THE SKEPTICS' GUIDE TO EMERGENCY MEDICINE

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SEASON 8

Introduction:

Welcome to the Skeptics' Guide to Emergency Medicine (TheSGEM). Meet 'em, greet 'em, treat 'em and street 'em. The goal of the SGEM has always been to cut the knowledge translation (KT) window down from over ten years to less than one year. It does this by using social media to provide you with high quality, clinically relevant, critically appraised, evidence based information. The SGEM wants you to have the best evidence so you can provide your patients with the best care.

Much of the SGEM content is a result of the Best Evidence in Emergency Medicine (BEEM) process. The BEEM process is a reliable and validated method of selecting relevant emergency medicine articles.
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The SGEM consists of a weekly podcast and blog. It also has a Facebook page, active Twitter feed, and YouTube channel.

So stop practicing medicine from ten years ago and start practising medicine based on the best evidence. Listen to the podcast and turn your car into a classroom. And always remember:

BE SKEPTICAL OF ANYTHING YOU LEARN, EVEN IF YOU LEARNED IT FROM THE SKEPTICS' GUIDE TO EMERGENCY MEDICINE

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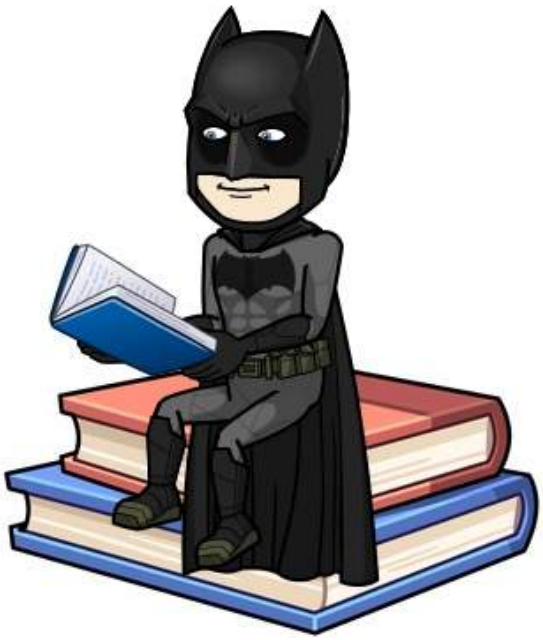

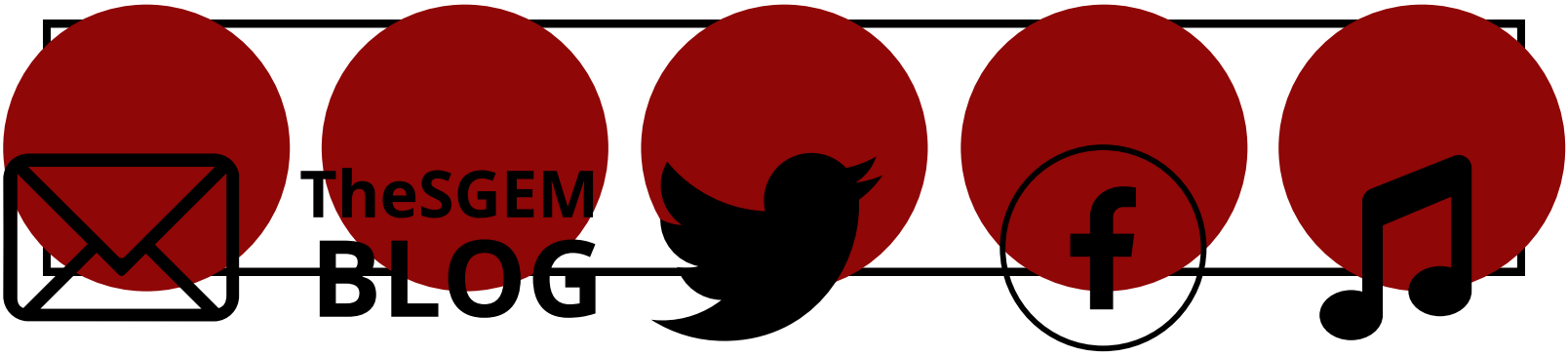

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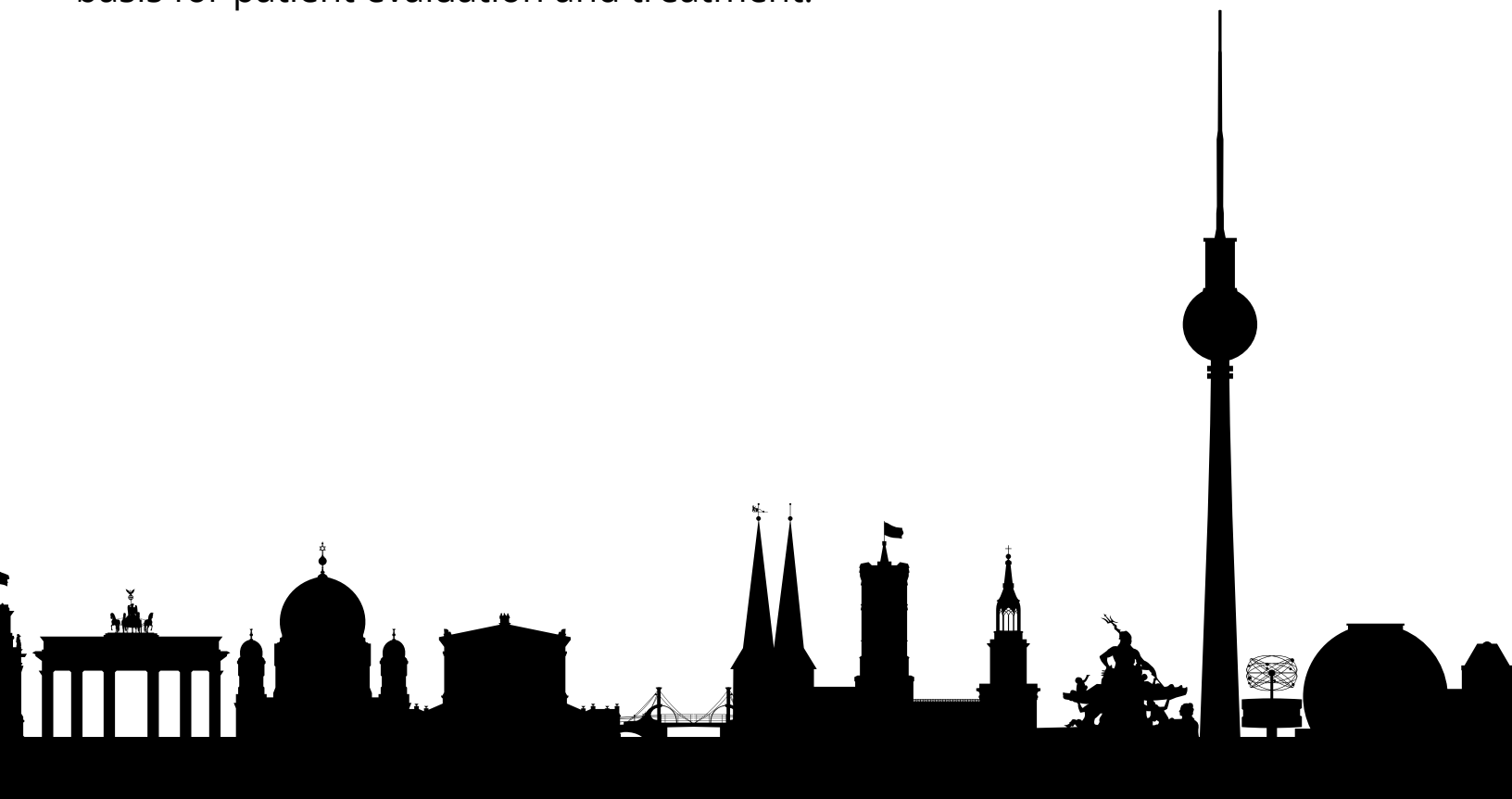


265 Total EcLiPSE of the Seizure - What a ConSEPT

Clinical Question:

Is Levetiracetam superior to Phenytoin as a second-line treatment for convulsive status epilepticus in children?

Bottom Line:

Levetiracetam is not statistically superior to phenytoin for the management of status epilepticus but its clinical suitability as a replacement or additional agent may still need further investigation.

Guest:

Dr. Tessa Davis is a Paediatrician specializing in Paediatric Emergency Medicine and currently practicing at the Royal London Hospitals. She is also the co-founder of Don't Forget the Bubbles and on the FeminEM Speaker Bureau.

Case Overview

Case: Julia is a 4-year-old girl with a history of seizures and developmental delay. She presents the emergency department with another seizure for more than five minutes and has not been aborted with two doses of midazolam intramuscularly.You know the guidelines recommend phenytoin as a second line agent, but the junior doctor asks you if levetiracetam would work faster with less side effects.

Background: Convulsive status epilepticus can be defined as a single seizure lasting greater than 20 to 30 minutes, or recurrent shorter seizures without recovery of consciousness between seizures.

Status epilepticus is a common paediatric emergency with significant consequences for the patients. Our focus on management of status is to stop the seizures quickly to avoid any complications.

Guidelines recommend benzodiazepines as the first line treatment, and we have plenty of evidence to back this up. Most guidelines recommend phenytoin or fosphenytoin as a second-line treatment, but the evidence base for its use is much weaker.

- CPS – Emergency management of the paediatric patient with generalized convulsive status epilepticus
- APLS – Advanced Life Support Group. Advanced paediatric life support: a practical approach to emergencies, 6th edn. Hoboken: Wiley-Blackwell, 2016.
- NICE – Epilepsies: diagnosis and management. London: National Institute for Health and Care Excellence, 2012.
- AES – Glauser T, Shinnar S, Gloss D, et al. Evidence-based guideline: treatment of convulsive status epilepticus in children and adults: report of the Guideline Committee of the American Epilepsy Society. Epilepsy Curr 2016

Phenytoin is linked to many adverse events including liver damage, Steven-Johnson syndrome, extravastion, pancytopenia, hypotension, arrhythmias, and death due to dosing errors.

Levetiracetam is an alternative to phenytoin for second line treatment of convulsive status epilepticus. It can be given more quickly, is more compatible with intravenous fluids, has less drug interactions, and has a lower risk of adverse events.

Although small studies suggest that levetiracetam is effective, there have been no comparison studies until now.

Reference: Dalziel et al. Levetiracetam versus phenytoin for second-line treatment of convulsive status epilepticus in children (ConSEPT): an open-label, multicentre, randomised controlled trial. The Lancet May 2019

Population: Children aged three months to 16 years of age presenting to 13 emergency departments in Australia and New Zealand in status epilepticus. Convulsive status epilepticus was defined as having a seizure for more than five minutes or two or more recurrent seizures without recovery of consciousness between seizures. Or three or more seizures within the preceding hour and a current seizure. They also had to have received two doses of benzodiazepines.

Intervention: Levetiracetam 40mg/kg (max 3g) IV or IO over five minutes.

Five minutes after the infusion finished, patients were assessed to see if the seizures had stopped. If the patient was still convulsing, then the other drug was given.

Exclusions: Being on regular phenytoin or levetiracetam; having already had a second-line treatment; known to be refractory to the medication; allergy; seizures secondary to a head injury; or seizure due to eclampsia in late pregnancy.

Comparison: Phenytoin 20mg/kg (max 1g) IV or IO over 20 minutes.

Outcome:

- **Primary Outcome:** Seizure cessation five minutes after the drug infusion
- **Secondary Outcomes:** Time to cessation of seizures; the need for other medications/interventions; adverse events; ICU admissions; airways complications; arrhythmias; length of hospital stay; or seizure status up to two months later.
- **Adverse Reactions:** Death, Stevens-Johnson syndrome, rash, airway complications, cardiovascular instability, extravasation injury, and extreme agitation, as well as those listed in the summary product characteristic of each treatment.

Authors' Conclusions

"Levetiracetam is not superior to phenytoin as a second line agent for convulsive status epilepticus."

Quality Checklist for Randomized Control Trials

- ☑ 1. The study population included or focused on those in the emergency department.
- ☑ 2. The teams were adequately randomized.
- ☑ 3. The randomization process was concealed.
- ☑ 4. The teams were analyzed in the groups to which they were randomized.
- ☑ 5. The study teams were recruited consecutively (i.e. no selection bias).
- ☑ 6. The teams in both groups were similar with respect to prognostic factors.
- ☒ 7. All participants (patients, clinicians, outcome assessors) were unaware of group allocation.
- ☑ 8. All groups were treated equally except for the intervention.
- ☑ 9. Follow-up was complete (i.e. at least 80% for both groups).
- ☑ 10. All (team) patient-important outcomes were considered.
- ☒ 11. The treatment effect was large enough and precise enough to be clinically significant.

Case Outcomes

Key Results:
There were 233 children identified, who met eligibility criteria and consented for this trial out of 639 and who presented to participating EDs with convulsive status epilepticus.

Of those enrolled, 114 assigned to phenytoin and 119 assigned to levetiracetam. The mean age was four years of age with close to ¾ presenting febrile.

- **Primary Outcome:** Cessation of seizures five minutes post the infusion.
  - 60% in the phenytoin group vs. 50% in the levetiracetam group
  - Risk difference –9·2% [95% CI –21·9 to 3·5]; p=0·16)

- **Secondary Outcomes:** There was no statistical difference in number needed to be intubated, other drug used in less than two hours, seizure stopping within two hours, intensive care unit admissions, intensive care unit length of stay or hospital length of stay.

- **Adverse Events:** No statistical differences in adverse events between the two groups was observed. One child died 27 days later but this was not thought to be due to the study drug.

Reference: Lytte et al. Levetiracetam versus phenytoin for second-line treatment of paediatric convulsive status epilepticus (EcLiPSE): A multicentre, open-label, randomised trial. The Lancet May 2019.

	Phenytoin	Levetiracetam	Difference (95% CI)	p Value
Intubation	18%	26%	7.6 (-3.0 to 18.3)	0.16
Other Drug <2hrs	37%	40%	3.5 (-9.0 to 16.0)	0.58
Seizure Stopped <2hrs	54%	51%	-3.1 (-15.9 to 9.7)	0.63
ICU Admission	30%	33%	2.9 (-9.0 to 14.9)	0.63
ICU LOS (hours)	20	33	12.8 (-2.8 to 28.2)	0.11
Hospital LOS (hours)	47	52	4.7 (-5.8 to 15.2)	0.38

2-in-1

Population: Children aged six months to 18 years of age presenting to 30 emergency departments in UK with convulsive status epilepticus. This was defined as generalized tonic-clonic, generalized clonic or focal clonic seizure). Participants also had to have received two doses of benzodiazepines.

Intervention: Levetiracetam 40mg/kg (max 2.5g) IV or IO over 5 minutes.

Exclusions: "Patients with absence, myoclonic, or non-convulsive status epilepticus, or infantile spasms; were known or suspected to be pregnant; had a contraindication or allergy to levetiracetam or phenytoin; had established renal failure; had received a second-line anticonvulsant during the presenting episode of convulsive status epilepticus, before screening; or were known to have been previously enrolled in the EcLiPSE trial."

Comparison: Phenytoin 20mg/kg (max 2g) IV or IO over 20 minutes.

Outcome:

- **Primary Outcome:** Time to seizure cessation (all visible signs of convulsive activity, defined as cessation of all continuous rhythmic clonic activity, as judged by the treating clinician)
- **Secondary Outcomes:** Need for other medications, rapid sequence intubation or ICU admissions.
- **Adverse Reactions:** These were defined as death, Stevens-Johnson syndrome, rash, airway complications, cardiovascular instability, extravasation injury, and extreme agitation, as well as those listed in the summary product characteristic of each treatment.

Authors' Conclusions

"Although levetiracetam was not significantly superior to phenytoin, the results, together with previously reported safety profiles and comparative ease of administration of levetiracetam, suggest it could be an appropriate alternative to phenytoin as the first-choice, second-line anticonvulsant in the treatment of paediatric convulsive status epilepticus."

Quality Checklist for Randomized Control Trials

- ☑ 1. The study population included or focused on those in the emergency department.
- ☑ 2. The teams were adequately randomized.
- ☑ 3. The randomization process was concealed.
- ☒ 4. The teams were analyzed in the groups to which they were randomized.
- ? 5. The study teams were recruited consecutively (i.e. no selection bias).
- ☑ 6. The teams in both groups were similar with respect to prognostic factors.
- ☒ 7. All participants (patients, clinicians, outcome assessors) were unaware of group allocation.
- ☑ 8. All groups were treated equally except for the intervention.
- ☑ 9. Follow-up was complete (i.e. at least 80% for both groups).
- ? 10. All (team) patient-important outcomes were considered.
- ☒ 11. The treatment effect was large enough and precise enough to be clinically significant.

Case Outcomes

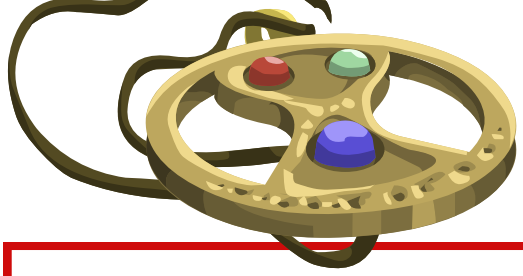
Key Results:
There were 286 patients included in the modified intention-to-treat analysis. The median age was 2.7 years, about ¾ presented with a generalized tonic-clonic seizure and 1/3 had pre-existing epilepsy.
Convulsive status epilepticus was terminated in 70% of patients receiving levetiracetam and 64% of patients receiving phenytoin.

- **Primary Outcome:** Median time from randomization to seizure cessation
  - 35 minutes levetiracetam vs. 45 minutes phenytoin (log-rank test p=0.20)

- **Secondary Outcomes:** There was no statistically significant differences were observed between phenytoin and levetiracetam.

- **Adverse Events:** There were five serious adverse events recorded in the trial. Three were in two patients receiving phenytoin, one in a patient receiving levetiracetam, and one in a patient who received both medications.

	Phenytoin	Levetiracetam	RR (95% CI)	p Value
Other Drugs	37.3%	37.5%	1.01 (0.74-1.36)	0.97
Intubation	35.1%	30.0%	0.83 (0.59-1.16)	0.27
ICU Admit	53.7%	63.8%	1.19 (0.97-1.45)	0.08



Time to Talk Nerdy

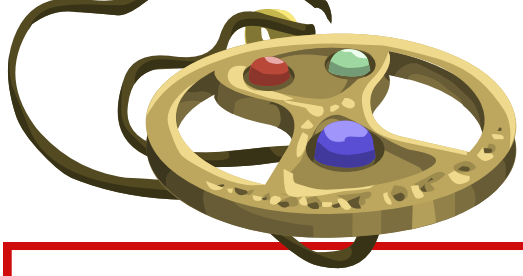
1. Selection Bias: It is possible that there was selection bias in ConSEPT. This is because they missed 127 children who presented to the ED with convulsive status epilepticus. Why were these children missed? In addition, they used opaque sealed envelopes rather than a computer-based system that assigned group allocation. Both of these could have introduced selection bias into the trial.

EcLiPSE could have also had some selection bias. There were 53 patients eligible but not randomly allocated. The reasons for not randomizing these children were included no trial-trained doctor available, loss of or failure to achieve intravenous access, clinical judgment, and treatment given before random assignment.

2. Lack of Blinding: ConSEPT and EcLiPSE physicians, research nurses and investigators were not masked to treatment assignment. This could have introduced bias into the study.

3. Outcome Assessment ConSEPT: The primary outcome was 5 minutes after the infusion. This would have been 25 minutes for phenytoin and 10 minutes in the levetiracetam group. Would this 15 minute difference in time have an impact on the results? Seizures tend to stop over time. Both groups already had two doses of benzodiazepines prior to enrolment. This bias should have favoured the control (phenytoin group). This makes me wonder if there would have been a difference or superiority to levetiracetam? However, there was no statistical difference in the number of patients whose seizure stopped in under two hours.

4. DOO vs. POO: Does any difference in time to termination of seizure activity have a clinically important impact? In ConSEPT, the median time to termination of seizure activity was 22 minutes for phenytoin vs. 17 minutes for levetiracetam.



Time to Talk Nerdy

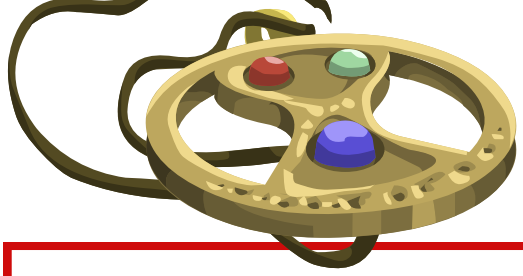
In EcLiPSE the difference was 10 minutes (35 minutes vs. 45 minutes). None of these time differences were statistically different, but would this disease-oriented outcome translate into a patient-oriented outcome?

5. Subjective Outcome: Clinicians decided in both trials if the seizure activity had stopped. While this is pragmatic it is also subjective. It would have been more objective to have EEGs to confirm termination of seizure activity.

6. Observer Bias: This can be defined as the tendency for the researcher to see what they expect to see or what they want to see. It is also called experimental bias or research bias. In this case, the researchers may have had a conscious or unconscious bias towards the efficacy of the intervention (levetiracetam). They attempted to minimize this by recording, if possible, the primary outcome assessment. This was reviewed by two emergency physicians and one neurologist who were blinded to group allocation. While this is an interesting way to address observer bias, only 2/3 of the cases were recorded.

7. Seizure Cessation Rates: Previous retrospective data had suggested a seizure cessation rate of 60% with phenytoin and both ConSEPT and EcLiPSE confirmed this number. In contrast, seizure cessation rate was expected to be 80% with levetiracetam based on previous retrospective studies. The rate observed in ConSEPT was only 50% and 70% in EcLiPSE. Why was the efficacy of levetiracetam less than expected? Is this because of the bias in the literature that new drugs seem more efficacious, but the magnitude of effect seems to decrease over time?

8. ITT Analysis vs. PP Analysis: Intention-to-treat (ITT) is preferred method of analysis in superiority trials because it is more conservative. Per-protocol (PP) analysis can bias the results towards the intervention group.



Time to Talk Nerdy

In ConSEPT both the ITT and PP analysis failed to demonstrate superiority of levetiracetam. EcLiPSE used a modified ITT analysis. This too would have tended to bias the results toward levetiracetam. Because both trials failed to demonstrate superiority compared to phenytoin using these statistical methods it strengthens our confidence in the results.

9. Adverse Event Rates: The adverse event rates in ConSEPT and EcLiPSE due to phenytoin was not as pronounced as previous reported. This is interesting and it makes me wonder if the concerns have been highlighted more for the older drug (phenytoin) in order to promote the newer drug (levetiracetam)?

10. Superiority and Equivalent Trials: Both of these trials were designed as superiority trials and failed to demonstrate superiority of levetiracetam to phenytoin. That does not mean equivalence can be claimed but rather we have to accept the null hypothesis that levetiracetam is not superior to phenytoin in these patients. To make the claim of equivalence the 95% confidence intervals of the point estimate of the intervention must fit between a pre-defined delta of the comparator.

Comment on Authors' Conclusion Compared to SGEM Conclusion: We generally agree with the authors' conclusions.

Clinical Application: Although not a direct safety analysis the results suggest that levetiracetam is unlikely to cause harm in children with status and therefore can be considered as treatment agent. How units amend their current protocols will depend on their current experience with levetiracetam, the local anasethetic and intensive care support and whether they feel amendment to national seizure guidance is necessary first.

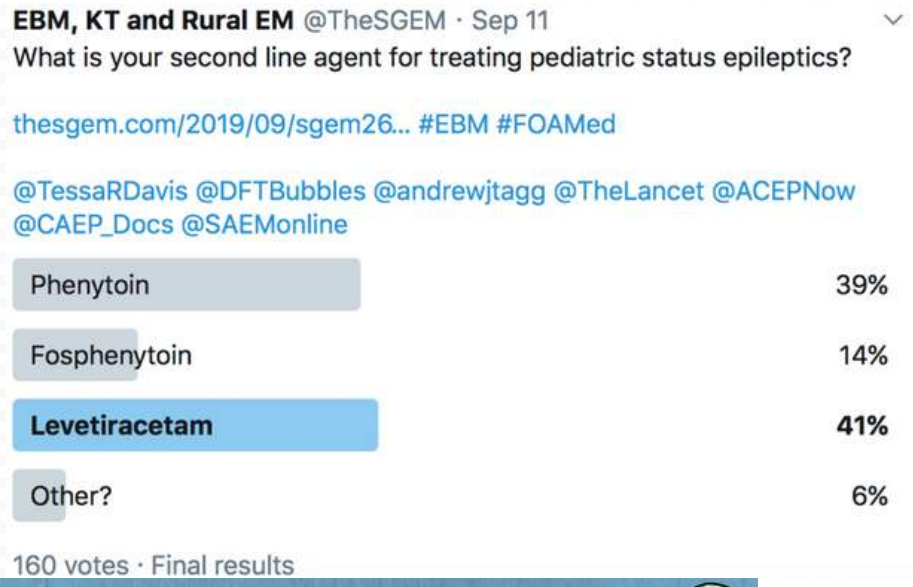
What Do I Tell the Parents? In a recent study another anti-seizure medication was demonstrated to have similar outcomes to phenytoin in children who have very prolonged seizures. We feel comfortable using the new drug if the phenytoin does not stop your child's seizure.

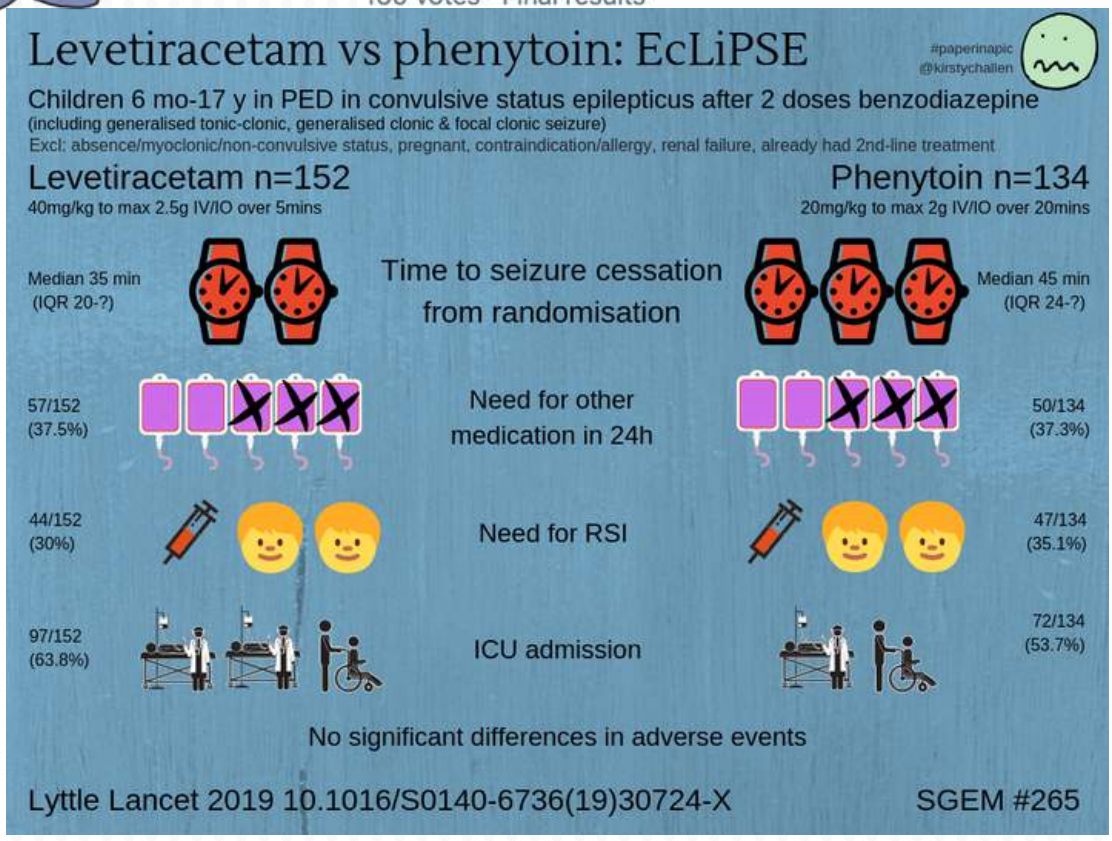
Case Resolution: You give the patient phenytoin 20mg/kg IV over 20 minutes. The seizure activity does not seem to stop after five minutes. You then start levetiracetam 40mg/kg over five minutes and at the end of the infusion the seizure activity seems to cease.

Episode End Notes

Other FOAMed:

- DFTB: Seizing the Truth
- REBEL EM: 2nd Line Therapy for Pediatric Status Epilepticus – EcLiPSE & ConSEPT
- First10EM: Levetiracetam versus Phenytoin in Status Epilepticus (ConSEPT and EcLiPSE)
- EMLitofNote: Levetiracetam vs. Phenytoin
- St. Emlyn's: Enter Sandman – Which Agent as Second Line in Paediatric Status Epilepticus?





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OLD MAN TAKE A LOOK AT THE CANADIAN CT HEAD RULE I'M A LOT LIKE YOU WERE

Clinical Question:

What is the diagnostic accuracy of the CCHR in patients 65 years of age or older in predicitng clinically important brain injuries?

Bottom Line:

This paper opens the door for further research to try to narrow the criteria in the Canadian Head CT Rule to further reduce unnecessary head CT imaging in the emergency department. However, further, high quality prospective studies are required prior to clinical application.

Guests:

Dr. Sarah Berg is a PGY-3 resident in Emergency Medicine at Washington University School of Medicine in St. Louis. She is interested in social determinants of health in the emergency department and health policy.

Dr. Ian Holley is also a PGY-3 resident in Emergency Medicine at Washington University School of Medicine in St. Louis. He is interested in ultrasound and international emergency medicine.

Case Overview

Case: It's a busy night in the emergency department, your next patient is a well appearing 70-year-old man, presenting after a mechanical fall from standing with loss of consciousness. He is neurologically intact with a Glasgow Coma Scale (GCS) of 15 one hour after the fall. There are no other external signs of trauma on your exam. He is not on anticoagulation and there is no history of seizures.

Background: Head trauma is an exceedingly common presenting complaint in the emergency department, with approximately 2.5 million emergency department visits in the US in 2014 [1], with the most significant proportion of visits occurring in the elderly ≥75 (1,682/100,000).

Head trauma can result in a spectrum of brain Injuries varying from mild to severe. In cases of severe injury, the decision to obtain head CT imaging is straight forward. In mild traumatic brain injury (mTBI), this decision is can be more difficult, as there may be no or minimal evidence of injury on exam. Traditionally CT imaging was obtained for fear of missing intracranial pathology.

In an attempt to improve resource utilization, emergency department length of stay, limit cost and improve outcomes, there have been multiple Clinical Decision Rules (CDRs) created to help guide clinicians in their decision-making process. Two of the most commonly used rules include the Canadian CT Head Rule (CCHR) and the New Orleans Criteria (NOC); other rules include NEXUS-II, the Neurotraumatology Committee of the World Federation of Neurosurgical Societies, the National Institute of Clinical Excellence guidelines, and the Scandinavian Neurotrauma Committee guideline.

We have covered the CCHR on the SGEM with the EM Swami and Dr. Emily Junck back on SGEM#106. It was a classic EM paper published in the Lancet back in 2001 by the Legend of Emergency Medicine, Dr. Ian Stiell. We also discussed three studies that compared CCHR to the NOC. The bottom line was while both rules are highly sensitive for positive CT findings and clinically important brain injuries, the CCHR had higher specificity and may be more clinically applicable given it is designed to

predict clinically important brain injuries.

The Canadian CT Head Rule is a clinical decision instrument to help you decide if a patient with a mild head injury requires a CT head. Minor head injury was defined as blunt head trauma, resulting in amnesia, loss of consciousness or an altered mental state (confusion or disorientation) with a GCS score ≥13. The CCHR only applies to those patients with minor head injury and is not applicable to non-traumatic cases, GCS less than 13, age less than 16 years, coumadin or bleeding disorder or obvious open skull fractures.

The CCHR is the most researched CDR in mTBI and has shown sensitivities and specificities from 99-100% and 48-77% [3]. The use of CDRs such as CCHR, have the ability to reduce the amount of unnecessary head CT imaging obtained in the emergency department.

Unfortunately, the CCHR uses age ≥ 65 as a high-risk criterion for obtaining head CT imaging in mTBI. This is based on the initial validation study which demonstrated an odds ratio (OR) of 4.1 for risk of clinically important brain injury (CIBI). CIBI is defined, per the CCHR, as “any acute brain finding revealed on CT and which would normally require admission to hospital and neurological follow-up”.

Given the ageing population, with an expected 60% increase in population >65 years old from 2015-2050 and the already rapidly rising rate of ED visits for TBI in this patient population which has shown a 120% increase from 2007-2013, it is important to look forward in finding decision aids or pathways that may further help clinicians risk stratify patients in this already higher risk cohort.

Reference: Fournier et al. Adapting the Canadian CT head rule age criteria for mild traumatic brain injury. Emergency Medicine Journal 2019.

Canadian CT Head Rule

CT head is only required for minor head injury patients with any one of these findings:

High Risk (for Neurological Intervention)

1. GCS score < 15 at 2 hrs after injury
2. Suspected open or depressed skull fracture
3. Any sign of basal skull fracture*
4. Vomiting ≥ 2 episodes
5. Age ≥ 65 years

Medium Risk (for Brain Injury on CT)

6. Amnesia before impact ≥ 30 min
7. Dangerous mechanism ** *(pedestrian, occupant ejected, fall from elevation)*

*Signs of Basal Skull Fracture

- hemotympanum, 'racoon' eyes, CSF otorrhea/ rhinorrhea, Battle's sign

** Dangerous Mechanism

- pedestrian struck by vehicle
- occupant ejected from motor vehicle
- fall from elevation ≥ 3 feet or 5 stairs

Rule Not Applicable If:

- Non-trauma cases
- GCS < 13
- Age < 16 years
- Coumadin or bleeding disorder
- Obvious open skull fracture

Stiell IG, et al. The Canadian CT Head Rule for Patients with Minor Head Injury. Lancet 2001;357:1391-96.

Population: Adult patients 65-years of age or older with confirmed mild TBI within the last 24 hours who received a head CT in the emergency department.

- Mild TBI was defined as blunt head trauma, resulting in amnesia, loss of consciousness or an altered mental state (confusion or disorientation) with a GCS score ≥13.

Intervention: Application of a modified Canadian CT Head Rule with cutoff ages of 65, 70, 75, 80 and 85 years old.

Exclusions: Patients with a coagulopathy, on anticoagulants, who did not undergo head CT or with a delay of >24 hours between the head injury and the emergency department visit.

Comparison: None

Outcome:

- **Primary Outcome:** Diagnostic accuracy of the modified CCHR for clinically important brain injuries (CIBI).
  - CIBI was defined as any acute brain finding revealed on CT and which would normally require admission to hospital and neurological follow-up.
- **Secondary Outcomes:** Reduction of CT scan usage.

Authors' Conclusions

"Adjusting the age criteria of the Canadian CT head rule to 75 years old could be safe while reducing radiation and ED resources. A future prospective study is suggested to confirm the proposed modification."

Quality Checklist for Clinical Decision Tools

- ☑ 1. The study population included or focused on those in the emergency department.
- ☑ 2. The patients were representative of those with the problem.
- ? 3. All important predictor variables and outcomes were explicitly specified.
- ☒ 4. This is a prospective, multicenter study including a broad spectrum of patients and clinicians (level II).
- ? 5. Clinicians interpret individual predictor variables and score the clinical decision rule reliably and accurately.
- ☒ 6. This is an impact analysis of a previously validated CDR (level I).
- ☒ 7. For Level I studies, impact on clinician behavior and patient-centric outcomes is reported.
- ☒ 8. The follow-up was sufficiently long and complete.
- ? 9.The effect was large enough and precise enough to be clinically significant.

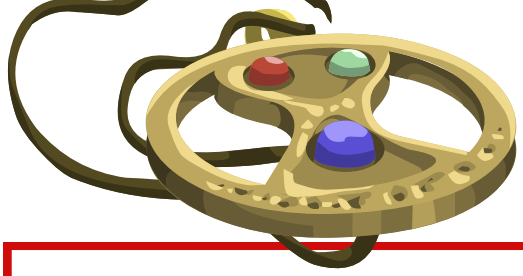
Case Outcomes

Key Results:
This retrospective chart review from a level 1 trauma center, in a French-Canadian population identified 104 patients with mTBI that met inclusion criteria. The mean age of the cohort was 77 years and 58% were male.
CCHR had a sensitivity of 100% and a specificity of 13.9% for 75 years old.

Overall, they identified 32 CIBI (30.7%, 95% CI 22-41%), 8 (25%) of which had no positive CCHR criteria apart from age. They found that GCS score less than 15 two hours post injury to have the largest association with CIBI (RR 2.35, 95%CI 1.36-4.09, p=0.0023) and dangerous mechanism to be the least predictive.

They calculated that the modified CCHR would decrease 10% of CT images obtained in patients >65 years old.

	65 Years	70 Years	75 Years	80 Years	85 Years
Sensitivity (95% CI)	100 (89.1-100)	100 (89.1-100)	100 (89.1-100)	90.6 (75-98)	75 (75.6-88.5)
Specificity (95% CI)	0 (0-5)	4.2 (0.9-11.7)	13.9 (6.9-24.1)	23.6 (14.4-35.1)	31.9 (21.4-44)
CTs Done (%)	104 (100%)	101 (97.1%)	94 (90.4%)	84 (80.8%)	73 (70.2%)
Missed CIBI (%)	0 (0%)	0 (0%)	0 (0%)	3 (9,4%)	8 (25%)



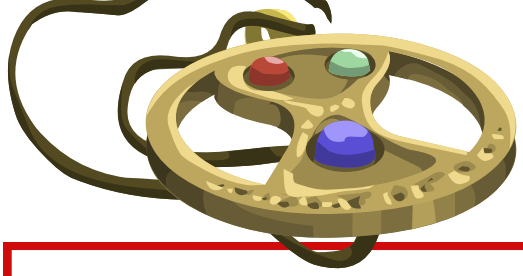
Time to Talk Nerdy

1. Chart Reviews: This is a single center, retrospective, chart review, with unclear methodological quality. Retrospective chart reviews are frequently biased by methods of data extraction. Gilbert et al published a chart review paper in 1995 to help improve methodological quality of chart reviews. Worster et al expanded the original list of eight to twelve quality indicators. This study incorporates seven of the proposed twelve criteria for a high-quality chart review:

1. Were the abstractors trained before the data collection? Yes
2. Were the inclusion and exclusion criteria for case selection defined? Yes
3. Did the abstractors use data abstraction forms? Yes
4. Was inter-observer reliability mentioned? Yes
5. Was the medical record database identified or described? Yes
6. Was the method of sampling described? Yes
7. Did they obtain ethics approval? Yes

The study did not use the remaining variables described by Gilbert et al and Worster et al; Blinding (which may bias interpretation of chart documentations to favor outcome), monitoring performance of research assistants (to improve accuracy), Interrater reliability testing (kappa value), management plan of missing or conflicting data and definition of variables.

Although variables were inherently defined in the CCHR and chart reviewers were documenting presence or absence of these on a standardized form, the absence of a particular variable in the chart does not necessarily indicate true absence of this variable clinically. The authors stated that when a criterion was not accurately reported in the medical record, it was considered absent. However, the absence of evidence is not the evidence of absence and taking this approach can result in a non-response bias, which could alter the validity of the results.



Time to Talk Nerdy

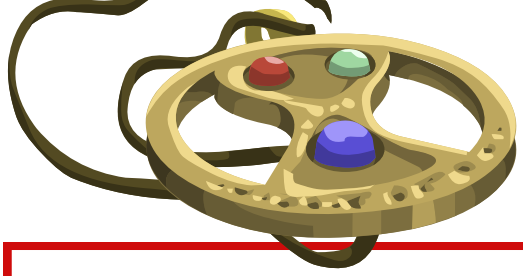
2. Excluded Patients: As previously mentioned, there were 13 patients with mTBI who were excluded from the study, as they did not receive head CT imaging. From this it can be inferred that there are clinicians from this patient population that are basing decisions to obtain CT imaging without the use of the CCHR. As a result, if one is not using the CDR, it is unlikely that all components of the rule be documented, worsening the non-response bias.

With some clinicians not following the CCHR, this also raises concern for selection bias of sicker patients, as those providers not using the CCHR would be more likely to obtain CT imaging in sicker patients than those who are more well appearing and did not have imaging obtained.

3. Wide Confidence Intervals: While the sensitivity for age 75 was 100% the lower 95% confidence interval was 89.1%. This means using this age adjusted CCHR could potentially miss more than 10% of CIBI. Is that an acceptable miss rate? It will all depend on where you work and patient expectations. A larger study could improve the precision of these results around the point estimate.

4.10% Reduction: The estimated reduction of CT utilization by raising the age to 75 years is 10%. This could possibly lead to less cost, radiation exposure and ED length of stay. However, this gets back to point #3, is that 10% reduction worth the potential risk of missing up to 10% of CIBI? The answer is probably different depending on many things including your medical legal environment. While it might be more acceptable in Canada to reduce utilization with the potential increase in miss rate, the zero-miss culture in the USA might find this trade off unacceptable.

5. Prospective Validation: We think this needs a prospective, multi-center validation study prior to clinical use. Numerous Clinical Decision Rules (CDRs)



Time to Talk Nerdy

have been thought to be effective on derivation studies but go on to fail external validation. Take the San Francisco Syncope Rule as an example – The derivation study showed a sensitivity of 96% and specificity of 62%. The subsequent validation studies demonstrated sensitivities and specificities of 74-87% and 52-57% respectively. Very few CDRs go the additional step and do an impact analysis. We look forward to seeing this hypothesis of raising the CCHR age cutoff to 75 years further explored in validation studies.

Comment on Authors' Conclusion Compared to SGEM Conclusion: Although we hope to one day see a modified CCHR (or head CT decision pathway), for our ageing populations, we do not feel that this study is able to provide clinical guidance in management of mTBI in the emergency department. However, it is relevant for hypothesis generation and further prospective studies are required prior to clinical incorporation.

Clinical Application: The original Canadian Head CT Rule that was published back in 2001 has successfully reduced the number of head CT imaging obtained in the emergency department for mTBI. One major limitation to the decision instrument is using 65 years of age or older as a high-risk criterion. While this new study attempting to increase the age cutoff to 75 years is interesting and hypothesis generating it is not yet ready for clinical application at this time.

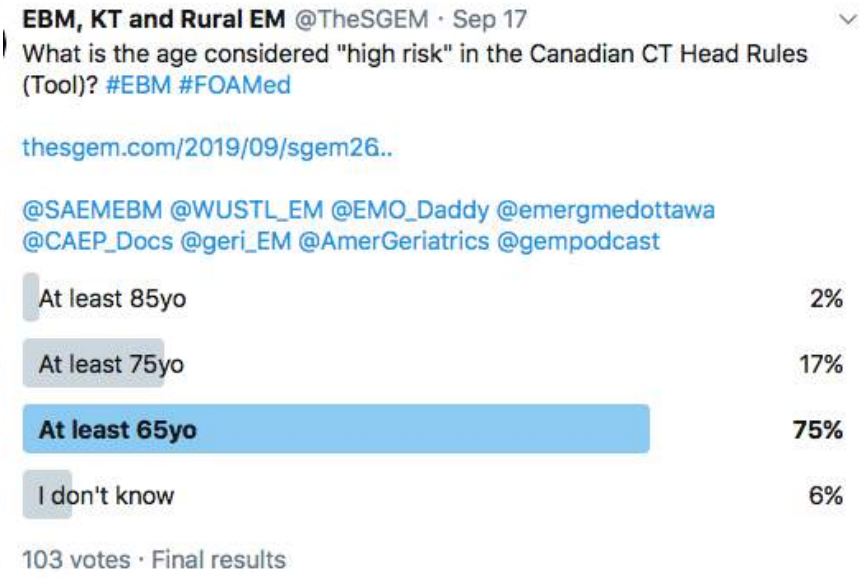
What Do I Tell the Patient? There is some new evidence suggesting that we do not need to CT all patients older than 65 who have minor traumatic brain injury. However, best practice evidence at this time, still indicates that CT imaging should be performed in this patient population given the increased prevalence of CIBI.

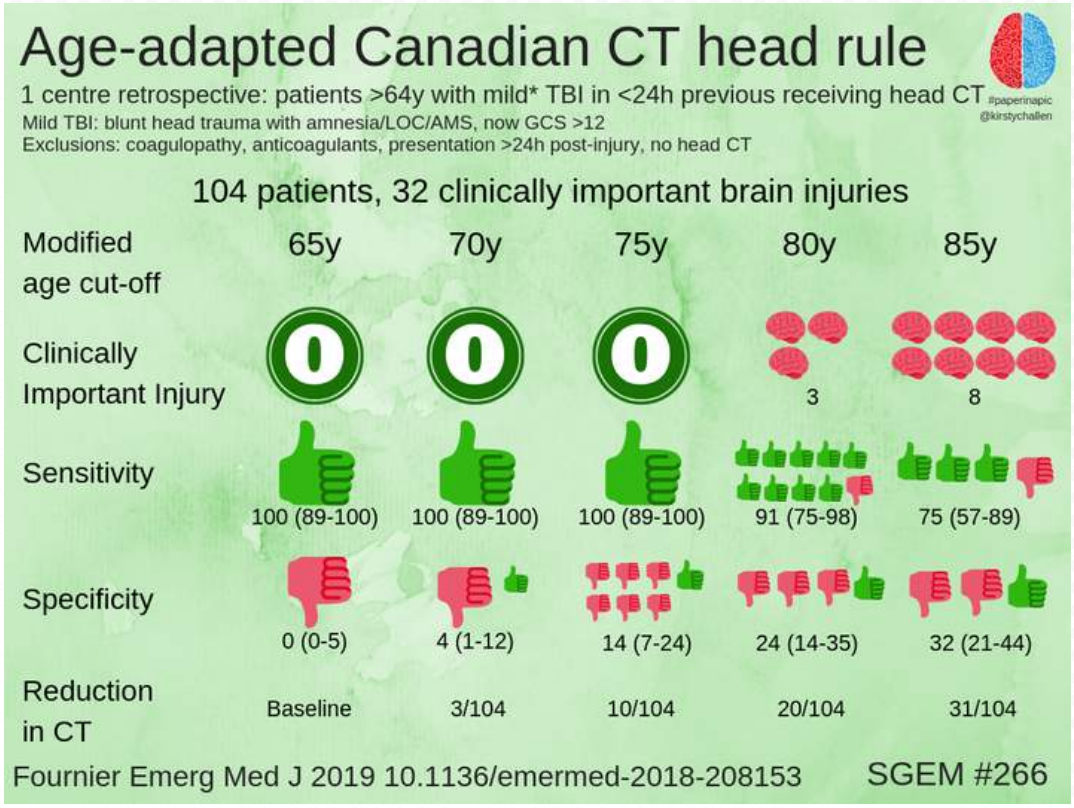
Case Resolution: Given the current evidence, and prevalence of CIBI in the patient population 65 years and older, you obtain head CT imaging. The CT scan is negative for acute pathology, both you and the patient are relieved. You provide the patient with return precautions and discharge him home.

Episode End Notes

Other FOAMed:

- Rebel EM – Canadian head CT rule vs New Orleans head CT rule
- CoreEM – Canadian Head CT rule
- CoreEM – New Orleans Head CT rule
- SGEM#106: O Canada- Canadian CT Head Rules for Patients with Minor Head Injury
- SGEM#225: NEXUS II – Validation of the Pediatric Head CT Decision Instrument





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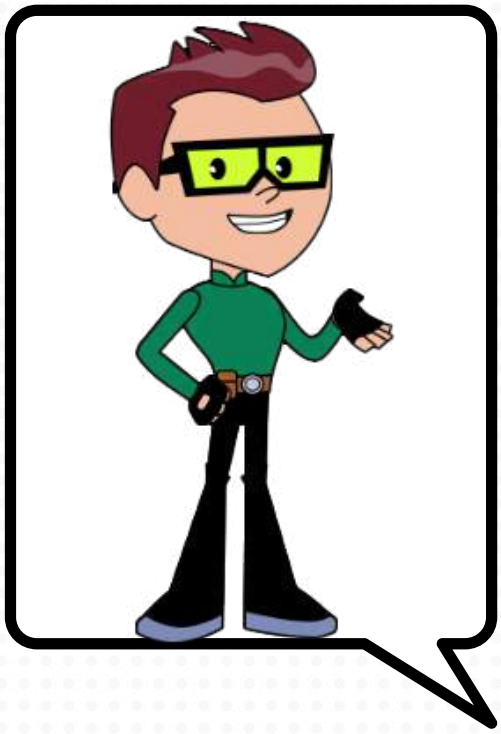
AFIB OF THE NIGHT - CHEMICAL VS. ELECTRICAL FIRST CARDIOVERSION

Clinical Question:

In emergency department patients with atrial fibrillation, is sinus rhythm achieved more rapidly with electrical-first rhythm control when compared with chemical-first rhythm control?



Bottom Line:

Consider implementing an electrical-first rhythm control strategy for low risk patients with atrial fibrillation.

Guest:

Dr. Chris Bond is an emergency medicine physician and clinical lecturer in Calgary. He is also an avid FOAM supporter/producer through various online outlets including TheSGEM

Case Overview

Case: A 55-year-old male presents to the emergency department with sudden onset of palpitations and pre-syncope starting one hour ago. He has no chest pain or shortness of breath and aside from a heart rate of 140 beats per minute, the rest of his vital signs appear within normal limits. His past medical history is significant for hypertension for which he takes perindopril. His ECG shows atrial fibrillation with a rapid ventricular response.

Background: Atrial fibrillation is the most commonly encountered significant dysrhythmia in the emergency department (1). We have covered this topic a number of times on the SGEM.

- SGEM#88: Shock Through the Heart (Ottawa Aggressive Atrial Fibrillation Protocol)
- SGEM#133: Just Beat It (Atrial Fibrillation) with Diltiazem or Metoprolol?
- SGEM#222: Rhythm is Gonna Get You – Into an Atrial Fibrillation Pathway
- SGEM#260: Quit Playing Games with My Heart – Early or Delayed Cardioversion for Recent Onset Atrial Fibrillation?

The most recent episode looked at whether late cardioversion is non-inferior to early cardioversion (SGEM#260) in acute atrial fibrillation. The SGEM bottom line from that episode was that the late approach was non-inferior to early approach and that both strategies achieve high rates of sinus rhythm at the 4-week follow up (>90%).

In uncomplicated patients with symptoms less than 48 hours and no stroke or TIA in the past six months, the 2018 Canadian Cardiovascular Society (CCS) guidelines permit rate or rhythm control (2).

There is significant variability in the management of patients with acute atrial fibrillation, with the proportion undergoing rhythm control ranging from 42-85% in Canadian academic centres (3). The rhythm control strategies typically employed are chemical cardioversion with procainamide infusion or electrical cardioversion with electrical countershock (3-6).

Both of these strategies appear safe from prior studies, but comparative effectiveness data is lacking. Thus, Canadian management varies, with 56% of patients receiving a chemical-first approach and 44% an electrical-first approach (3).

Reference: Scheuermeyer et al. A Multicenter Randomized Trial to Evaluate a Chemical-first Cardioversion Strategy for Patients with Uncomplicated Acute Atrial Fibrillation. AEM Sept 2019

Population: Adults between 18 and 75 years of age with atrial fibrillation less than 48 hours duration and a CHADS2 score less than two.

Exclusions: Hemodynamic instability, atrial flutter, CHADS2 score greater than or equal to two, patients with an acute underlying medical illness, recent cardiac procedure, acute intoxication or withdrawal from alcohol or illicit substances. They also excluded those who attended the emergency department for other reasons (eg. trauma, gout) who were incidentally found to be in atrial fibrillation.

Intervention: Chemical cardioversion with procainamide (a dose of 17mg/kg up to a maximum of 1500mg infused over one hour was recommended). This was followed by electrical cardioversion if chemical cardioversion was unsuccessful.

Comparison: Electrical cardioversion using a synchronized biphasic waveform sequence of 100J to 150J to 200J to a maximum of three shocks were allowed. Patients were sedated at the physicians' discretion. The study recommended an initial propofol bolus of 0.50 mg/kg, with further slow boluses of 0.25 mg/kg every minute until adequate sedation was achieved.This was followed by chemical cardioversion with procainamide if electrical cardioversion was unsuccessful.

Outcome:

- **Primary Outcome:** Proportion of patients discharged within four hours of emergency department arrival.
- **Secondary Outcomes:** Additional median time intervals, emergency department-based adverse events, and thirty-day patient-centred outcomes.

Authors' Conclusions

"In uncomplicated ED AF patients, chemical-first and electrical-first strategies both appear to be successful and well tolerated; however, an electrical-first strategy results in a significantly shorter ED length of stay. Our results should encourage clinicians to initially consider an electrical-first approach for such patients."

Quality Checklist for Randomized Control Trials

- [x] 1. The study population included or focused on those in the emergency department.
- [x] 2. The teams were adequately randomized.
- [x] 3. The randomization process was concealed.
- [x] 4. The teams were analyzed in the groups to which they were randomized.
- [ ] 5. The study teams were recruited consecutively (i.e. no selection bias).
- [x] 6. The teams in both groups were similar with respect to prognostic factors.
- [ ] 7. All participants (patients, clinicians, outcome assessors) were unaware of group allocation.
- [x] 8. All groups were treated equally except for the intervention.
- [x] 9. Follow-up was complete (i.e. at least 80% for both groups).
- [x] 10. All (team) patient-important outcomes were considered.
- [x] 11. The treatment effect was large enough and precise enough to be clinically significant.

Case Outcomes

Key Results:
Overall, 222 eligible patients were screened and 84 were ultimately enrolled and randomized (41 chemical-first and 43 electrical-first). The median age was in the late 50's, more than a third were female and three-quarters had a history of atrial fibrillation.

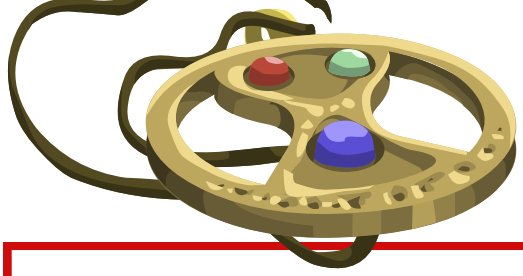
1/3 of patients were discharged in four hours with chemical-first group compared to 2/3 in the electrical-first group.

- **Primary Outcome:** Proportion of patients discharged within four hours of emergency department arrival.
  - In the chemical-first group, 13 of 41 (32%) were discharged within four hours, compared with 29 of 43 (67%) in the electrical-first group. Difference 36% (95% CI 16-56%, P<0.001) for a number needed to treat of 3.

- **Secondary Outcomes:** Additional median time intervals, emergency department-based adverse events and thirty-day patient-centred outcomes.

- **Adverse Events:**
  - Chemical-first group had 10 adverse events (24%) and electrical group had 11 (26%). All had minimal-risk outcomes.
  - There were no strokes or deaths in either group at 30 days.
  - Quality of life scores at 3 and 30 days were similar for both groups across all domains.

This is an SGEMHOP episode which means we have the lead author on the show. Dr. Frank Scheuermeyer is an emergency physician researcher director at St. Paul's Hospital in Vancouver, BC. He is also the associate director of research for the University of British Columbia Department of Emergency Medicine, and the Cardiovascular Emergencies lead for the British Columbia Emergency Medicine Network.



Time to Talk Nerdy

1) Consecutive Patients – You did not have consecutive recruitment of patients. Recruitment depended on whether or not a research assistant was available. That often means no nights, weekends or holidays. This could have introduced some selection bias. How do you think this may have impacted your results? (note it was only 8/135 eligible patients)

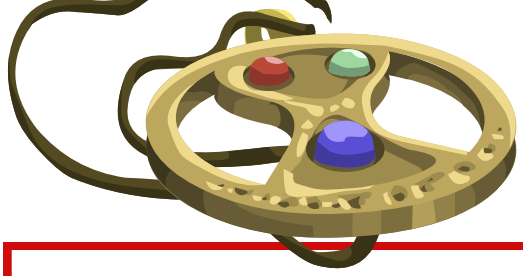
2) More than an ECG – For this study, you encouraged physicians to obtain an ECG, complete blood count, electrolytes, creatinine, TSH, troponin and chest x-ray on all patients. Do you recommend this in practice, and with high sensitivity troponins, wouldn't you obtain many intermediate elevations from the tachycardia if it was prolonged?

3) Exclusion – You excluded patients over the age of 75. My good friend and geriatric emergency medicine guru Dr. Chris Carpenter may accuse you of practicing ageism. Why did you exclude these older patients?

4) Outcomes – One outcome we found interesting was the emergency department re-visits at 3 and 30 days. The numbers were not statistically significant, but for chemical vs. electrical cardioversion they were 5 vs. 1 at 3 days and 9 vs. 3 at 30 days. Is there any literature to support a difference in recurrence rate for the two methods?

Speaking of outcomes, you changed your primary outcome. Originally you had emergency department length of stay. This was then changed to the proportion of patients discharged within four hours of emergency department arrival. Can you explain why you made this change?

5) External Validity – I absolutely love this study as an emergency medicine practitioner in Calgary. We are about as pro-electricity as you can get. Why do you think there is such variation in use of electrical vs. chemical first



Time to Talk Nerdy

ardioversion across Canada and worldwide?

I also really liked that your study sites ranged from big tertiary referral centres like with all the resources, to small community hospitals where I work with no on-site cardiologist. This really strengthens the external validity to different Canadian emergency departments. However, do you think this trial has external validity to other countries like the USA, Australia and European countries different practice environments?

Comment on Authors' Conclusion Compared to SGEM Conclusion:
We agree with the authors conclusions.

Clinical Application: This study provides support for an electrical-first rhythm control strategy in patients with uncomplicated atrial fibrillation to reduce emergency department length of stay.

What Do I Tell the Patient? Your heart is in an abnormal rhythm called atrial fibrillation and is going too fast. This is why you are feeling lightheaded and like your heart is racing. We have several safe methods to get you out of this rhythm, which include making you sleepy and giving your heart some electricity or giving you intravenous medication. The electrical method is more effective on the first attempt and will generally result in you going home 1-2 hours sooner than the intravenous medication. For the electricity method, we will give you an anesthetic that will make you forget the procedure in most cases. If one method doesn't work, then we generally try the other method afterward.

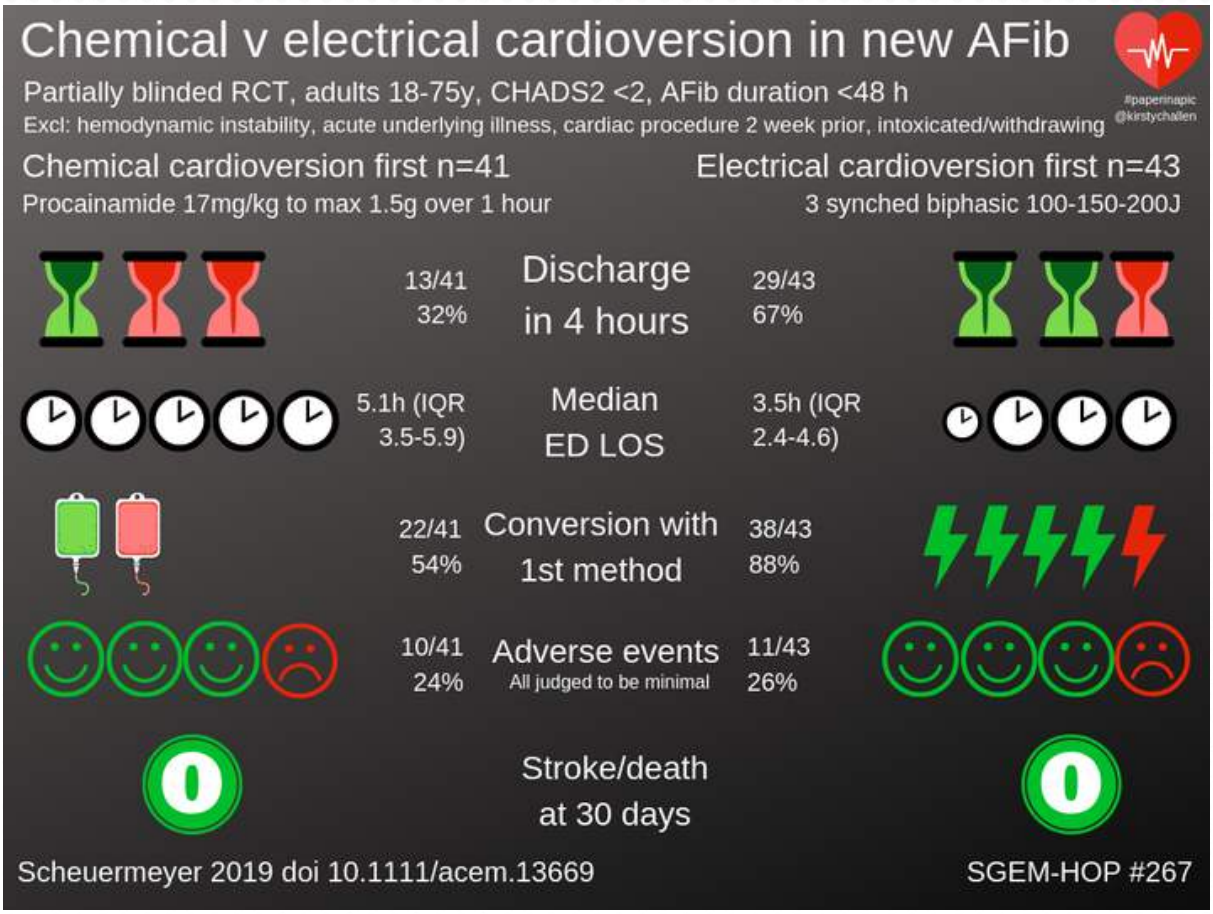
Case Resolution: This study provides support for an electrical-first rhythm control strategy in patients with uncomplicated atrial fibrillation to reduce emergency department length of stay.

Episode End Notes

What's your usual 1st strategy for acute uncomplicated AF? thesgem.com/2019/09/sgem26... #FOAMed doi.org/10.1111/acem.1... #SGEMHOP #EBM

Chemical Convert	21%
Electrical Convert 100J	12%
Electric Convert 200J	20%
Rate control NOT convert	**47%**

197 votes · Final results



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VITAMIN C NOT READY FOR GRADUATION TO ROUTINE USE

Clinical Question:

Does the administration of vitamin C to an adult critically ill ICU patient or cardiac surgery patients decrease mortality?

Bottom Line:

There is not enough evidence to support the routine use of vitamin C in critically ill patients.

Guests:

Dr. Erin Willard is a PGY-3 Emergency Medicine Resident, Department of Emergency Medicine, University of Arkansas for Medical Sciences.

Dr. Carly Eastin is an Associate Professor, Division of Research and Evidence Based Medicine, Department of Emergency Medicine, University of Arkansas for Medical Sciences.

Case Overview

Case: A 45-year-old female in the emergency department is being admitted to the intensive care unit (ICU) for septic shock secondary to urinary tract infection (UTI). She has been given fluids, antibiotics, and is currently maintaining adequate mean arterial pressure (MAP) on low-dose vasopressors. You are ready to call the ICU and get her admitted. But you remember seeing in the news there was a study claiming vitamin C could cure sepsis. You wonder if giving vitamin C will affect her outcome?

Background: There was a huge buzz in the media a few years ago about a vitamin C cocktail (vitamin C, hydrocortisone and thiamine) as a possible cure for sepsis. This was because of a well-known critical care physician Dr. Paul Marik.

Dr. Marik published a retrospective before and after study that included a vitamin C cocktail reporting an impressive number needed to treat of 3 to prevent one death due to sepsis.

For the scientific rationale why vitamin C therapy may help septic patients check out Dr. Josh Farkas' post on PulmCrit.

We reviewed Dr. Marik's observational study on SGEM#174. A dozen skeptics commented about the validity of the study including my EBM mentor Dr. Andrew Worster who started BEEM and Legend of Emergency Medicine Dr. Jerome Hoffman.

The SGEM Bottom Line was that Vitamin C, hydrocortisone and thiamine was associated with lower mortality in severe septic and septic shock patients in this one small, single centred retrospective before-after study but causation has yet to be demonstrated.

A number of clinical trials are currently underway in an attempt to replicated Dr. Marik's findings. The existing evidence to support vitamin C use in patients with septic shock is weak and has been summarized in a systematic review meta-analysis.

Reference: Putzu et al. The Effect of Vitamin C on Clinical Outcome in Critically Ill Patients: A Systematic Review with Meta-Analysis of Randomized Controlled Trials. Critical Care Medicine. June 2019.

Population: Randomized trials examining critically ill adult ICU or cardiac surgery patients

Exclusions: Inappropriate setting (cardiac or ICU) or study design (RCT), pediatrics, non-critically ill

Intervention: Any type of vitamin C formulation or regimen

Comparison: Placebo or no therapy.

Outcome:

- **Primary Outcome:** Mortality at the longest follow-up available
- **Secondary Outcomes:** Acute kidney injury, supraventricular tachycardia, ventricular arrhythmia, stroke, ICU and hospital length of stay.

Authors' Conclusions

"In a mixed population of ICU patients, vitamin C administration is associated with no significant effect on survival, length of ICU or hospital stay. In cardiac surgery, beneficial effects on postoperative atrial fibrillation, ICU or hospital length of stay remain unclear. However, the quality and quantity of evidence is still insufficient to draw firm conclusions, not supporting neither discouraging the systematic administration of vitamin C in these populations. Vitamin C remains an attractive intervention for future investigations aimed to improve clinical outcome."

Quality Checklist for Therapeutic Systematic Reviews

- ✓ 1. The clinical question is sensible and answerable.
- ✓ 2. The search for studies was detailed and exhaustive.
- ? 3. The primary studies were of high methodological quality.
- ✓ 4. The assessment of studies were reproducible.
- ✓ 5. The outcomes were clinically relevant.
- ✗ 6. There was low statistical heterogeneity for the primary outcomes.
- ✗ 7. The treatment effect was large enough and precise enough to be clinically significant.

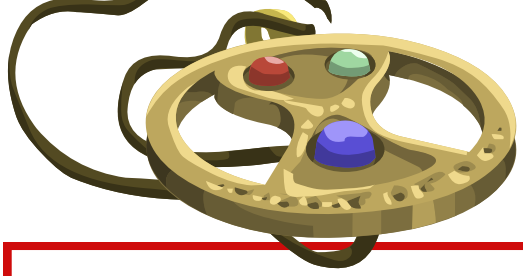
Case Outcomes

Key Results:
They included 44 randomized studies with 16 from the ICU setting (n=2,857) and 2 from cardiac surgery (n=3,598).

No statistical difference in mortality wiht the administration of vitamin C.

- **Primary Outcome:** Mortality
  - ICU: No statistical difference 28% in the vitamin C group vs 29% in the control group. RR 0.90 (95% CI 0.74-1.10; p=0.31)
  - Cardiac Surgery: No statistical difference in post-operative mortality

- **Secondary Outcomes:**
  - ICU: No statistical difference in AKI, ICU or hospital LOS
  - Cardiac Surgery: Less post-operative atrial fibrillation, ICU and hospital LOS. No statistical difference in AKI, stroke or ventricular arrhythmias.



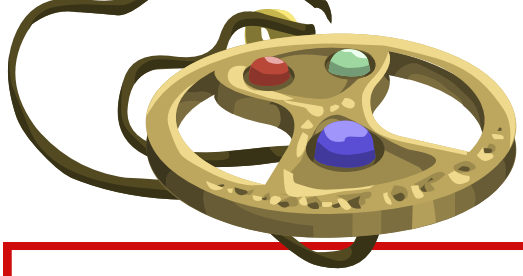
Time to Talk Nerdy

1) Focused Question: We would have preferred to have a much more focused question. This SRMA looked at critically ill patient whether they were in the ICU or post-operative cardiac surgery patients. There is a possibility that vitamin C could have a patient oriented benefit identified through a SRMA. However, the heterogeneity of the included population could hide any subgroup demonstrating efficacy. We would have like to have the question of whether or not in patients suffering from severe sepsis or septic shock would have a mortality benefit from the administration of vitamin C.

2) Quality of Trials: One of the weaknesses of a SRMA is the quality of the included trials. The vast majority (36/44) of the included trials were deemed to be of high-risk of bias. There is this hierarchy of evidence-based medicine where SRMA are considered better than randomized control trials. However, we would have more confidence in a well designed multi-centered, blinded, randomized, placebo-controlled trial than a SRMA containing poor quality studies. Mashing low quality studies in a meat grinder does not get us any closer to the “truth”.

3) Heterogeneity: The statistical heterogeneity represented by the I2metric was moderately high. This relates to the 1stnerdy point and the variety of patients included in the study. There was also a great deal of variability in vitamin C regimen (dose and route of administration). If the result demonstrated benefit this would strength our confidence in the effect of vitamin C in a variety of critically ill patients at a variety of dosages. Because they failed to demonstrate efficacy we still do not know if there is a mortality or other benefit to vitamin C.

4) Harm: As with many studies, there was limited data on harm of the intervention. Most of the studies included in this SRMA did not systematically assess advents due to vitamin C administration. While it is probably safe it



Time to Talk Nerdy

would be intellectually inaccurate to claim safety.

5) Burden of Proof: In epistemology the burden of proof is on those making the claim. Advocates of vitamin C claim that it provides a patient-oriented benefit. Research studies are set up with a null hypothesis (no effect). Evidence needs to be presented to reject the null hypothesis. At this point in time the burden in support of vitamin C has not been met. That does not mean we can make the claim that vitamin C does not work but rather we do not have sufficient evidence to warrant rejecting the null.

Comment on Authors' Conclusion Compared to SGEM Conclusion: We agree that there appears to be no mortality benefit but that the secondary outcomes should only be viewed as hypothesis generating.

Clinical Application: Vitamin C may prove beneficial in the prevention of post-operative supraventricular arrhythmia. However, the available evidence has significant limitations and should be viewed as hypothesis generating for our cardiology colleagues. Further high-quality research is needed in this area before we can confidently reject the null hypothesis.

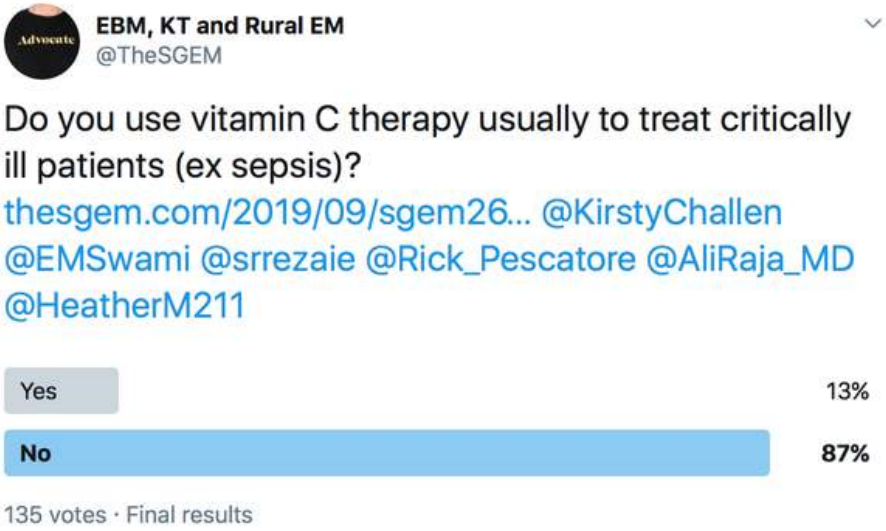
What Do I Tell the Patient? We are going to admit you to the ICU and give you IV antibiotics for your serious infection. You may have heard in the media about vitamin C being a cure for sepsis (severe infections). We hope that is true but at this time we do not have good enough evidence to routinely give it to patients.

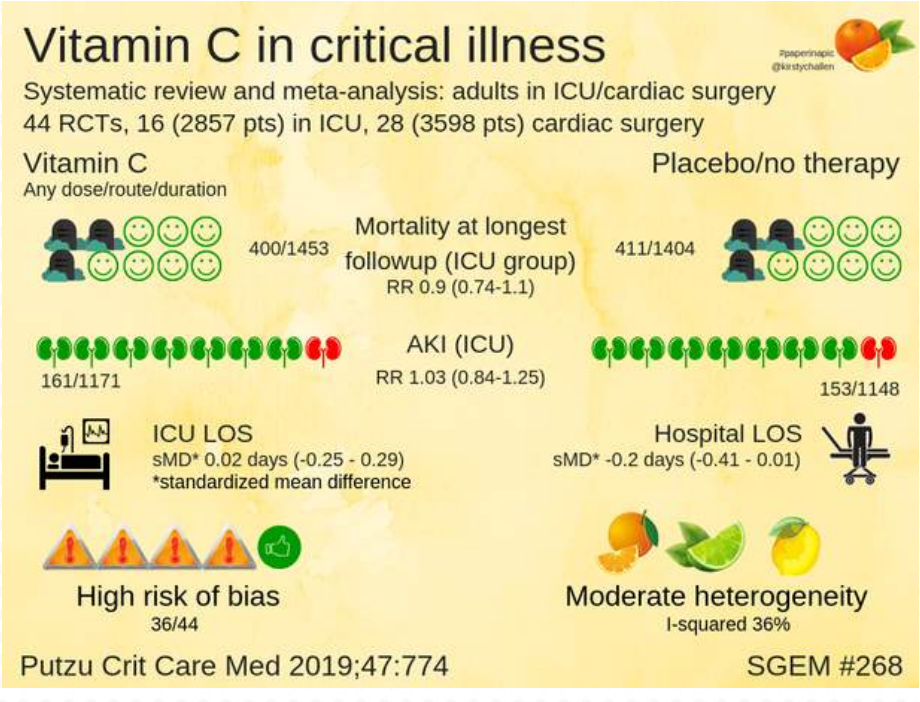
Case Resolution: You remember that there is no good evidence that vitamin C treatment in critically ill patients like sepsis has benefit and chose not to this therapy. The patient is transitioned to the floor the following day and ultimately discharged home without end-organ damage.

Episode End Notes

Other FOAMed Resources:

- The Bottom Line: An Orange a Day Keeps Sepsis at Bay?
- EMLit of Note: Vitamin C for Sepsis
- EMCrit: Paul Marik on the Metabolic Resuscitation of Sepsis
- EMCrit: Metabolic sepsis resuscitation: the evidence behind Vitamin C
- Pharmacy Joe: Vitamin C, Hydrocortisone, and Thiamine for Severe Sepsis and Septic Shock
- Everyday EBM: Vitamin C in Sepsis – Splashes in the Popular Press
- Emlyn's: Vitamin SCepTiC?
- REBEL EM: The Marik Protocol: Have We Found a "Cure" for Severe Sepsis and Septic Shock?
- ZdoggMD: Vitamin C Cures Sepsis and other fake news?





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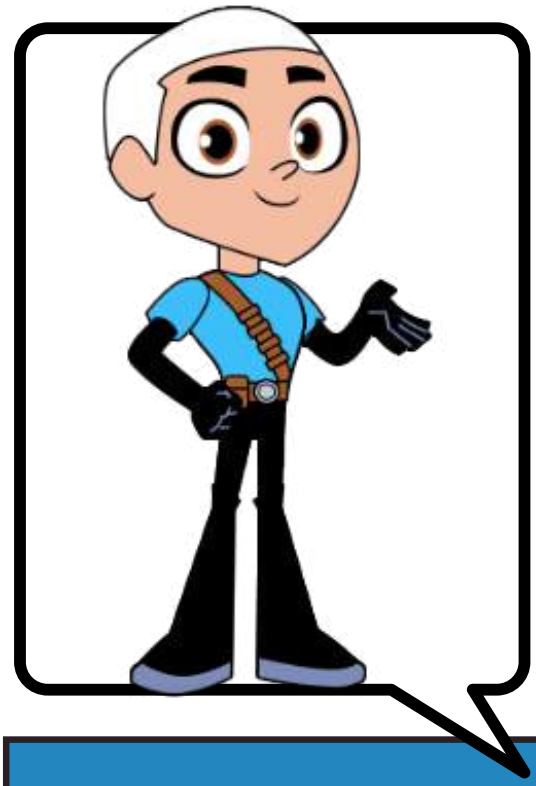
PRE-HOSPITAL NITROGLYCERIN FOR ACUTE STROKE PATIENTS?

Clinical Question:

Does early administration of glyceryl trinitrate (nitroglycerin) by paramedics in the pre-hospitaal setting improve neurologic outcome in patients with presumed acute stroke?



Bottom Line:

Very early application of transdermal nitroglycerin by paramedics in the pre-hospital setting cannot be recommended at this time in patients with a suspected stroke.

Guests:

Clay Odell is a Paramedic/RN for New London Hospital EMS in New Hampshire, USA which provides 9-1-1 coverage and Mobile Integrated Healthcare for seven rural communities. He's been involved in EMS for over 30 years in a variety of roles and is a strong advocate for evidence-based EMS protocols.

Case Overview

Case: Your ambulance responds to a 9-1-1 call for a 75-year-old male experiencing abrupt onset of left sided weakness. You arrive to find the patient awake and alert, with a facial droop, slurred speech and left-sided arm drift (FAST-ED score = 3). He has a history of hypertension. His vital signs are heart rate 90 beats per minute, blood pressure 162/96 mmHg, respiratory rate 14 breaths per minute, SpO2 96% on room air, capillary blood glucose 120 mg/dl (6.7 mmol/L). His 12-lead ECG shows a normal sinus rhythm without ST abnormality or ectopy. While preparing for transport you contemplate administering nitroglycerin due to the likelihood of stroke.

Background: We have covered stroke many times on the SGEM (SGEM#29: Stroke Me, Stroke Me; SGEM#70: The Secret of NINDS; SGEM Xtra:Thrombolysis for Acute Stroke; SGEM Xtra: No Retreat, No Surrender; and SGEM Xtra: The Walk of Life). This episode will not debate the use of tPA for acute ischemic stroke. Rather we will be discussing whether lowering the blood pressure of a patient suspected of having a stroke in the pre-hospital setting will have a net beneficial patient-oriented outcome (POO).

Hypertension is common in acute stroke and is a predictor of poor outcome [1]. There is still some controversy on whether or not it is beneficial to lower the blood pressure in these cases [2].

Previous studies suggested that Nitric Oxide (NO) donors, such as transdermal glyceryl trinitrate (GTN – also known as nitroglycerin), reduced blood pressure, improved cerebral blood flow and reduced stroke lesion size if administered early [3 and 4].

There have been five randomized trials looking at nitroglycerin with four not showing superiority for functional outcome. One phase 2 trial done in the pre-hospital setting

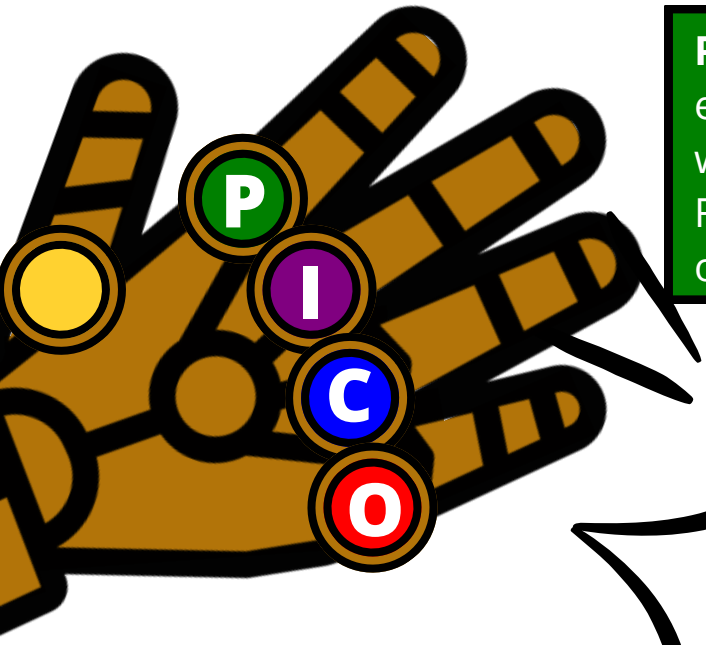
(RIGHT: Rapid Intervention with Glyceryl trinitrate in Hypertensive stroke Trial) did suggest a benefit to nitroglycerine [5].

The RIGHT study was a subgroup analysis of the ENOS (Efficacy of Nitric Oxide in Stroke) that looked at nitroglycerin within 6 hours of stroke. It too failed to demonstrate a statistical benefit [6].

However, a SRMA of individual patient data in these five trials suggested that earlier administration of nitroglycerin was associated with better outcomes in both ischemic and intracerebral hemorrhage stroke. It also was associated with lower mortality, disability, cognitive impairment, mood disturbance and poor quality of life (QOL) [7].

The conclusion to the RIGHT study was that a larger trial is needed to determine if nitroglycerin improves survival with good neurologic outcome.

Reference: Bath PM et al. Prehospital transdermal glyceryl trinitrate in patients with ultra-acute presumed stroke (RIGHT-2): an ambulance-based, randomized, sham-controlled, blinded, phase 3 trial. The Lancet March 2019.



Population: Adult patients who called emergency services for presumed stroke within 4 hours of onset of symptoms and a FAST score of 2 or 3, systolic blood pressure of equal or greater than 120 mmHg

Intervention: Application of a 5.0 mg Transidermal-Nitro patch

Exclusions: Nursing home patients, Glasgow Coma Scale <8, hypoglycemia or witnessed seizure, life expectancy < 6 months, known to have taken PDE5 inhibitor in the previous days and sensitivity to the Transidermal-Nitro patch or DuoDERM hydrocolloid dressing.

Comparison: Application of a sham DuoDERM hydrocolloid dressing

Outcome:

- **Primary Outcome:** Functional outcome measured by Modified Rankin Scale (mRS) at 90 days.
- **Secondary Outcomes:** Barthel Index, cognition, quality of life and mood.
- **Safety Outcomes:** All-cause mortality, cause specific mortality,hypotension or hypertension occurring during the first 4 days.

Authors' Conclusions

"Prehospital treatment with transdermal GTN does not seem to improve functional outcome in patients with presumed stroke. It is feasible for UK paramedics to obtain consent and treat patients with stroke in the ultra-acute prehospital setting."

Quality Checklist for Randomized Control Trials

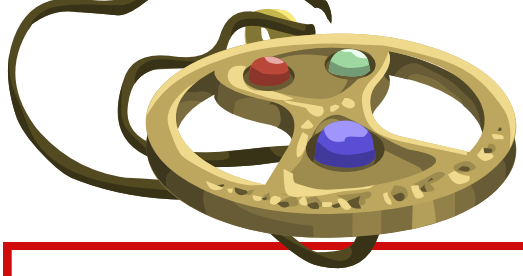
- ☒ 1. The study population included or focused on those in the emergency department.
- ☑ 2. The teams were adequately randomized.
- ? 3. The randomization process was concealed.
- ☑ 4. The teams were analyzed in the groups to which they were randomized.
- ? 5. The study teams were recruited consecutively (i.e. no selection bias).
- ☑ 6. The teams in both groups were similar with respect to prognostic factors.
- ☒ 7. All participants (patients, clinicians, outcome assessors) were unaware of group allocation.
- ☑ 8. All groups were treated equally except for the intervention.
- ☑ 9. Follow-up was complete (i.e. at least 80% for both groups).
- ☑ 10. All (team) patient-important outcomes were considered.
- ☒ 11. The treatment effect was large enough and precise enough to be clinically significant.

Case Outcomes

Key Results:
They enrolled 1,149 patients into RIGHT-2. The median time to randomization was 71 minutes. The cohort had slightly more men and the mean age was in the early 70's. Ischemic strokes were diagnoses in 52%, intracerebral hemorrhage in 13%, TIAs in 9% and stroke mimics in 26%. The mean change in blood pressure after the initial treatment was 5.8 mmHg systolic and 2.6 mmHg diastolic compared to the sham group. This drop in blood pressure represents a disease-oriented outcome (DOO) or surrogate outcome.

- **Primary Outcome:** Functional outcome measured by Modified Rankin Scale (mRS) at 90 days.
  - Odds Ratio 1.04 (95% CI; 0·84 to 1·29) p=0·69

- **Secondary Outcomes:** There were no statistically differences between groups.
- **Safety Outcomes:** There were no statistical difference between the two groups (ex: in mortality or serious adverse events). The nitroglycerine group did have more hypotension at day 4.



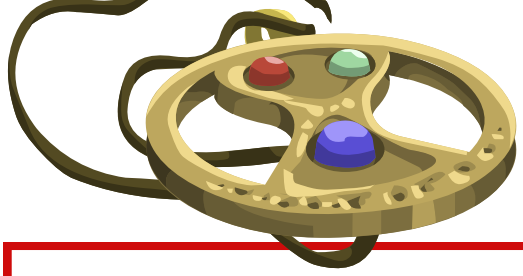
Time to Talk Nerdy

1. Enrollment/Randomization: We are unsure if consecutive patients were randomized due to the possible lack of concealment. Ambulance stations were randomized with blocks of four packs (two active and two control). Paramedics got an envelope at the beginning of their shift and returned unopened ones at the end of their shift. They did not mention if the envelopes were opaque. Even if the envelopes were opaque there is recent evidence of paramedics opening trial envelopes until they found the intervention group. It is possible that paramedics could have known which treatment group they had at the start of their shift and returned it unopened.

2. Blinding: This trial was not completely blinded. Paramedics and treating clinicians knew which group patients were assigned. The patients and outcome assessors were unaware of group allocation. However, there is no confirmation in the study that blinding was maintained. Unmeasured factors in the management of the patient could be possible. In addition, if the patient knew which group they were assigned and the study hypothesis that could have introduced bias favoring the intervention. It would have been easy to ask participants at the end of the study which group they thought they were assigned.

3. Outcome Assessment: The primary outcome was the mRS. The reliability of the mRS is only moderate in trained clinicians and its validity has been questioned [8 and 9]. This trial outcome assessment was done by telephone with a trained blinded assessor. If the patient could not be reached by phone, a questionnaire was mailed for the patient to complete. No information could be found on how many patients had to fill out the questionnaire and how many patients were interviewed over the phone.

4. Intervention: The study design was for four placements of the active or sham patch. However, there was significant falloff following the initial



Time to Talk Nerdy

treatment. While there was 99% adherence to protocol by paramedics, only 55% of the subjects received a second treatment (in the hospital), and less than 50% got all four intended treatments.

Even the fall in blood pressure for the 99% who received the first treatment was lower than prior studies. It is possible with a larger dose of nitroglycerine dropping the blood pressure greater and better adherence to treatment protocols that a benefit could be demonstrated.

5. ITT vs. mITT: They divided the study up into two cohorts. Cohort 2 included all the patients and represents a true ITT. The primary outcome was no statistical difference. Cohort 1 removed all the patients with TIAs (9%) or stroke mimics (26%) for a total of 35%. The remaining 65% of patients were analyzed as a from modified ITT of the targeted disease (ischemic or hemorrhagic stroke). This mITT also failed to superiority of nitroglycerine.

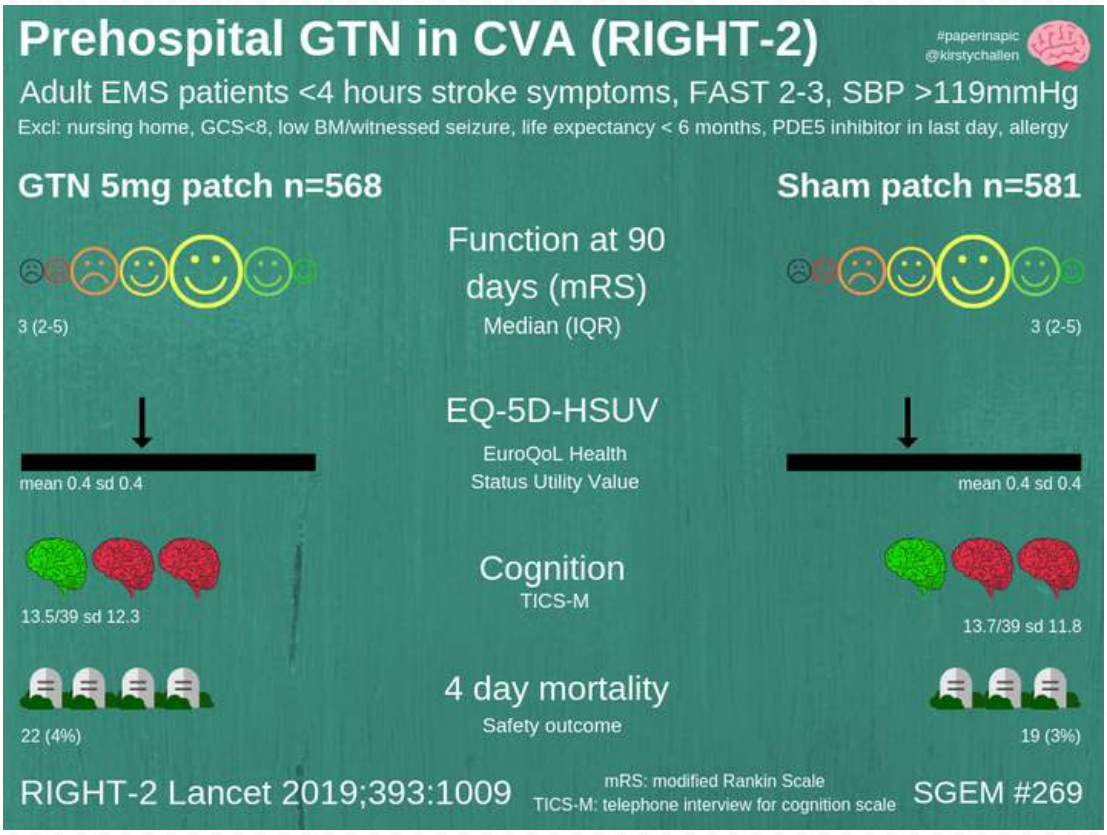
Comment on Authors' Conclusion Compared to SGEM Conclusion: We agree with the authors' conclusions about lack of efficacy but are not sure why they needed to include the statement about feasibility.

Clinical Application: This is another example of pre-hospital treatment not resulting in a patient-oriented outcome (POO). Other examples include IV fluids (SGEM#246) and IV antibiotics (SGEM#207) in septic patients and therapeutic hypothermia (SGEM#183), endotracheal intubation (SGEM#247) and epinephrine (SGEM#238) for OHCA. We need to focus on things that have been proven to make a difference in the pre-hospital setting by paramedics like high-quality CPR and early defibrillation.

What Do I Tell the Patient? It looks like you might be having a stroke. We are going to monitor you closely and transport you to the hospital emergency department where they will assess you and treat whatever is causing your weakness.

Case Resolution: An intravenous line is established in the patient's right forearm and he is transported to the closest hospital with stroke care capability.

Episode End Notes



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CRASH-3 TXA FOR TRAUMATIC HEAD BLEEDS?

Clinical Question:

Does TXA have mortality benefit in patients with isolated head trauma?

Bottom Line:

We cannot recommend the routine use of TXA for patients with isolated brain injuries at this time.

Guests:

Dr. Salim Rezaie currently works as a community emergency physician at Greater San Antonio Emergency Physicians (GSEP), where he is the director of clinical education. He is also the creator and founder of REBEL EM and REBEL Cast, a free, critical appraisal blog and podcast that tries to cut down knowledge translation gaps of research to bedside clinical practice.

Case Overview

Case: A 42-year-old man falls off a backyard deck. He arrives at the emergency department via EMS with a Glasgow Coma Scale (GCS) score of 10 and both pupils reactive. He is hemodynamically stable and sent for a STAT head CT. It demonstrates a traumatic intracranial hemorrhage. You wonder if you should give tranexamic acid (TXA) while you wait for neurosurgery to call you back.

Background: TXA is a synthetic derivative of lysine that inhibits fibrinolysis and thus stabilizing clots that are formed. We have covered TXA as a treatment for bleeding a number of times on the SGEM. The evidence for TXA providing a patient-oriented outcome (POO) has been mixed. It seems to work for epistaxis, fails to cause a decrease in all-cause mortality in post-partum hemorrhage, does not demonstrate an improved neurologic outcome in hemorrhagic strokes but does have 1.5% absolute mortality reduction in adult trauma patients.

- Epistaxis – SGEM#53 and SGEM#210
- Post-Partum Hemorrhage – SGEM#214
- Stroke due to Intracranial Hemorrhage – SGEM#236
- CRASH-2 Trial – SGEM#80

REBEL EM has also looked at TXA for those conditions plus a few others. It is unclear if it provides a benefit for gastrointestinal bleeds (GIB). Nebulized TXA shows promise for both post-tonsillectomy bleeding and hemoptysis. However, better studies are needed to confirm these observations.

Zehtabchi et al published a SRMA of TXA for traumatic brain injuries (TBI). They found only two high-quality randomized control trials with 510 patients having TBI that met inclusion

criteria. The results were no statistical difference in in-hospital mortality or unfavorable neurologic functional status. However, there was a statistical reduction in intracranial hematoma expansion size with TXA compared to placebo.

Reference: CRASH-3 Trial Collaborators. Effects of tranexamic acid on death, disability, vascular occlusive events and other morbidities in patients with acute traumatic brain injury (CRASH-3): a randomised, placebo-controlled trial. The Lancet October 2019

Tranexamic Acid (TXA) for Everything That Bleeds?

TXA Use	Yes or No	Dosing
Trauma ≤3hrs • Thinking MTP	YES	1g IV over 10min • 1g IV over 8hr
ICH	NO	---
PPH	+/-	1g IV over 10min
GIB	+/-	???
Epistaxis	YES	500mg Soaked Pledget
Post-Tonsillectomy	YES	250mg Nebulized (<25kg) OR 500 - 1000mg Nebulized (≥25kg)
Hemoptysis	YES	250mg Nebulized (<25kg) OR 500 - 1000mg Nebulized (≥25kg)

Population: Adult patients 16 years and older with traumatic brain injuries with GCS score of 12 or lower or any intracranial bleed on CT scan and no extracranial bleeding treated within 3 hours of injury

Exclusions: Age less than 16 years of age, extracranial bleeding, or greater than 8 hours since injury (limited to greater than 3 hours from September, 2016)

Intervention: TXA 1g infused over 10 minutes followed by an infusion of another 1g over 8 hours

Comparison: Saline placebo

Outcome:

- **Primary Outcome:** Head injury-related deaths within 28 days
- **Secondary Outcomes:** Early head injury deaths (<24hrs), all-cause and cause specific mortality, disability, vascular occlusive events (myocardial infarctions, stroke, venous thromboembolism), seizures, complications, neurosurgery, days in the intensive care unit (ICU), adverse events within 28 days and subgroup analyses.

Authors' Conclusions

"Our results show that tranexamic acid is safe in patients with TBI and that treatment within 3 h of injury reduces head injury-related death. Patients should be treated as soon as possible after injury."

Quality Checklist for Randomized Control Trials

- ☑ 1. The study population included or focused on those in the emergency department.
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- ☑ 8. All groups were treated equally except for the intervention.
- ☑ 9. Follow-up was complete (i.e. at least 80% for both groups).
- ☑ 10. All (team) patient-important outcomes were considered.
- ? 11. The treatment effect was large enough and precise enough to be clinically significant.

Case Outcomes

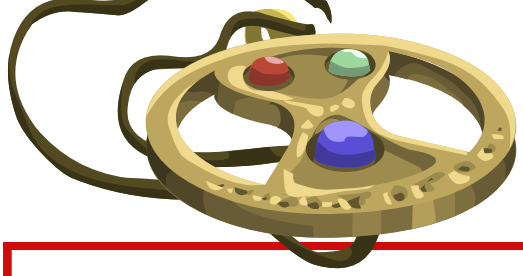
Key Results:
The CRASH-3 investigators randomly allocated 12,737 patients with TBI to receive either TXA or placebo. There were 9,202 (72%) who were enrolled within 3 hours of injury. The mean age was 42 years, 80% were male, 80% had both pupils reactive and about 2/3 had a GCS less than 12.

No statistical difference in head-injury related mortality with TXA compared to placebo.

- **Primary Outcome:** Death due to head injury
  - 18.5% TXA vs. 19.8% placebo, RR 0.94 (95% CI 0.86 to 1.02)

- **Secondary Outcomes:** The two statistically significant results were less head injuries deaths within the first 24 hours and in the subgroup of patients with milder injuries (GCS 9-15). Disability was similar between both groups. There was no evidence of increased vascular events, seizures, complications or adverse events. We could not find the data on neurosurgery or days in the ICU.

	TXA vs. Placebo	RR (95% CI)
Head Injury Death <24hrs		0.81 (0.69-0.95)
All-Cause Mortality		0.96 (0.89-1.04)
Head Injury Death GCS 3-8	39.6% vs. 40.1%	0.99 (0.91-1.07)
Head Injury Death GCS 9-15	5.8% vs 7.5%	0.78 (0.62-0.95)
Head Injury Death (exclude GCS 3 or bilateral unreactive pupils)	12.5% vs. 14.0%	0.89 (0.80-1.00)



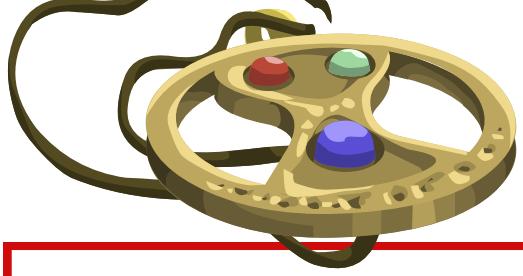
Time to Talk Nerdy

This was a large multinational study looking at a very important question. The CRASH-3 Trial Collaborators need to be commended for successfully completing this study. All studies will have some limitations that need to be considered when interpreting the results. Here are five that we identified and wanted to discuss:

1. Selection Bias: We are unsure if there was any selection bias in CRASH-3. Patients were eligible if the recruiting clinician was uncertain as to the appropriateness of TXA. No denominator was provided for how many people were screened. They state that "almost all patients with TBI who met inclusion criteria were recruited" but do not provide the actual number. Because of the subjective nature of the inclusion and exclusion (based on recruiting clinicians' uncertainty) this could have introduced selection bias into the study.

2. Wide-Confidence Intervals: The confidence intervals were wide for point estimate of the primary outcome (relative risk head injury related death). It ranged from a large effect size (0.86) but also crossed the line of no difference (1.02). That does not mean we can conclude TXA does not work but rather it did not demonstrate a statistical benefit. The point estimate did favour TXA over placebo (RR 0.94). The width of the 95% confidence interval and the upper limit crossing the 1.0 decreases the certainty of any conclusion that can be made.

3. All-Cause vs. Head Injury Mortality: The authors considered many patient-oriented outcomes. While their primary outcome was head-injury related mortality, a more important POO would be overall mortality. The patient and their family usually do not care what they died from but whether or not they did die. We saw this in the WOMAN trial where the overall mortality was not decreased but the paper highlighted the statistically



Time to Talk Nerdy

significant decrease in post-partum hemorrhage related deaths.

4. External Validity: The study was done in 29 countries with the majority being middle to low income countries. Canada had one centre and the USA had no participating centres. They did do an analysis based on income that was not pre-specified. This did not show a statistical difference. However, the question remains on whether TXA would have a clinically important impact in the USA healthcare setting.

5. Subgroup Analysis: While the subgroup analyses were pre-specified, they are underpowered to draw any strong conclusions. We should be cautious not to over-interpret these results.

Comment on Authors' Conclusion Compared to SGEM Conclusion: We agree that TXA does appear to be safe but think the claim about decreased head-injury related death is misleading. This is because it was only for a subgroup of patients. If TXA is given, then giving it as soon as possible seems reasonable.

Clinical Application: Clinicians will have different thresholds of evidence that will convince them to change practice. The effect size of TXA in patients with TBI was small, the confidence intervals were wide and the upper end of the 95% confidence interval crossed the line of no statistical difference. The evidence was even less convincing when looking at the more patient-oriented outcome of all-cause mortality. While the subgroup analyses showing efficacy in certain cohorts was interesting, the groups were underpowered to provide a clear answer on how to apply this information.

We have a number of concerns how this trial will be interpreted and applied. One aspect is the "spin" on the article. People may highlight the "significant" relative reduction of death in a subgroup rather than focusing on the lack of statistical difference of an absolute reduction in overall mortality. This was seen in the WOMAN trial and we need to be cautious not to do this with CRASH-3 by over hyping the results.

It is also well recognized that the efficacy of treatment decreases when applied outside the strict environment of a research trial. Applying this protocol in the community setting would likely dilute and negate any possible benefit of TXA for patients with isolated TBI.

We are also concerned that a quality metric will be created to monitor adherence to providing TXA to these adult isolated TBI patients within 3 hours. This could be tied to physician or hospital pay despite the weak underlying evidence. We have seen this happen with tPA for acute ischemic stroke and the 30cc/kg of IV crystalloid within the first hour in septic patients.

Let us not forget about cognitive load and attention. Adding an additional treatment which may or may not provide a patient-oriented benefit is just one more thing to consider when managing a trauma patient. While we are paying more attention to that individual, we will be decreasing our attention to the many other undifferentiated patients in the department. Those other patients

Clinical Application: might have time dependent emergencies whose treatment could be impacted negatively.
The low cost of TXA may also be used as an argument for using it in these patients. However, this is irrelevant if it does not provide a patient-oriented outcome. There are also millions of people who suffer from TBI every year worldwide. A small number multiplied by millions of patients will add up to a lot of money.

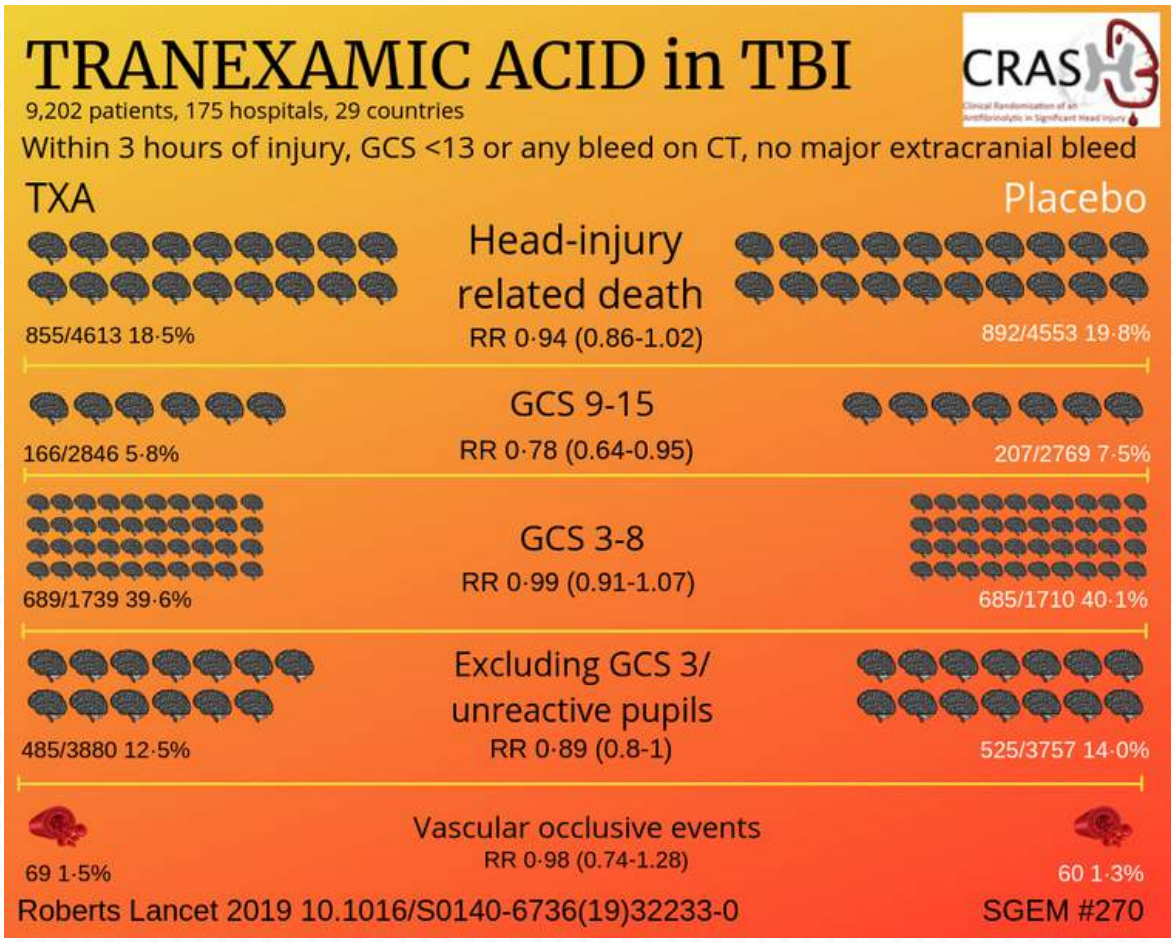
What Do I Tell the Patient? You tell the family that their loved one has a serious brain injury. You have called the neurosurgeons and they are coming shortly to talk about the best treatments.

Case Resolution: You decide not to give TXA and decide to leave it up to the neurosurgeon.

Episode End Notes

Other FOAMed:

- St. Emlyn's: Tranexamic Acid (TXA) in Head Injury.
- PulmCrit: Tranexamic acid for traumatic brain injury (CRASH3)
- EM Nerd: The Case of the Indecisive Antidote
- EM Literature of Note: CRASH-3
- BadEM: CRASH-3
- First10EM:CRASH-3 TXA is no Wonder Drug



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BOUGIE WONDERLAND FOR FIRST PASS SUCCESS

Clinical Question:

Does using a bougie increase first pass intubation success?

Bottom Line:

The use of a bougie is associated with increased first pass success rates for intubations in the emergency department but an RCT is needed to further explore this topic.

Guest:

Missy Carter, former City of Bremerton Firefighter/Paramedic, currently a physician assistant practicing in emergency medicine in the Seattle area and an adjunct faculty member with the Tacoma Community College paramedic program.

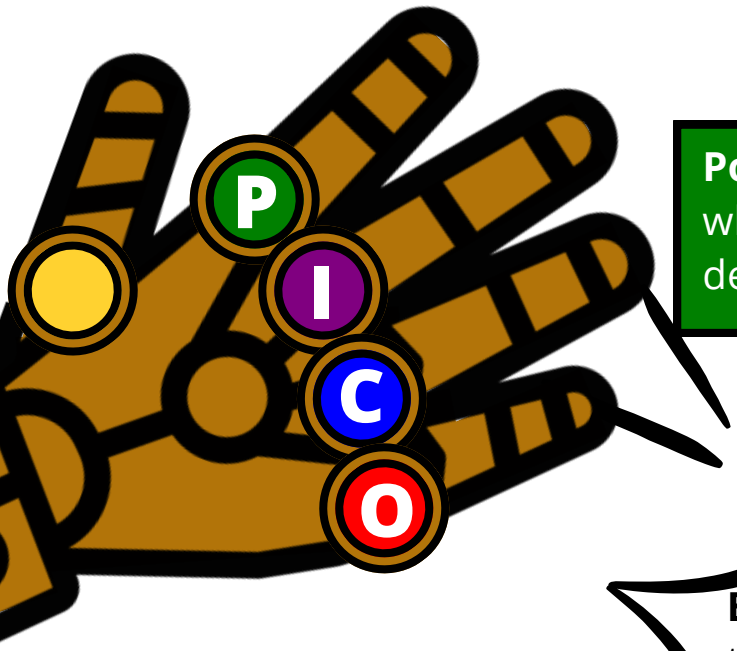
Case Overview

Case: You are preparing for a rapid sequence intubation in a patient suffering from respiratory distress. While doing your airway assessment you notice some difficult airway characteristics (obese patient with a small mouth opening). In the past you've had failed first pasts attempts on a similar patient and used a bougie as your back up device. You wonder if this time you would be more successful using the bougie for your first attempt.

Background: We have covered airway a number of times on the SGEM. This has included supraglottic airways for OHCA (SGEM#247), POCUS for confirming endotracheal tube placement (SGEM#249) and non-invasive positive pressure ventilation for OCHA (SGEM#96) just to name a few. However, we have never covered the issue of using a bougie for intubation.

For many years the bougie has been considered a back up or "rescue" airway tool and only pulled out after one or even several failed intubation attempts. Many studies have shown that multiple intubation attempts can increase mortality and morbidity, so we are always striving to increase our first pass intubation success rates to improve patient care.

Reference: Driver et al. The Bougie and First-Pass Success in the Emergency Department. Annals of Emergency Medicine 2017



Population: Adult patients (age > 17 years) who underwent intubation in the emergency department

Exclusions: Patients with missing videos that recorded the intubation, cases in which a bougie was used with a hyper angulated video laryngoscope blade (GlideScope) or were intubated before arrival to the emergency department

Intervention: Bougie with Macintosh or CMAC laryngoscope

Comparison: Intubation with endotracheal tube and stylet

Outcome:

- **Primary Outcome:** First-pass success rates
- **Secondary Outcomes:** Duration of attempts, hypoxia and esophageal intubations

Authors' Conclusions

"Bougie was associated with increased first-pass intubation success. Bougie use may be helpful in ED intubation."

Quality Checklist for Observational Study

- ☑ 1. Did the study address a clearly focused issue?
- ☑ 2. Did the authors use an appropriate method to answer their question?
- ☑ 3. Was the cohort recruited in an acceptable way?
- ☑ 4. Was the exposure accurately measured to minimize bias?
- ☑ 5. Was the outcome accurately measured to minimize bias?
- ☑ 6. Have the authors identified all-important confounding factors?
- ☑ 7. Was the follow up of subjects complete enough?
- ☑ 8. How precise are the results? Fairly precise given the small sample size
- ☑ 9. Do you believe the results?
- ☑ 10. Can the results be applied to the local population?
- ☑ 11. Do the results of this study fit with other available evidence?

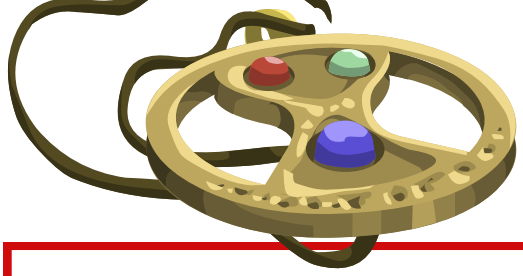
Case Outcomes

Key Results:
There were 543 patients included in this cohort. The median age was in the late 40's and more than two-thirds were male. The vast majority (~95%) of the intubations were performed by a senior resident.

First-pass success was greater with than without a bougie

- **Primary Outcome:** First-pass success
  - 95% with bougie vs. 86% without bougie
  - Absolute difference 9% (95% CI; 2% to 16%)

- **Secondary Outcomes:**
  - Median first-attempt duration was higher with than without bougie (40 seconds vs. 27 seconds) with a difference of 13 seconds (95% CI; 11 to 16).
  - Hypoxia 17% with and 13% without bougie
  - Esophageal intubation 1 with and 1 without bougie



Time to Talk Nerdy

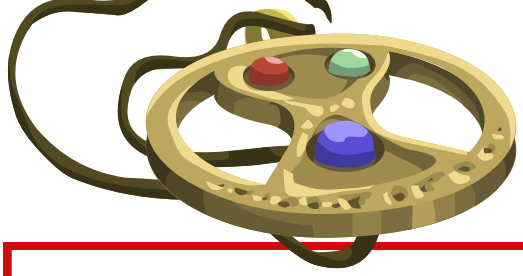
1. External Validity: This is clearly a bougie center of excellence. Of the 543 intubations included in this study, 435 used the bougie as the first-time airway tool. This raises the question of generalizability. If providers in this center are more proficient with the use of a bougie than the average emergency medicine clinician, would we see different results if we put the bougie in the hands of someone who does not use it regularly?

In addition, 95% of the intubations were done by residents. Does this have external validity to non-teaching sites where the attending physician is performing the intubations?

2. Missing Data: Although these cases were consecutive; 83 cases had to be excluded due to missing video. The videos in addition to chart review were the primary data collection tools. The authors addressed this limitation with a sensitivity analysis that showed the bougie would still be superior.

3. Associations: The retrospective nature of this study makes it difficult to eliminate bias. The reviewers did their best to mitigate this by using multiple reviewers for the videos looking from multiple angles. Three separate investigators watched all cases from three cameras. They were blinded to the study goals and simply reported information on a standardized form. However, it was not a randomized trial and so we cannot claim causation only association between bougie and first pass success rates.

4. Why Use the Bougie: It is unknown why the bougie was used in each case. The authors' attempted to identify difficult airway characteristics (obesity, cervical spine immobilization, presence of abnormal anatomy, facial trauma, masses, and body fluids) that could have influenced the operators' decision. They also screened for hypoxia and esophageal intubations. These



Time to Talk Nerdy

characteristics were about the same between groups which suggests the providers used bougie as first line device regardless of difficult airway characteristics.

5. Patient-Oriented Outcomes: They used first pass success rates, duration and hypoxia as surrogate markers. Important patient-oriented outcomes would have been survival and survival with good neurological function.

While there was a longer time for ETT insertion with a bougie than without (13 seconds) it is unlikely this was a clinically important difference.

Rates of hypoxia among the two groups were similar (13% with bougie and 17% without). Unfortunately, there is missing data on hypoxia in a total of 181 cases (114 missed on video feed and 67 were missed due to poor wave forms). It's possible that this missing information may have shown a significant increase in hypoxia for our bougie patients.

Comment on Authors' Conclusion Compared to SGEM Conclusion:
We agree with the authors' conclusions.

2-in-1

Reference: Driver et al. Effect of Use of a Bougie vs Endotracheal Tube and Stylet on First-Attempt Intubation Success Among Patients With Difficult Airways Undergoing Emergency Intubation. A Randomized Clinical Trial. JAMA May 2018

Population: Adult patients (>17 years of age) who underwent intubation in the emergency department and the attending emergency physician planned to use a Macintosh laryngoscope blade on the first attempt

Intervention: Bougie with Macintosh or CMAC laryngoscope

Exclusions: Prisoners, suspected or known pregnant patients and patients with known distortion of the upper airway or glottic structures

Comparison: Intubation with endotracheal tube and stylet

Outcome:

- **Primary Outcome:** First-attempt intubation success
- **Secondary Outcomes:** Duration of attempts, hypoxemia (SpO_2 <90% or a 10% decrease) and esophageal intubation

Authors' Conclusions

"In this emergency department, use of a bougie compared with an endotracheal tube + stylet resulted in significantly higher first-attempt intubation success among patients undergoing emergency endotracheal intubation. However, these findings should be considered provisional until the generalizability is assessed in other institutions and settings."

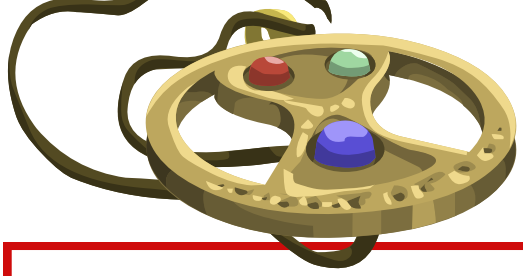
Quality Checklist for Randomized Control Trials

- [x] 1. The study population included or focused on those in the emergency department.
- [x] 2. The teams were adequately randomized.
- [x] 3. The randomization process was concealed.
- [x] 4. The teams were analyzed in the groups to which they were randomized.
- [x] 5. The study teams were recruited consecutively (i.e. no selection bias).
- [x] 6. The teams in both groups were similar with respect to prognostic factors.
- [ ] 7. All participants (patients, clinicians, outcome assessors) were unaware of group allocation.
- [x] 8. All groups were treated equally except for the intervention.
- [x] 9. Follow-up was complete (i.e. at least 80% for both groups).
- [ ] 10. All (team) patient-important outcomes were considered.
- [x] 11. The treatment effect was large enough and precise enough to be clinically significant.

Case Outcomes

Key Results:
They enrolled 757 patients that included 380 with a difficult airway characteristic. The mean age was in the mid-40's with more than two-thirds being male. The vast majority (85%) were intubated by a senior resident or fellow. Only 1% were intubated by emergency medicine faculty. The rest were intubated by junior residents.

- **Primary Outcome:** First-attempt intubation success
  - 96% with bougie group and 82% without bougie
  - Absolute difference of 14% (95% CI; 8-20)
-
- **Secondary Outcomes:**
  - Median first-attempt duration was similar (38 seconds vs 36 seconds)
  - Hypoxemia was similar (13% vs 14%)
  - Esophageal intubations (0 vs 3)



Time to Talk Nerdy

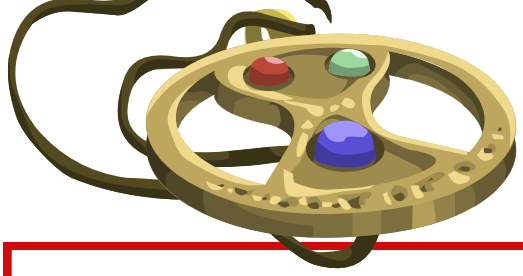
1. External Validity: The big money question we all have here is about generalizability. This trial was performed in a single center that has a known love affair with the bougie so healthy skepticism for bias is warranted. This raises the question if adding the bougie in a center which is unfamiliar with the device would be beneficial. Sometimes the best method is simply the method you know best.

Another thing is that only 1% of the intubations were done by the attending physician. Would the bougie be as helpful to a seasoned physician working in a non-teaching community setting.

Perhaps the bougie would help the rural clinician in the critical access hospital who does not intubate often?

2. Intention-to-Treat Analysis: This was an ITT analysis with 98% adherence in the bougie arm and 92% adherence in the stylet arm, meaning some physicians in the stylet arm chose bougie for first pass attempt due to their clinical judgement. There were 25 cases of crossover from stylet to bougie and only 4 cases of crossover to stylet from the bougie arm. This was a 7% protocol violation in favor of using bougie for difficult airways or need for rapid intubation per the article. This did not affect the study's final results as these intubations had high first pass success for the stylet group.

3. Secondary Outcomes: Various secondary outcomes were explored including hypoxia and incidence of pneumothorax were assessed in this trial. Unlike the observational trial which raised concern for hypoxia in the bougie group this study did not show a difference between the groups. There have been previous studies suggesting an association between bougie use and pneumothorax due to trauma while inserting to the carina. Those trials used a



Time to Talk Nerdy

straight bougie whereas this trial used a coude' tip. In this study complications were rare, pneumothorax after intubation without known cause was seen in in 9 patients in each group, esophageal intubation was seen in 3 patients in the stylet group and 0 in the bougie group. None of these complications were significant (table 5)

4. Subgroup Analyses: Although the trial was powered for success rates with difficult intubations, they did an interesting sub-group analysis of success rates as follows: Patients without difficult characteristics (99% vs. 92%), in-line immobilization (100% vs. 78%), obese patients (96% vs. 75%), and patients with Cormack-Lehane grades 2-4 (97% vs. 60%). Each favored the bougie suggesting routine bougie use as beneficial in all airways but some much more than others.

5. Patient-Oriented Outcomes: The outcomes were only measured until 1 minute after the end of the first intubation attempt. Again, they used first pass success rates, duration and hypoxia as surrogate markers. Patients may have considered mortality or survival with good neurological function more patient-oriented.

Comment on Authors' Conclusion Compared to SGEM Conclusion:
We generally agree with the authors' conclusions.

Clinical Application: It all depends. I personally use a bougie only as a rescue device and have only missed one airway in 24 years. There is one doctor in my shop who uses it all the time. I think if you are comfortable with it and having great success then carry on with what works. If you have struggled in the past and found yourself reaching for the bougie more often than you would like as a rescue device than consider using it for the first attempt.

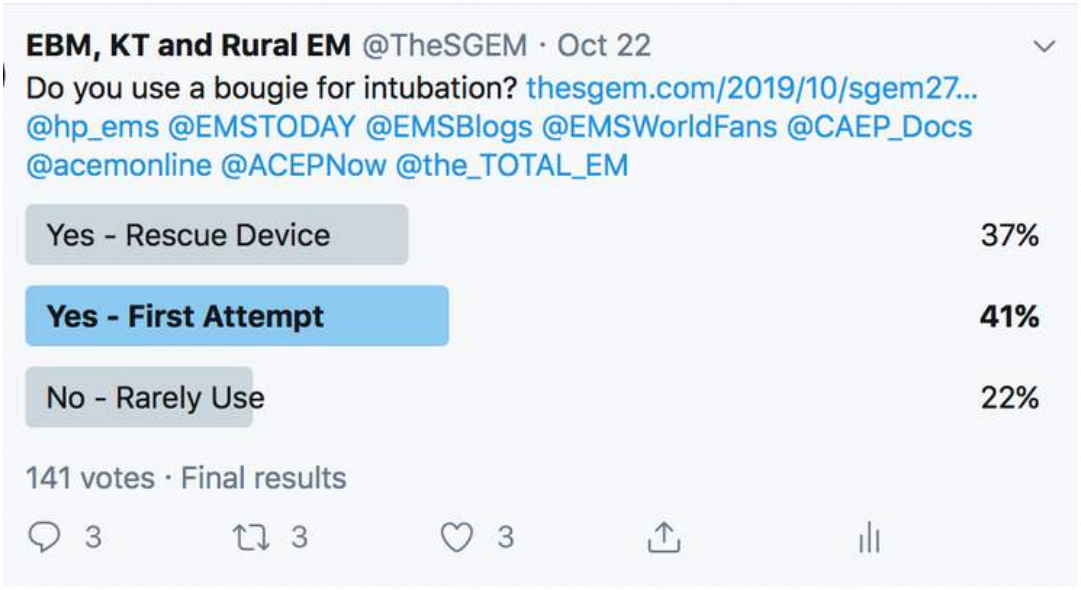
What Do I Tell the Patient? Probably not a whole lot to tell your patient since they are likely preoccupied with breathing or are unresponsive.

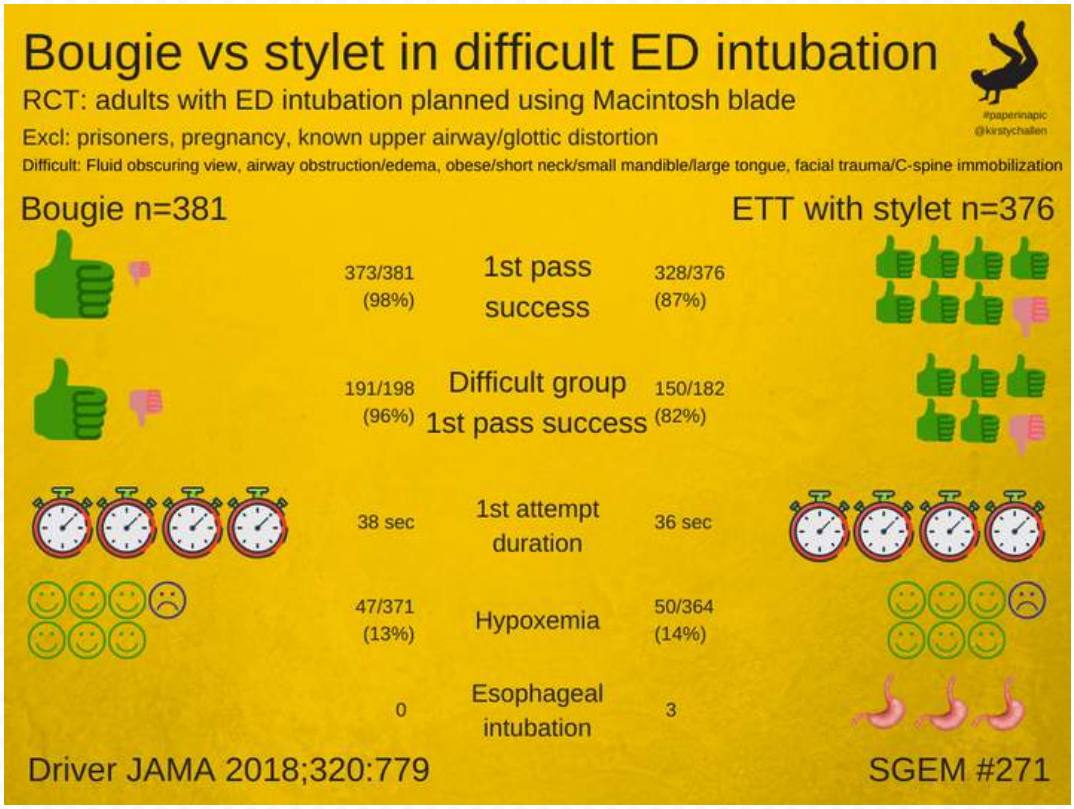
Case Resolution: You decide to use the bougie on your first attempt for this patient in hope you will get the tube on your first attempt. You make sure your team is ready with the ETT. You visualize a grade 2 view and slip the coude' tip under the epiglottis and through the cords. You feel the rumble strips as you advance to the hold up at the carina. The respiratory therapist slides the tube over the bougie, and you advance it to the proper depth. You have equal lung sounds on both sides and confirmation with wave form capnography.

Episode End Notes

Other FOAMed:

- REBEL EM: Bougie Use in Emergency Airway Management
- EMCrit: Bougie and Positioning





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TAKE THE MONEY AND RUN WITHOUT GETTING A CT

Clinical Question:

Do financial incentives, together with potential risk and potential benefit information, influence patient preference for diagnostic testing?

Bottom Line:

The potential risk, the potential benefit, and money can influence people's behavior in making healthcare decisions.

Guest:

Dr. Justin Morgenstern is an emergency physician and the creator of the excellent #FOAMed project called First10EM.com

Case Overview

Case: A 21-year-old comes into the emergency department after being knocked unconscious while playing rugby. The patient is now feeling great, or as they say in New Zealand "sweet as". He had no pain, nausea, or neurologic symptoms. His exam is normal. You aren't worried, but his dad is the coach of the American national rugby team and says that his players always get a CT when this happens. You wonder what factors might influence a patient's preference for imaging?

Background: The CT scan is arguably one of the most important pieces of diagnostic technology that we use in emergency medicine. It allows for incredibly rapid identification of a myriad of life-threatening conditions.

However, likely because it is such a valuable tool, there seems to be little doubt that we overuse it. For example, one study that looked retrospectively at all head CTs ordered for trauma concluded that more than 1/3 were unnecessary based on the Canadian CT head rule [1].

Not only does unnecessary testing reduce efficiency and add costs, it also directly harms patients with unnecessary radiation [2]. Many imaging decisions are obvious – the patient either clearly requires or clearly does not require imaging.

One way to decrease CT scans of the head is to use a clinical decision instrument like the Canadian CT Head Rule (CCHR). The SGEM covered the classic paper on the CCHR by the Legend of Emergency Medicine Dr. Ian Stiell on SGEM#106.

We also recently reviewed a paper that looked at increasing the CCHR age criteria from 65 years of age to 75 years of age (SGEM#266). The bottom line

was that this paper opens the door for further research to try to narrow the criteria in the CCHR to further reduce unnecessary head CT imaging in the emergency department. However, further, high quality prospective studies are required prior to clinical application.

There is a great deal of uncertainty in emergency medicine, which leaves a sizeable number of patients in a grey zone – where harms and benefits are closely matched, qualitatively different, or just unknown. For these patients, shared decision making is probably the best route forward.

Even when it seems clear to the physician that imaging isn't required, we can be met with resistance from our patients. In addition, if we are working in a zero-miss culture, we may be more likely to order CT scans that are not medically necessary. Thus, it is important to know what factors influence patients' decision to undergo CT.

This study by Iyengar and colleagues examines the impacts of financial incentives, as well as varying levels of risk and benefit, on patient preference for CT imaging in the setting of low risk head injury [3].

Reference: Iyengar R et al. The Effect of Financial Incentives on Patient Decisions to Undergo Low-value Head Computed Tomography Scans. AEM October 2019.

Population: A convenience sample of adult patients presenting to the University of Michigan emergency department.

Exclusions: Patients with chest pain or head trauma (because those were the conditions in the hypothetical cases presented). They also excluded patients with altered mental status, with contact precautions, or in resuscitation bays.

Intervention and Comparison: Patients were all presented with a hypothetical low risk head trauma scenario. The scenario was designed such that the Canadian Head CT rule suggests against imaging. Three aspects of the scenario were randomized:

- Benefit: This was presented as either 1% or 0.1%
- Risk: This was presented as either 1% or 0.1%
- Incentive: Patients were offered either $100 to forgo the CT, or $0.
    - All risk and benefit information were provided in multiple formats, include percentages (0.1%), ratios (1 in 1,000), and in visual depictions.

Outcome:

- **Primary Outcome:** The percentage of patients that chose to receive a CT scan.
- **Secondary Outcomes:** They performed multiple regressions to control for potential confounders.

Authors' Conclusions

"Providing financial incentives to forego testing significantly decreased patient preference for testing, even when accounting for test benefit and risk. This work is preliminary, hypothetical, and requires confirmation in larger patient cohorts facing these actual decisions."

Quality Checklist for Randomized Control Trials

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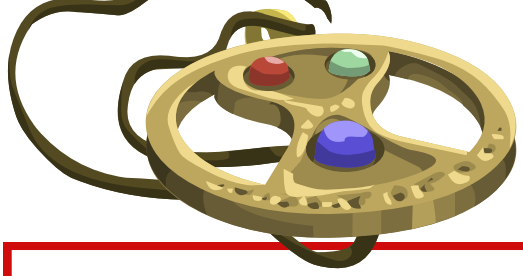
- ☑ 8. All groups were treated equally except for the intervention.
- ☑ 9. Follow-up was complete (i.e. at least 80% for both groups).
- ☑ 10. All (team) patient-important outcomes were considered.
- ☑ 11. The treatment effect was large enough and precise enough to be clinically significant.

Case Outcomes

Key Results:
They enrolled 913 patients, with a median age of 45 years of age and 56% of the population was female. The vast majority of this population identified as Caucasian and had attended at least some college. Overall, 54.2% of patients elected to receive a CT scan.

- **Primary Outcome:** The percentage of patients that chose to receive a CT scan.
  - If the benefit was reported as 0.1% then 49.6% of people wanted a CT, whereas if it was 1% then 58.9% wanted a CT. (OR 1.48 95% CI 1.13 – 1.92)
  - If the risk was reported as 0.1% then 59.3% of people wanted a CT, whereas if it was 1% then 49.1% wanted a CT. (OR 0.66 95% CI 0.51-0.86)
  - If no cash incentive was offered then 60% of people wanted a CT, whereas if 100$ was offered to forgo the CT then 48.3% of people wanted a CT. (OR 0.64 95% CI 0.49-0.83)

- **Secondary Outcomes:** The results remained consistent when adjusted for various potential confounders including age, gender, race, income, level of education, and prior history of health problems.



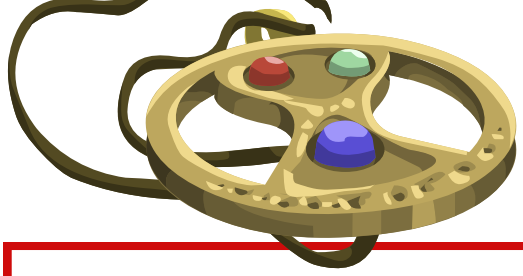
Time to Talk Nerdy

This is an SGEMHOP episode which means we have one of the authors on the show. Dr. William Meurer is an emergency physician. His focus is on the treatment of acute neurological emergencies, both as a researcher and clinician. He has been part of the University of Michigan Acute Stroke Team since 2006. In addition, Dr. Meurer has experience enrolling patients in acute trials and has served as a local PI for the CLEAR-ER trial (a trial enrolling acute stroke patients in the ED that tested a reperfusion strategy). He is on the executive team of the Strategies to Innovate EmeRgENcy Care Clinical Trials Network (SIREN). Dr. Meurer has other active or recently completed NIH funded clinical trials involving acute vertigo in the emergency department, hypertension, and therapeutic hypothermia after cardiac arrest.
Jessica Winkels

Jessica Winkels is the second author on this AEM publication and also joins us on the podcast. She is a fourth-year medical student at the University of Michigan. Jessica is planning on going into emergency medicine after she graduates in the spring. Publishing in AEM should certainly help with her application.

1. Sample Size: Your sample size was based on the feasibility of medical students being able to complete a summer research project. This would give an approximate power of 85% to 90% to detect a 10% absolute change in the proportion of subjects desiring testing from a baseline test acceptance rate of 50%. Do you think that a 10% difference reflects a real clinically important difference?

2. Statistics: You performed a series of nested regression analyses for your primary statistical analysis. I'll be honest, we got a little lost in the math. In our relatively simple mind, there were only a couple variables, with a simple yes or no answer regarding CT. It seems like presenting the raw numbers would



Time to Talk Nerdy

have been easier to understand than the odds ratios that you ended up using. Can you explain your choice of statistics to me?

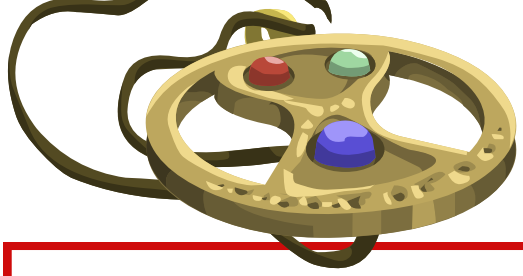
3. External Validity: The vast majority of this population was highly educated and white. There was also a very high percentage (24%) that worked in healthcare. How might that affect the external validity of the results?

4. External Validity 2: We was incredibly surprised than half of these patients wanted a CT. In Canada and New Zealand, a CT would not even have been offered to these patients (given that they passed the Canadian CT head rule). We often explain why a CT isn't needed, and the vast majority are fine with that. We definitely haven't experienced 50% of my patients asking for a CT. We therefore wonder how these results might apply in other countries.

5. Hypothetical Numbers: You chose to use hypothetical risks and benefits, rather than using known benefit and harm data. The hypothetical numbers could make these results less applicable in real clinical settings. You discuss it briefly in the paper, but could you explain the choice to use 1% and 0.1% and your numbers?

6. Real World Shared Decision Making: As you mention in the discussion, unlike the exact risk and benefit numbers you present here, it is often incredibly difficult to determine the exact risk and benefit of a test for the patient in front of you. Personally, we think that is the hardest part of this job. How do you think that uncertainty in real world practice would impact these results?

7. Health Inequities: This really isn't a nerdy question you can answer from your data, but we wonder whether offering cash incentives could result in inequities for our patients. It seems like the $100 incentive is more likely to be enticing to someone making minimum wage than someone earning a six-figure salary. Do we want healthcare to be distributed base on something other than the benefits and harms of the intervention itself?



Time to Talk Nerdy

8. Thought Experiment or Practical Plan: We wonder whether you see this as just a thought experiment at this point, or are you thinking that people should actually institute some kind of cash incentive to reduce CT use? Where would the $100 come from? I imagine getting a patient out of the hospital earlier, and freeing up their stretcher, might actually generate more than the $100 needed to incentivize them not having the scan. Have you thought about the overall economics of this model?

9. Health Literacy: We think you did a very good job explaining the risk in multiple ways – including both numbers and images. However, one number really jumped out at me. In the group with a 0.1% benefit and a 1% harm, 50% of people still wanted a CT scan. We had explicitly told patient that their chance of harm was 10x their chance of benefit, and they still wanted to be scanned. We think that number needs attention. Does it mean that your participants really didn't understand the numbers you were giving them? Is it

just a representation of the harms and benefits being qualitatively different (the benefit is immediate whereas the harm is delayed)? Or is there something else going on, because we find that number shocking.

10. Anything Else: Is there anything else you would like the SGEMers to know about your study?

Comment on Authors' Conclusion Compared to SGEM Conclusion: We agree with the authors conclusions as it applies to this patient population but are not sure about its external validity to other healthcare systems. It certainly is interesting and does require confirmation in other populations.

Clinical Application: I don't think I will be offering my patients financial incentives as part of medical decision making any time soon. However, I use shared decision making every shift. For this patient, a patient that passes the CCHR, I wouldn't actually perform shared decision making, because I think the decision is clear. A CT isn't needed.
But if the choice was unclear, I would perform shared decision making, presenting the risks and benefits in multiple formats, like the authors did here.

What Do I Tell the Patient? I am not sure if you need a CT scan at this point.I think chance that we are missing an important injury is about 1%. A CT would catch that injury, but it exposes you to radiation, and so your risk might be 0.1%. Another option would be to stay in the ED for a couple more hours so I can keep an eye on you and perform some repeat neurologic testing.

Case Resolution: You explain to the patient that he is very low risk for a serious head injury based on the CCHR. After discussing the risks of CT and the negligible chance of benefit, the patient (and his dad) are happy to observe his symptoms and only get a CT if he gets worse.

Episode End Notes

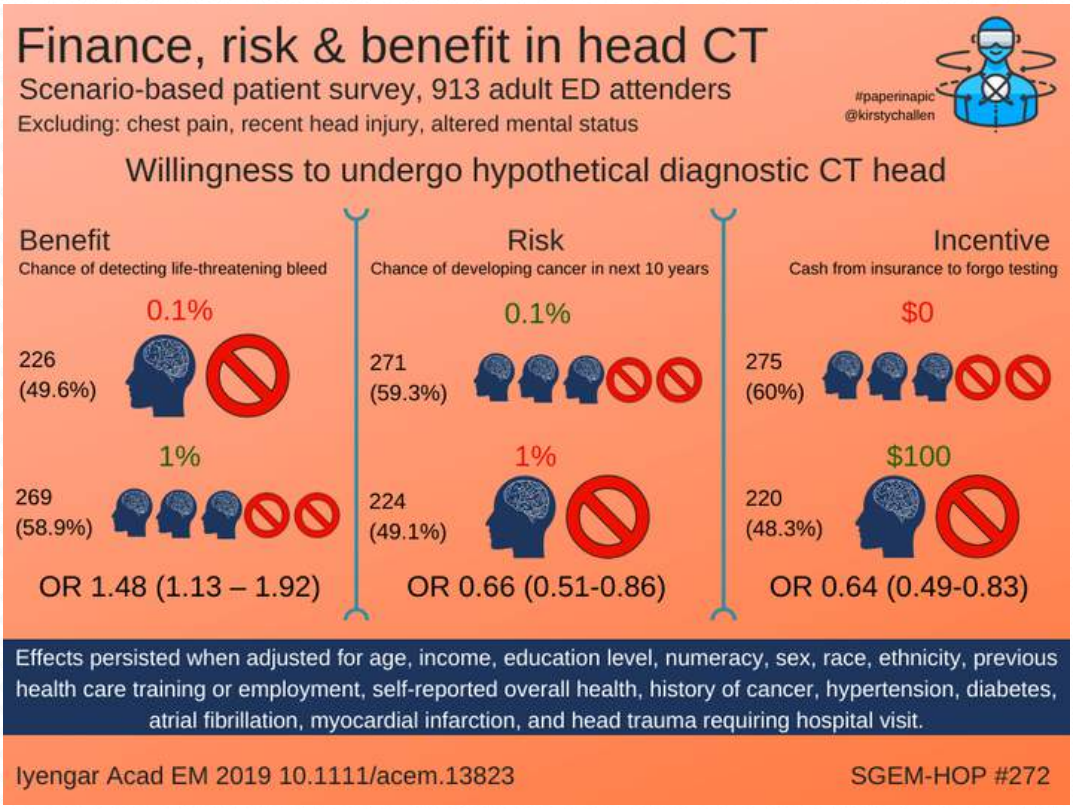
Should we be offering $$$ to patients not to get a CT scan of their head that is not clinically indicated based on the CCHR to decrease inappropriate CT utilization? onlinelibrary.wiley.com/doi/abs/10.111... #SGEMHOP @SAEMonline @AcademicEmerMed @AliRaja_MD @First10EM @ACEPNow @CAEP_Docs

Yes 16%

No 84%

69 votes · Final results

9:08 AM · Oct 29, 2019 · Twitter Web App



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MY BUDDY (TAPE) FOR BOXER'S FRACTURES

Clinical Question:

Is buddy taping an uncomplicated boxer's fracture just as effective as a plaster cast?

Bottom Line:

Consider offering patients with uncomplicated boxer's fractures buddy taping.

Guest:

Martha Roberts is a critical and emergency care, triple certified nurse practitioner, currently living and working in western Massachusetts. She is the host of EM BOOTCAMP in Las Vegas, as well as a usual speaker and faculty member for The Center for Continuing Medical Education (CCME). She writes a blog called The Procedural Pause for Emergency Medicine News and is the lead content editor and director for the videos series soon to be included in Roberts & Hedges Clinical Procedures in Emergency Medicine. Martha also serves as an adjunct professor for both Georgetown University and Marymount University in the Washington D.C. area.

Case Overview

Case: A 26-year-old right-handed male presents to the emergency department on Friday night with a swollen right hand after punching a wall.The x-ray confirms an uncomplicated boxer's fracture. You explain to him the traditional management which includes adequate pain control, immobilization with a cast and referral to a hand surgeon. He does not want any opioids because a friend was addicted to oxycocet. He is fine with going to see a hand surgeon in clinic, but asks if he really needs a cast. He is concerned that it will interfere with going to work on Monday morning.

Background: Boxer's fractures are common hand injuries. They are usually due to punching a solid object with a closed fist. For clarity, in this SGEM episode: when we say boxer's fracture, we are referring to a fracture of the neck of the fifth metacarpal.

There has been some controversy on the best way to manage an uncomplicated boxer's fracture. This is typically defined as a minimally displaced closed fracture with angulation up to 70 degrees.

Poolman et al (Cochrane 2005) did a SRMA and pooled together five studies with a total of only 252 patients. Most of the studies were of poor quality and functional outcome was not used in any of the studies. Because of the lack of good evidence, no treatment modality could be recommended over another.

Another systematic review meta-analysis was done by Dunn et al (Orthopedics 2016). They found that cast immobilization is not superior to soft wrap without reduction in most cases.

No study had investigated whether or not buddy taping would be superior to casting for functional outcomes in patients with boxer's fractures.

Reference: Pellatt et al. Is Buddy Taping as Effective as Plaster Immobilization for Adults With an Uncomplicated Neck of Fifth Metacarpal Fracture? A Randomized Controlled Trial. Annals of EM 2019

Population: Adults (18-70 years of age) with uncomplicated fractures of the fifth metacarpal neck (boxer's fracture).

- Uncomplicated Fractures: These were defined as fractures confirmed by radiograph with at least two views showing a closed fracture (NOT comminuted, NOT intra-articular) with fracture angulation less than 70 degrees, less than one week old, did not have tendon involvement and with no polytrauma or other significant injury.

Intervention: Buddy taping of the ring finger and little finger.

Exclusions: Patients less than 18 years of age or older than 70 years. Fractures that were open, gross rotational deformity, comminuted intra-articular, associated with polytrauma or other significant injuries. Patients were also excluded if the fracture angulation was greater than 70 decrease and the injury was older than one week.

Comparison: Cast immobilization in an ulnar gutter cast applied in a position of safety.

Outcome:

- **Primary Outcome:** Hand function at 12 weeks using the QuickDASH.
  - QuickDASH is a validated tool to evaluate a patient's ability to perform certain upper limb activities. DASH stands for Disabilities of the Arm, Shoulder and Hand. The original questionnaire has 30 items while the QuickDASH has only 11. The patient reports their functional ability on a 5-point Likert scale. The patient's overall disability is rated between 0 and 100. The higher the score, the greater the disability. The minimal detectable change (MDC) is 11% while the minimal clinical important difference (MCID) is 8%.

- **Secondary Outcomes:** Pain, satisfaction, return to work, return to sports, and quality of life.

Authors' Conclusions

"We found that patients with boxer's fractures who were randomized to buddy taping had functional outcomes similar to those of patients randomized to plaster cast at 12 weeks. We advocate a minimal intervention such as buddy taping for uncomplicated boxer's fractures."

Quality Checklist for Randomized Control Trials

- ✓ 1. The study population included or focused on those in the emergency department.
- ✓ 2. The teams were adequately randomized.
- ✓ 3. The randomization process was concealed.
- ✓ 4. The teams were analyzed in the groups to which they were randomized.
- ? 5. The study teams were recruited consecutively (i.e. no selection bias).
- ✓ 6. The teams in both groups were similar with respect to prognostic factors.
- ✗ 7. All participants (patients, clinicians, outcome assessors) were unaware of group allocation.
- ✓ 8. All groups were treated equally except for the intervention.
- ✗ 9. Follow-up was complete (i.e. at least 80% for both groups).
- ✓ 10. All (team) patient-important outcomes were considered.
- ? 11. The treatment effect was large enough and precise enough to be clinically significant.

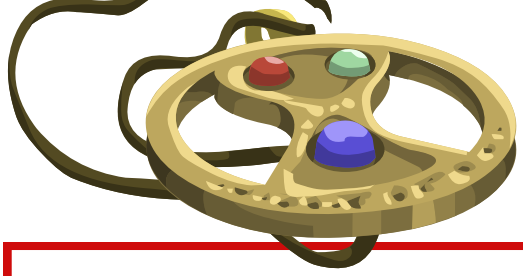
Case Outcomes

Key Results:
They assessed 506 patients for eligibility with 126 randomized. The mean age was in the mid-twenties, 85% were male and 90% were right hand dominant.

No statistical difference in the QuickKDASH score between buddy tape and plaster casting.

- **Primary Outcome:** Median QuickDASH score at 12 weeks
  - 0 buddy tape vs. 0 plaster cast (95% CI; 0 to 0)

- **Secondary Outcomes:**
  - **Pain –** Both groups reported absence of pain at 12 weeks
  - **Satisfaction –** Both groups reported high satisfaction scores with treatment
  - **Return to Work –** Buddy tape patients missed no days of work while those in a cast missed a median of two days of work
  - **Return to Sports –** No difference between the two groups
  - **Quality of Life –** No difference between the two groups



Time to Talk Nerdy

1. Selection Bias: There is a possibility of selection bias. There were 41 eligible patients who were not recruited and 34 who declined to participate. The patients who were missed were because the emergency department was too busy and there were other clinical priorities. The demographics of the missed patients were similar to the included patients suggesting that selection bias would be unlikely.

2. Loss to Follow-Up: One quality indicator is whether or not there were more than 20% of patients lost to follow-up. They reported 21% of patients being lost to follow-up (18% in the buddy tape group and 23% in the plaster cast group). This threatens the validity of the conclusions.

3. Non-Inferiority Trial: This was designed as a superiority trial. The real question could have been: is buddy taping non-inferior (not worse) that casting. A smaller sample size would be needed to demonstrate non-inferiority. This should help with nerdy point #5 about replication.

4. QuickDASH: We had some questions and concerns about the QuickDASH assessment tool. It's reliability is 0.9 and its validity is 0.7. This could have an impact of the precision of the results.

5. Replication: This study would need to be replicated in other healthcare systems for external validity. The patient population is probably the same, but their expectations may be different. What impact would this have on emergency department length of stay and cost. Would local specialists agree with such a change in management?

Comment on Authors' Conclusion Compared to SGEM Conclusion:
We agree that they demonstrated buddy taping had similar functional outcomes to plaster casting in patients with a boxer's fracture. However, we would not advocate for buddy taping uncomplicated boxer's fractures at this time based on one RCT.

Clinical Application: This small trial provides some evidence that buddy taping uncomplicated 5th metacarpal fractures is reasonable. It is not enough to change my routine practice of putting patients in an ulnar gutter. The orthopedic surgeon or plastic surgeon can decide how to manage these patients once they see them in clinic. If the patient requests not having a cast, I will bring up the buddy taping idea. We think this type of treatment needs to be validated and confirmed before offering this routinely to patients.

What Do I Tell the Patient? There is another option besides casting. One small study of less than 100 patients done in Australia put half the people in casts and half of them had their 4th and 5th finger buddy taped together. Both groups had the same functional outcome at three months. The study needs to be confirmed here and our hand surgeons need to be on board. The traditional way is still to cast these broken bones. Let me know If you really want to try buddy taping.

Case Resolution: You inform him there is another treatment option called buddy taping and in form him of the limitations of the evidence. He decides to try buddy taping instead of a plaster cast.

Episode End Notes

What do you do usually for uncomplicated boxer's fractures? thesgem.com/2019/11/sgem27... @proceduralpause @CAEP_Docs @ACEPNow @ketaminh @Rick_Pescatore @KirstyChallen @AliRaja_MD @AnnalsofEM @MDaware @HeatherM211 @emergmedottawa @meganranney @srrezaie @EMSwami @TChanMD @BEEMcme

Cast/splint	**71%**
Buddy tape	29%

94 votes · Final results

Buddy taping for boxer's fracture

#paperinapic @kirstychallen

Adults 18-70yo patients with uncomplicated fractures of 5th metacarpal neck

Excl: open, gross rotational deformity/>70 degree angulation, comminuted/intra-articular, tendon injury, >1 week old, polytrauma or other significant injuries.

Buddy taping n=48		Ulnar gutter cast n=49
Median 0-100 IQR 0-2.3	Quick-DASH at 12 weeks	Median 0-100 IQR 0-4
Median 0/10 IQR 0-0	Pain	Median 0/10 IQR 0-1
Median 9/10 IQR 8-10	Satisfaction	Median 9/10 IQR 8-10
Median 0 IQR 0-7	Missed work days	Median 2 IQR 0-14

Pellatt Ann EM 2019;74:88

SGEM #273

274

HOCUS POCUS FOR APPENDICITIS?

Clinical Question:

What are the diagnostic performance of point of care ultrasonography (EP-POCUS) for diagnosing acute appendicitis?

Bottom Line:

EP-POCUS has the potential to diagnose acute appendicitis especially in pediatric populations and appears to be better at ruling in rather than ruling out

Guest:

Chip Lange is an Emergency Medicine Physician Assistant (PA) working primarily in rural Missouri in community hospitals. He also hosts a great #FOAMed blog and podcast called TOTAL EM. Chip is the CEO of an ultrasound education company called Practical POCUS which is based in the United States but is expanding into an international market.

Case Overview

Case: A 6-year-old boy comes into your emergency department at around midnight with his parents complaining of abdominal pain. His mother reports that the symptoms began a couple of days ago and he did not eat today. Now, the patient has been vomiting for the last couple of hours. Initially, he would point to the periumbilical area, but his father says that now he points to the right lower portion of the abdomen as his area of pain. You do not have an ultrasound tech available at night and you are thinking of using your point of care ultrasound (POCUS) skills to look for a possible appendicitis, but you are unsure how accurate this test would be especially compared to other modalities such as radiology performed ultrasound.

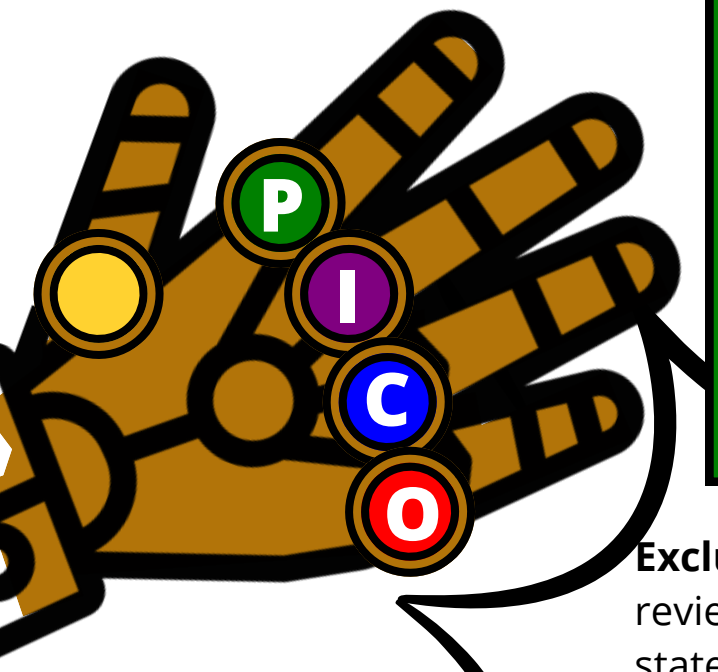
Background: We have reviewed papers on POCUS many times over the years on the SGEM. This has included performing lumbar punctures, diagnosing acute abdominal aneurysms, acute heart failure, pediatric fractures, retinal detachments and endotracheal tube placement.

- SGEM#41: Ultra Spinal Tap (Ultrasound Guided Lumbar Puncture)
- SGEM#94: You Better Think Ultrasound for Acute Abdominal Aneurysm
- SGEM#97: Hippy Hippy Shake – Ultrasound Vs. CT Scan for Diagnosing Renal Colic
- SGEM#119: B-Lines (Diagnosing Acute Heart Failure with Ultrasound)
- SGEM#124: Ultrasound for Skull Fractures – Little Bones
- SGEM#153: Simulation for Ultrasound Education
- SGEM#177: POCUS –A New Sensation for Diagnosing Pediatric Fractures
- SGEM#245: Flash-errrs (POCUS for Retinal Detachments)
- SGEM#249: Ace in the Hole –Confirming Endotracheal Tube Placement with POCUS

Ultrasound, especially in the pediatric population, has been a common form of imaging for the diagnosis of appendicitis. It avoids the concerns for radiation and contrast that is seen with CT. MRI is not practical in many situations, especially in rural or remote environments.

However, ultrasound does have its limitations especially in obese patients or those unable to comply with the exam for reasons such as pain.

Reference: Lee and Yun. Diagnostic Performance of Emergency Physician-Performed Point-of-Care Ultrasonography for Acute Appendicitis: A Meta-Analysis. AJEM 2019.



Population: Patients in original research articles with right-lower quadrant (RLQ) abdominal pain with EP-POCUS being performed as the index test and the use of surgical or pathological findings as the reference standard for acute appendicitis. There had to be sufficient information to reconstruct a 2×2 contingency table regarding sensitivity and specificity.

Intervention: EP-POCUS for diagnosing acute appendicitis.

Exclusions: Case reports, case series, review articles, guidelines, consensus statements letters, editorials, clinical trial, and conference abstracts. Additionally, studies that did not pertain to the field of interest, insufficient data to create the 2×2 tables, POCUS was not performed by emergency physicians (EPs), and studies that only used the radiologists' final report.

Comparison: Radiologist-performed ultrasonography (RADUS)

Outcome:

- **Primary Outcome:** Diagnostic parameters of EP-POCUS for acute appendicitis (sensitivity, specificity and likelihood ratios).
- **Secondary Outcomes:** Subgroup analysis of pediatric patients comparing EP-POCUS to radiologist-performed ultrasonography (RADUS).

Authors' Conclusions

"The diagnostic performances of EP-POCUS and radiologist-performed ultrasonography (RADUS) were excellent for AA, with EP-POCUS having even better performance for pediatric AA. Accurate diagnoses may be achieved when the attending EP is the initial POCUS operator and uses a 7mm cut-off value."

Quality Checklist for Systematic Review Diagnostic Studies

- ✓ 1. The diagnostic question is clinically relevant with an established criterion standard.
- ✗ 2. The search for studies was detailed and exhaustive.
- ✓ 3. The methodological quality of primary studies were assessed for common forms of diagnostic research bias.
- ✓ 4. The assessment of studies were reproducible
- ✗ 5. There was low heterogeneity for estimates of sensitivity or specificity.
- ? 6. The summary diagnostic accuracy is sufficiently precise to improve upon existing clinical decision-making models.

Case Outcomes

Key Results:
Their search identified 17 studies involving 2,385 patients. The mean age ranged from 6 to 37 years of age and the mean proportion of male patients were 26% to 61%.

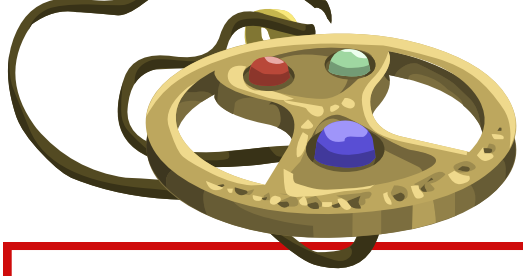
EP-POCUS exhibited a pooled sensitivity fo 84% and a pooled specificity of 91%, with a positive likelihood ratio of 7.0 and a negative likelihood ratio of 0.22 for diagnosing acute appendicitis.

There was better diagnostic performance for pediatric acute appendicitis with a sensitivity of 95% (95% CI: 75%-99%) and specificity of 95% (95% CI: 85%-98%).

A direct comparison revealed no statistical differences (p=0.18-0.85) between the diagnostic performances of EP-POCUS (sensitivity: 81%, 95% CI: 61%-90%; specificity: 89%, 95% CI: 77%-95%) and RADUS (sensitivity: 74%, 95% CI: 65%-81%; specificity: 97%, 95% CI: 93%-98%).

The meta-regression analyses revealed that study location, acute appendicitis proportion, and mean age were sources of heterogeneity. Higher sensitivity and specificity tended to be associated with an appendix diameter cut-off value of 7 mm and the EP as the initial operator.

	Sens. (95%CI)	Spec. (95%CI)	LR+ (95%CI)	LR- (95%CI)
EP-POCUS	0.81 (0.61–0.90)	0.89 (0.77–0.95)	7.0 (3.2–15.3)	0.22 (0.12–0.42)
RADUS	0.74 (0.65–0.81)	0.97 (0.93–0.98)	21.6 (10.4–44.7)	0.27 (0.20–0.36)



Time to Talk Nerdy

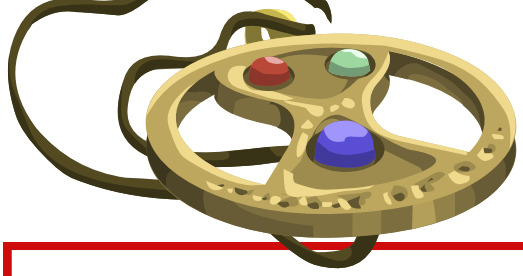
1. Wide Range of Cut-Offs: There was a wide range of cut-offs for appendicitis including the diameter and the concurrent findings. This has helped attribute to the heterogeneity of the studies. We care about this primarily because it makes it more difficult to see if certain parameters are most beneficial for diagnostic cut-offs. However, from this particular data set, the 7mm cut-off for appendiceal diameter seems to be better than the 6mm cut-off used in other studies.

2. Heterogeneity: There was large heterogeneity as reported by the I2 metric. It was 94% for sensitivity and 89% for specificity. This will affect pooled estimates and we see this all with the wide confidence intervals that were present. It is reasonable to question whether or not these studies should have been meta-analysed given the large heterogeneity. We should be skeptical of these results, especially given the data used.

3. Likelihood Ratios: We like to see LR+ greater than 10 to rule in a diagnosis and LR- less than 0.1 to rule out a diagnosis. Only the RADUS had a LR+ of >10. Neither RADUS nor EP-POCUS had a LR- of less than 0.1.

4. Clinicians: Like most studies regarding POCUS, this used resident and attending physicians in academic centers and does not speak to the abilities of other types of clinicians (such as PAs and NPs or those in rural or remote environments). It would be fantastic to see future studies that addressed these issues specifically to see how much of an impact there is with these groups of clinicians.

5. Pediatric Patients: The evidence for EP-POCUS is strongest for pediatric examinations. This may primarily be related to body habitus. The larger the patient, the harder it is to visualize abdominal organs, especially the



Time to Talk Nerdy

appendix. Also, in small pediatric patients the high-frequency linear probe is frequently used which provides even more detailed visualization of the appendix compared to the more classically use lower-frequency curvilinear or phased array probes.

Comment on Authors' Conclusion Compared to SGEM Conclusion:
We think that the diagnostic accuracy of EP-POCUS is good but not excellent for diagnosing acute appendicitis. It is better in pediatric populations and that the use of a 7mm cut-off appears to be more accurate.

Clinical Application: POCUS continues to play an important role in emergency medicine and is being embraced more over time. We should consider using ultrasound for a variety of conditions including for the diagnosis of appendicitis. Given the issues of operator experience, study heterogeneity and wide confidence intervals we do not think EP-POCUS should be the sole criteria in diagnosing acute appendicitis.

What Do I Tell the Parents? I would tell the parents and patient that we are going to use a special machine that uses sound waves to look into his abdomen to see if his appendix, a small tube in his stomach that can become sick and be causing his symptoms. It is a good test, but it is far from a perfect test. If I see a swollen appendix with the ultrasound machine your son probably has appendicitis. If I do not see his appendix, we probably will need to do more testing.

Case Resolution: With consent from the parents and patient, you are able to use your bedside ultrasound and find an 8mm non-compressible and aperistaltic appendix. You call the pediatric general surgeon who takes the patient to the OR for further management including appendectomy.

Episode End Notes

EBM, KT and Rural EM @TheSGEM · Nov 12

Are you using POCUS to diagnose acute appendicitis?

thesgem.com/2019/11/sgem27... #FOAMed #ebm

@proceduralpause @the_TOTAL_EM @CAEP_Docs @ACEPNow @ultrasoundpod @PracticalPOCUS @ButterflyNetInc @Rick_Pescatore @AliRaja_MD

Yes	27%
No	**73%**

97 votes · Final results

EP ultrasound for appendicitis: review

17 diagnostic accuracy studies, 2385 patients with RLQ pain

Excl: case series, non-EP POCUS, radiologist findings as gold standard

#paperinapic
@kirstychallen

Sensitivity	Specificity		LR +	LR -
84% (72-92%)	91% (85-95%)	Overall	7.0 3.2-15.3	0.22 0.12-0.42
95% (75-99%)	95% (85-98%)	Pediatrics 7 studies		
81% (61-90%)	89% (77-95%)	Direct comparison: EP 5 studies	7.0 3.2-15.3	0.22 0.12-0.42
74% (65-81%)	97% (93-98%)	Direct comparison: radiology	21.6 10.4-44.7	0.27 0.2-0.36

Significant heterogeneity — Q=100.575: related to study location, proportion with appendicitis and age

Lee Am J EM 2019;37:696

LR+: positive likelihood radio LR-: negative likelihood ratio

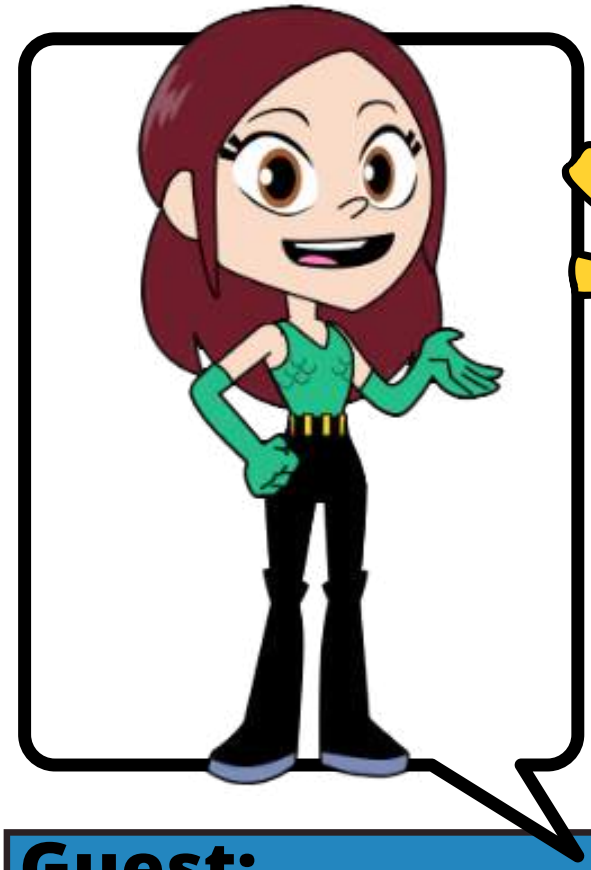
SGEM #274

275

10TH AVENUE FREEZE OUT - THERAPEUTIC HYPOTHERMIA AFTER NON-SHOCKABLE CARDIAC ARREST

Clinical Question:

Does therapeutic hypothermia improve survivla with good neurologic outcome in patients who achieve ROSC after non-shockable cardiac arrest?



Bottom Line:

We do not have good evidence to routinely recommend TTM in patients with non-shockable cardiac arrests.

Guest:

Dr. Laura Melville (@lmelville535) is an emergency physician in Brooklyn, New York, is a part of the New York ACEP Research Committee, ALL NYC EM, and is the NYP-Brooklyn Methodist Resident Research Director.

Case Overview

Case: A 59-year-old woman comes is brought into your emergency department (ED) by EMS in cardiac arrest. She had a witnessed arrest, and CPR was initiated by bystanders. Her initial rhythm in the field was reported as pulseless electrical activity (PEA) by EMS. The patient achieved return of spontaneous circulation (ROSC) on arrival to the ED. You call your hyperthermia team to initiate targeted temperature management (TTM), which in your hospital means 33C for 24 hours followed by slow rewarming for 24 hours. Your senior resident asks you "should we really be cooling our patient to 33C, doesn't the data suggest 36C is just as good? And if she was not in a shockable rhythm at arrest, will she be likely to benefit from this treatment?" The patient's family has separately mentioned they heard she might have a better chance of being "normal" if she gets cooled down. What do you say? Do you continue with the ICE Code? What do you tell the patient's family?

Background: We have covered therapeutic hypothermia many times on the SGEM. This has been or out-of-hospital cardiac arrests (OHCA). Therapeutic hypothermia has not been demonstrated to have benefit in the pre-hospital setting (SGEM#54 and SGEM#183).

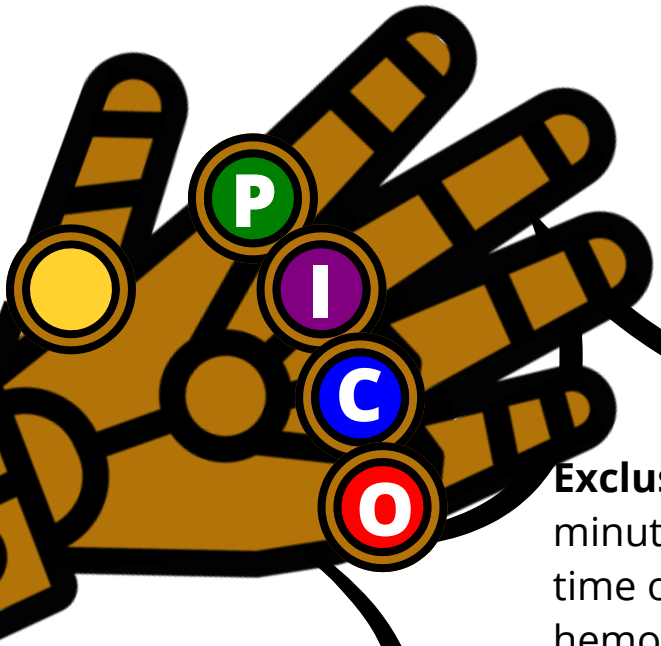
But two earlier randomized controlled trials (Hypothermia after Cardiac Arrest Study Group 2002 and Bernard et al 2002) showed benefit for good neurologic outcome when TTM was initiated in the hospital after ROSC was achieved. In those studies, the temperature goal was 32C-34C and 33C respectively.

The SGEM covered the targeted temperature management (TTM) trial published in the NEJM. It showed cooling patients to 33C was not superior to 36C for the primary outcome (SGEM#82).

The most recent time we have looked at therapeutic hypothermia was SGEM#199. This was a trial looking to see if there was a neuroprotective effect of hypothermia in patients with status epilepticus. Unfortunately, that study failed to demonstrate a benefit of therapeutic hypothermia for adult patients admitted to the ICU with convulsive status epilepticus.

It seems like TTM is a good example of an intervention that “makes sense” but doesn’t always work. There are many examples like this in the literature where something makes sense from a pathophysiologic standpoint but is not demonstrated to work when properly tested.

Reference: Lascarrou et al. Targeted Temperature Management for Cardiac Arrest with Nonshockable Rhythm. NEJM Oct 2019



Population: Adults (18 years and older) with OHCA or IHCA of any cause, with non-shockable rhythm and a Glasgow Coma Scale (GCS) score of 8 or lower.

Exclusions: No flow time of more than 10 minutes (collapse to starting CPR), low-flow time of more than 60 minutes, major hemodynamic instability (continuous vasopressor infusion), time from cardiac arrest to screening >300 minutes, moribund condition, severe hepatic dysfunction, pregnant or breast-feeding, prisoner, lack of health insurance and decide not to participate (by next of kin)..

Intervention: Targeted temperature management to 33C (+/- 0.5C) was started post arrest and then maintained for 24hrs. Cooling protocol was determined by each of the 25 participating sites. Slow rewarming of 0.25-0.5C/hr to target of 36.5-37.5C, which was maintained for 24hrs.

Comparison: Targeted normo-therapy to 36.5-37.5C for 48 hours

Outcome:

- **Primary Outcome:** Survival to good neurologic outcome at 90 days as defined by Cerebral Performance Category (CPC) scale score of 1 or 2.

- **Secondary Outcomes:** clinicaltrials.gov listed 20 outcomes (NCT01994772). The methods section only mentioned six (mortality, mechanical ventilation, length of stay in the ICU and hospital, infection and hematologic adverse events).

Authors' Conclusions

"Among patients with coma who had been resuscitated from cardiac arrest with nonshockable rhythm, moderate therapeutic hypothermia at 33C for 24 hours led to a higher percentage of patients who survived with a favorable neurologic outcome at day 90 than was observed with targeted normothermia."

Quality Checklist for Randomized Control Trials

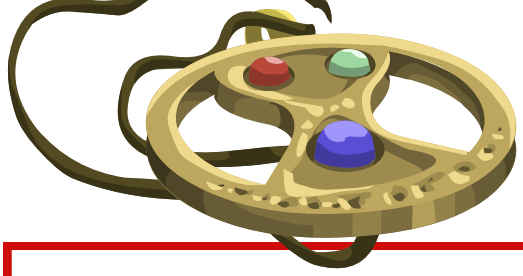
- [x] 1. The study population included or focused on those in the emergency department.
- [x] 2. The teams were adequately randomized.
- [x] 3. The randomization process was concealed.
- [x] 4. The teams were analyzed in the groups to which they were randomized.
- [x] 5. The study teams were recruited consecutively (i.e. no selection bias).
- [x] 6. The teams in both groups were similar with respect to prognostic factors.
- [x] 7. All participants (patients, clinicians, outcome assessors) were unaware of group allocation.
- [x] 8. All groups were treated equally except for the intervention.
- [x] 9. Follow-up was complete (i.e. at least 80% for both groups).
- [x] 10. All (team) patient-important outcomes were considered.
- [x] 11. The treatment effect was large enough and precise enough to be clinically significant.

Case Outcomes

Key Results:
The screened 2,723 patients for eligibility and 584 underwent randomizations. The median age was 67 years, two-thirds were male, and three-quarters were OHCAs.

- **Primary Outcome:** Survival to discharge with good neurological outcome as measured by a CPC score of 1 or 2 was statistically better in the TTM group compared to the Usual Care group.
  - 10.2% TTM vs. 5.7% Usual Care (absolute difference 4.5%), p=0.047 which gives an NNT of 22
  - Hazard ratio 4.5 (95% CI; 0.1 to 8.9) and a fragility index of 1

- **Secondary Outcomes:** There was no statistical differences in any of the secondary outcomes
  - Mortality at 90 days 81.3% TTM vs. 83.2% Usual Care (95% CI; −8.0 to 4.4).
  - No statistical difference was reported for mechanical ventilation, length of stay in the ICU and hospital, infection and hematologic adverse events.



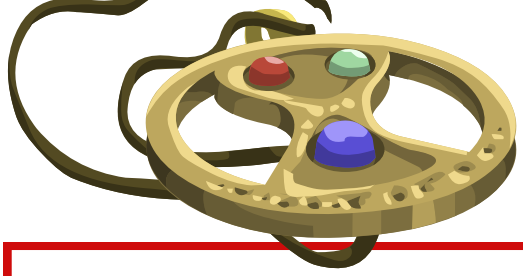
Time to Talk Nerdy

1) Statistics: They based their sample size calculation on the assumption that there would be survival with good neurologic function in 23% of the TTM and 14% of the usual care. This would mean they expected a 9% absolute difference. The actual result was only 10.2% for TTM and 5.7% in usual care (4.5% absolute difference). This often happens in research. My EBM mentor Dr. Andrew Worster who taught me also told me if you want to make an outcome rare all you need to do is study that outcome. Here they thought they would have a higher prevalence of the primary outcome and yet in this population it was less than half.

Besides basing their sample size on this expected outcome, they also fell a few patients short of their target. The goal was to get 584 participants but three withdrew consent so left them with 581. Again, because their outcome of interest occurred less often than anticipated, and the difference between the two groups was half what was expected, the study was underpowered.

2) P-Values and Fragility Index: We have discussed the problem with being dichotomous about p-values and the utility of the fragility index. They did report a statistical difference between the two groups for the primary outcome, but the p value was 0.047. That does not mean therapeutic hypothermia works or does not work but rather needs to be interpreted as the probability of false rejecting the null hypothesis and making a type I error.

The fragility index is linked mathematically to the p-value and is another way of representing the data. In this study the fragility index was 1. This means that changing the outcome of one participant would have made the results statistically non-significant on a subjective outcome measure susceptible to bias due to lack of blinding and reliability of the CPC score.



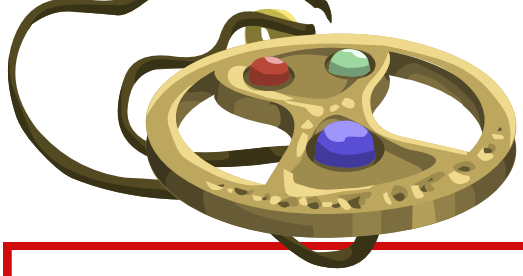
Time to Talk Nerdy

3) Lack of Blinding: This is a huge limitation of this study. While the unconscious patients and the outcome assessor were blinded to group allocation, the clinicians were not blinded. This introduces bias that would probably be directed towards treatment. The hypothesis was that TTM would provide a patient-oriented benefit (superior to usual care). Patients could have consciously or unconsciously been treated differently by the clinicians. These potential subtle differences in management could be responsible for the fragile statistical difference demonstrated.

4) Temperature Management: The true duration of temp control seemed at first like both groups were exposed to temperature management for the same amount of time (48 hours). However, temperature management was performed between 8-16 hours longer in the 33C group, due to additional time required for re-warming.

In addition, a number of patients had their body temperatures rise above 38C, in particular after the period of TTM. This could have impacted the results and suggests the target should have been 36C for the usual care to prevent hyperthermia.

5) Outcome Assessment: This builds on nerdy point #3. The outcome was done by a single psychologist. They were blinded to the group allocation, but the patient was not. They were being questioned on their neurologic function and could have known if they were or were not in the treatment group thought to be superior. The CPC is a subjective assessment not objective and was done over the telephone. There would be a bias for the patient to say they were better if allocated to the TTM group.



Time to Talk Nerdy

In addition, the inter-rater reliability of the CPC score in post-arrest cases is known to be poor. One study from Grossestreuer et al (Resuscitation 2016) demonstrated disagreement between assessors more than 1 in 5 times (22%) giving a kappa of only 0.66. If another psychologist conducted the assessments, it is very likely they would not have assigned the same CPC score for the survivors. This nerdy point comes from our #FOAMed friend Dr. Josh Farkas from PulmCrit.

Comment on Authors' Conclusion Compared to SGEM Conclusion:
We would say that limited data suggests that patients with OHCA/IHCA with a non-shockable rhythm had a statistically higher chance of a good neurologic outcome with TTM.

Clinical Application: These results are too fragile to change practice. However, most institutions are applying their ICE protocols to all OCHA/IHCA patients that achieve ROSC and meet inclusion/exclusion criteria without regard to initial rhythm. The major take-away from this is that 37C may be a poor choice of target as it seems to allow for fever to develop. Otherwise we cannot say if TTM to 33C or 36C will improve outcomes for patient likelihood of survival with good neurological outcome at 90 days.

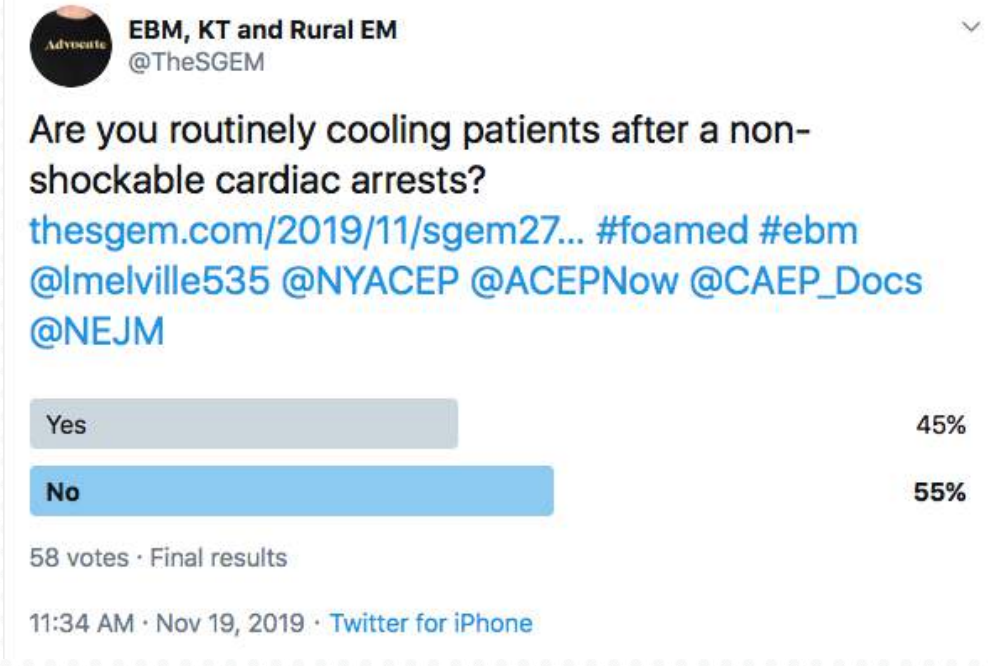
What Do I Tell the Patient? You tell the patient's family that their loved one has experienced a cardiac arrest, but that her heart is now beating on its own. You explain she has been put into a targeted temperature control protocol, and that her prognosis is grave. Right now, there is no clear data to help us know if her initial rhythm will have any influence on how she will do, but the fact that she got bystander CPR could be very helpful.

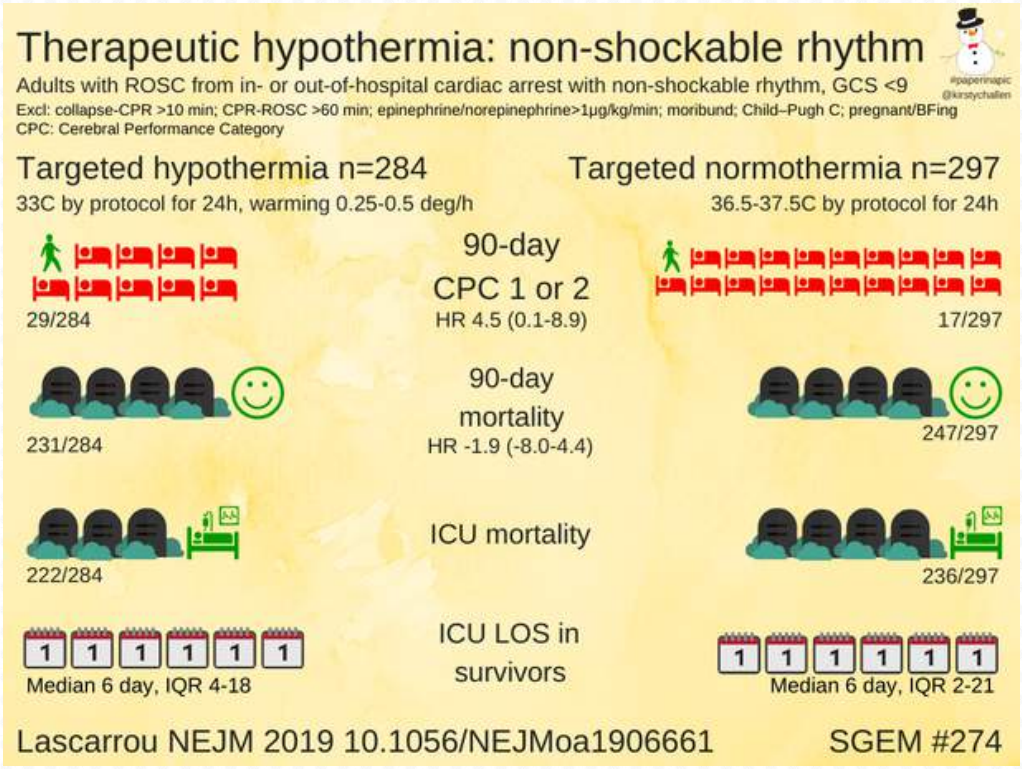
Case Resolution: You initiate your ICE protocol based on your current guidelines, not influenced by the patient's initial rhythm.

Episode End Notes

Other FOAMed:

- PulmCrit – HYPERION
- REBEL EM





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FOCUS ON PE IN PATIENTS WITH ABNORMAL VITAL SIGNS

Clinical Question:

In patients presenting to the ED with suspected PE, who have abnormal vital signs, what is the sensitivity of FOCUS for PE?

Bottom Line:

Focused cardiac ultrasound does not have good enough diagnostic accuracy even in patients with abnormal vital signs to safely rule in or out PE.

Guest:

Dr. Corey Heitz is an emergency physician in Roanoke, Virginia. He is also the CME editor for Academic Emergency Medicine.

Case Overview

Case: You are caring for a 45-year-old male patient in the emergency department with pleuritic chest pain. You suspect he has a pulmonary embolism (PE), and the CT scanner is currently being used up by a multi-patient multiple-trauma pan-scan which promises to take hours. Your patient has a heart rate of 105 bpm and a systolic blood pressure of 95 mmHg. You pull the department's ultrasound machine to the bedside and prepare to do a focused cardiac ultrasound to decide if you want to treat for a PE while waiting for the scanner to free up.

Background: We have covered the issue of PE many times on the SGEM. This has included outpatient management (SGEM#51 and SGEM#126), catheter directed thrombolysis (SGEM#163) and even discussed the PERC rule with its creator, Dr. Jeff Kline (SGEM#219).

We may have covered it so often because PE is commonly suspected in patients presenting the ED with chest pain, shortness of breath, or other symptoms. The current gold standard test is a CT angiogram of the pulmonary arteries (CTA), but this test cannot be performed immediately in some patients due to renal function, availability of the equipment, or contrast allergies.

There are concerns about doing CTAs in pregnant patients due to the radiation exposure to both the mother and fetus. We have a show coming up soon looking at a pregnancy adapted YEARS criteria to help minimize the number of CTAs ordered in this patient population.

In addition, patients with hemodynamic instability may not be appropriate to take out of the resuscitation bay. Focused cardiac ultrasound (FOCUS) can show

findings of right ventricular strain caused by a PE, but in all patients suspected of PE, it is relatively insensitive. However, it has been suggested that in patients with hemodynamic instability, the sensitivity may be higher.

Reference: Daley et al. Increased Sensitivity of Focused Cardiac Ultrasound for Pulmonary Embolism in Emergency Department Patients With Abnormal Vital Signs. AEM November 2019

Population: Adult patients (>17 years old) undergoing evaluation for PE who are tachycardic (HR >100bpm) and/or hypotensive (systolic BP <90mmHg)

Exclusions: Prisoners, wards of the state, non–English-speaking patients, and those where investigators could not obtain any ECHO data due to technical challenges.

Intervention: Focused cardiac ultrasound (FOCUS)

Comparison: CT angiography of the pulmonary arteries

Outcome:

- **Primary Outcome:** Sensitivity of FOCUS for PE patient with a HR ≥ 100 beats/min or sBP < 90 mm Hg (n = 136) and those with a HR ≥ 110 beats/min (n = 98).
- **Secondary Outcomes:** Specificity and likelihood ratios of FOCUS for PE in each population.

Authors' Conclusions

"A negative FOCUS exam may significantly lower the likelihood of the diagnosis of PE in most patients who are suspected of PE and have abnormal vital signs. This was especially true in those patients with a HR ≥ 110 BPM. Our results suggest that FOCUS can be an important tool in the initial evaluation of ED patients with suspected PE and abnormal vital signs."

Quality Checklist for Observational Study

1. Did the study address a clearly focused issue?
2. Did the authors use an appropriate method to answer their question?
3. Was the cohort recruited in an acceptable way?
4. Was the exposure accurately measured to minimize bias?
5. Was the outcome accurately measured to minimize bias?
6. Have the authors identified all-important confounding factors?
7. Was the follow up of subjects complete enough?
8. How precise are the results? Fairly precise given the small sample size
9. Do you believe the results?
10. Can the results be applied to the local population?
11. Do the results of this study fit with other available evidence?

Case Outcomes

Key Results:
They screened 143 patients who underwent CTA with 136 subjects enrolled in the study. The mean age was in the mid-50's, 59% were female, 23% had a previous VTE, 40% had cancer in the previous 6 months and 15% had signs or symptoms of a DVT.

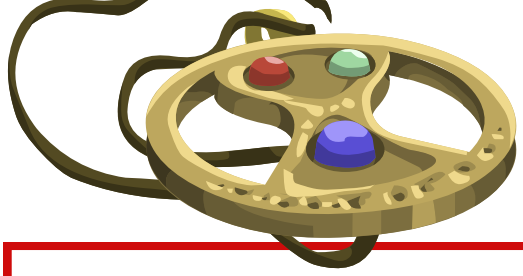
- **Primary Outcome:**
  - Sensitivity of FOCUS for PE in all patient with a HR ≥ 100 beats/min or sBP < 90 mm Hg was 92% (95%CI; 78% to – 98%)
  - Sensitivity of FOCUS for PE in patients with a HR ≥ 110 beats/min (n = 98) was 100% (95%CI; 88% to 100%)

- **Secondary Outcomes:** There was substantial interobserver agreement for FOCUS (kappa = 1.0, 95% CI = 0.31 to 1.0) when they were only required to call it positive or negative.

Table 2
Diagnostic Test Characteristics of FOCUS and Its Components for PE in Subjects With a HR ≥ 100 beats/min and/or sBP < 90 mm Hg (*n* = 136)

	Sensitivity, % (95% CI)	Specificity, % (95% CI)	Positive Likelihood Ratio (95% CI)	Negative Likelihood Ratio (95% CI)
FOCUS	92 (78–98)	64 (53–73)	2.5 (1.9–3.3)	0.13 (0.04–0.38)
TAPSE threshold (cm)				
2.0	88 (72–97)	73 (63–82)	3.3 (2.3–4.7)	0.17 (0.07–0.42)
1.7	66 (48–82)	85 (76–91)	4.5 (2.6–7.6)	0.39 (0.24–0.64)
RVE	51 (34–68)	86 (77–92)	3.6 (2.0–6.3)	0.57 (0.40–0.80)
Septal flattening*	43 (27–61)	93 (86–97)	5.9 (2.7–13.2)	0.61 (0.46–0.82)
TR	50 (26–74)	75 (62–86)	2.0 (1.1–3.8)	0.67 (0.41–1.08)
McConnell's sign†	35 (20–53)	99 (94–100)	33.7 (4.6–249)	0.66 (0.52–0.83)

FOCUS = focused cardiac ultrasound; HR = heart rate; PE = pulmonary embolism; RVE = right ventricular enlargement (appearance of right ventricle as being equal to or larger than the left ventricle); TAPSE = tricuspid annular plane systolic excursion; TR = tricuspid regurgitation (any regurgitant jet visualized on color Doppler).
*Abnormal flattening of the interventricular septum during systole.
†Visualization of hypokinesis of the right ventricle with apical sparing.



Time to Talk Nerdy

1. Convenience Sample: This was a convenience sample. We always like to see consecutive patients recruited but understand the reality of research. Do you think this could have impacted the results in any meaningful way?

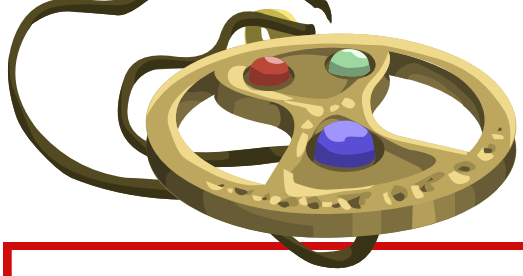
2. Spectrum Bias: Sensitivity depends on the spectrum of disease, while specificity depends on the spectrum of non-disease. Because they looked at sicker patients (tachycardic and hypotensive) this could falsely raise the sensitivity of FOCUS. Did you consider doing a multivariable model which could have told us what the association of these vital signs with PE are and not have had to prespecify arbitrary cut points?

3. Blinding: The clinicians obtaining the images (staff, residents and medical students) were not blinded to the hypothesis. There are some subjective aspects to FOCUS when obtaining images. In addition, investigators we unblinded to the results in two cases because the patient were getting a heparin infusion when FOCUS was performed. These things could have biased the operators and made the diagnostic parameters look better than if they did not know the purpose of the study or that the patients had a PE.

4. Primary Outcome: You have what seems to be two primary outcomes, meaning the sensitivity in two patient groups. Can you explain the decision not to define one as the primary and the other as a secondary?

5.Missing Data: How researchers handle missing data is important. There were times when data was missing. Can you explain how that could impact your results?

6. Precision: There were fairly wide 95% confidence intervals around the point estimates for the primary outcome. The lower limits of your sensitivity calculations in patients with HR >100 or BP <90 mmHg are in the 70s. How does this affect your recommendation for using FOCUS to evaluate for PE in these patients?



Time to Talk Nerdy

7. Sensitivity and Specificity: While these statistics provide additional information using likelihood ratios can be more helpful to clinicians. We like to see LR+ more than 10 to confidently rule in a condition and LR- less than 0.1 to rule out a condition. FOCUS did not demonstrate robust enough diagnostic accuracy to help make clinical decisions.

8. Inter-Rater Reliability: Your study had seven ultrasound trained attendings, three EM residents and three medical students. All had different degrees of experience. The inter-rater reliability for FOCUS being positive or negative by two separate sonographers was substantial with a kappa statistic of 1.0 (95% CI = 0.31 to 1.0). How did the attendings compare to the residents and medical students?

9. Resource Poor Facilities: You hypothesized in the discussion that FOCUS could play a role in rural locations that lack access to CTA. I have worked my entire career in locations without a CT scanner. Those locations without a CT do not have a high volume of patients presenting with a suspected PE. Would this not make it difficult to maintain FOCUS skills and lower the diagnostic accuracy of this test?

10. Anything Else: Any other thoughts or comments you think the SGEM audience needs to know about your study? Have you considered a head to head comparison of FOCUS vs. CT for PE?

Comment on Authors' Conclusion Compared to SGEM Conclusion: We generally agree with the authors' conclusions especially since they used the word "may" which can also mean "may not".

Clinical Application: In patients with abnormal vital signs, bedside FOCUS may help guide empiric therapy in patients with suspected PE but cannot make a definitive diagnosis to rule in or out a PE.

What Do I Tell the Patient? The ultrasound I just performed tells me that you likely do not have a pulmonary embolism, and I think it's too risky to provide anticoagulation at this time. Once the CTA results are back, we can decide on definitive therapy.

Case Resolution: Your FOCUS exam on your patient shows an essentially normal RV. You delay anticoagulation therapy at this time, choosing to await the CTA results.

We face this all the time with patients needing to be transported to another facility for the CTA. This typically takes about three hours. It is my routine not to anticoagulated prior to transportation.

Episode End Notes

Do you use FOCUS to help diagnose PE? onlinelibrary.wiley.com/doi/full/10.11... #SGEMHOP @SAEMonline @AcademicEmerMed @CHeitzMD

Yes	33%
No	**34%**
What's FOCUS	33%

64 votes · Final results

Focused Cardiac Ultrasound for Pulmonary Embolism ED patients with abnormal vitals

#paperinapic
@kirstychallen
Josh Lupton

Prospective observational multicenter cohort study, 136 patients

Adults ≥ 18y with heart rate ≥ 100 bpm and/or systolic blood pressure <90 mmHg undergoing CTA for possible PE
Exclusions: Prisoners, state wards, non-English speaking,US images not be obtained due to technical issues

HR ≥ 100 bpm and/or SBP <90

Sensitivity analysis: HR ≥ 110 bpm n=98

FOCUS:
RV dilation
McConnell's sign
Septal flattening
Tricuspid regurgitation
TAPSE

70 +ve FOCUS	66 -ve FOCUS	51 +ve FOCUS	47 -ve FOCUS
36 -ve CTPA	34 +ve CTPA	63 -ve CTPA	3 +ve CTPA	27 -ve CTPA	24 +ve CTPA	47 -ve CTPA	0 +ve CTPA

Sens: 92% (78-98) | Spec: 64% (53-73)
+ LR: 2.5 (1.9-3.3) | -LR: 0.13 (0.04-0.38)

Sens: 100% (88-100) | Spec: 63% (51-74)
+ LR: 2.7 (2.0-3.7)

Daley doi 10.1111/acem.13774

Sens: sensitivity Spec: specificity LR: Likelihood ratio

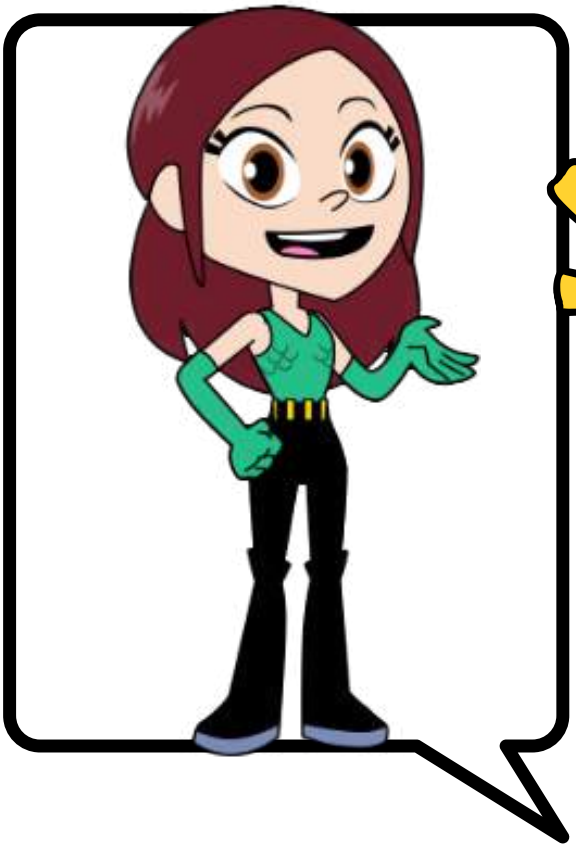
SGEM-HOP #276

277

IN THE PREGNANT YEARS - DIAGNOSING PULMONARY EMBOLISM

Clinical Question:

Can the YEARS algorithm, which utilizes the D-dimer test, be used in pregnant women to rule out the diagnosis of pulmonary embolism?



Bottom Line:

The pregnancy-adapted YEARS algorithm has the potential to safely rule out PE and decrease CTPA studies but requires external validation.

Guest:

Dr. Theresa Robertson-Chenier is currently an Emergency Physician practicing at the Peterborough Regional Health Centre. She is also an adjunct faculty member with Queen's University, Department of Family Medicine.

Case Overview

Case: A 32-year-old female, G1P0, who is 22 weeks pregnant, presents to your local emergency department with the chief complaint of shortness of breath. She states that for the last one week she has had progressive shortness of breath on exertion. She denies any chest pain, fever, cough or leg swelling. She has no history of venous thromboembolic (VTE) disease like deep vein thrombosis (DVT) or pulmonary embolism (PE). But recently she drove seven hours from London, Ontario to Montreal, Quebec. She is worried about the possibility of a PE. She is otherwise healthy, takes only prenatal vitamins and has no allergies. She is terrified about any radiation exposure in pregnancy and has read on google that there is a blood test you can order to rule out PE.

Background: We have covered VTE a number of times on the SGEM. This has even included a few of episodes with the PE guru and PERC rule creator Dr. Jeff Kline. However, we have never looked at the YEARS criteria study published by Van der Hulle T et al (The Lancet 2017).

- SGEM#51: Home (Discharging Patients with Acute Pulmonary Emboli Home from the Emergency Department)
- SGEM#126: Take me to the Rivaroxaban – Outpatient treatment of VTE
- SGEM#163: Shuffle off to Buffalo to Talk Thrombolysis for Acute Pulmonary Embolism
- SGEM#219:Shout, Shout, PERC Rule Them Out

The YEARS algorithm starts with the clinician suspecting an acute PE. Then they order a D-dimer and apply the YEARS clinical decision instrument. It has three items with each getting one point:

1. Clinical signs of DVT
2. Hemoptysis
3. PE most likely diagnosis

If there are zero YEARS items and the d-dimer is <1,000ng/ml then a PE is excluded. If there are zero YEARS items but the d-dimer is equal to or greater than 1,000ng/ml then a CT pulmonary angiography (CTPA) scan is needed to rule out a PE.

If there are one or more YEARS items and the d-dimer is <500ng/ml then a PE is excluded. If there are one or more YEARS items but the d-dimer is equal to or greater than 500ng/ml then a CTPA scan is needed to rule out a PE.

While this publication was interesting, it was a prospective observational study from the Netherlands. There was a study by Kabrhel et al (AEM 2018) that was done in 17 hospitals in the USA. They compared usual care for possible PE vs. YEARS criteria. They enrolled 1,789 patients and 84 (4%) had a PE. Using standard d-dimer criteria, 53% would not have been imaged (2 misses). YEARS avoided imaging in 67%, but had 6 misses. Standard care had a sensitivity 97.6% vs, 92.9% for YEARS. It would be better if there was a randomized control trial comparing usual care to YEARS. In addition, the case you presented was of a pregnant woman. In the original YEARS study from 2017 it said pregnancy was an exclusion.

Clinically, it can be difficult to diagnosis PE in pregnancy because of the overlap of symptoms due to the physiological changes in pregnancy (tachycardia, shortness of breath and leg swelling) with the signs and symptoms of PE. The incidence of PE is reported to be 1.72 cases per 1,000 deliveries, and it accounts for approximately one death in every 100,000 deliveries.

In addition, the diagnostic tests used to diagnosis PE come with their own risks to mom and fetus. The radiation dose to the maternal breast can be potentially carcinogenic owing to the radiosensitive nature of the glandular breast during pregnancy. A CTPA study can increase the risk of breast cancer by 1.5% in a 25-year-old woman (see reference on last page).

Reference: van der Pol et al. Pregnancy-Adapted YEARS Algorithm forDiagnosis of Suspected Pulmonary Embolism. NEJM 2019

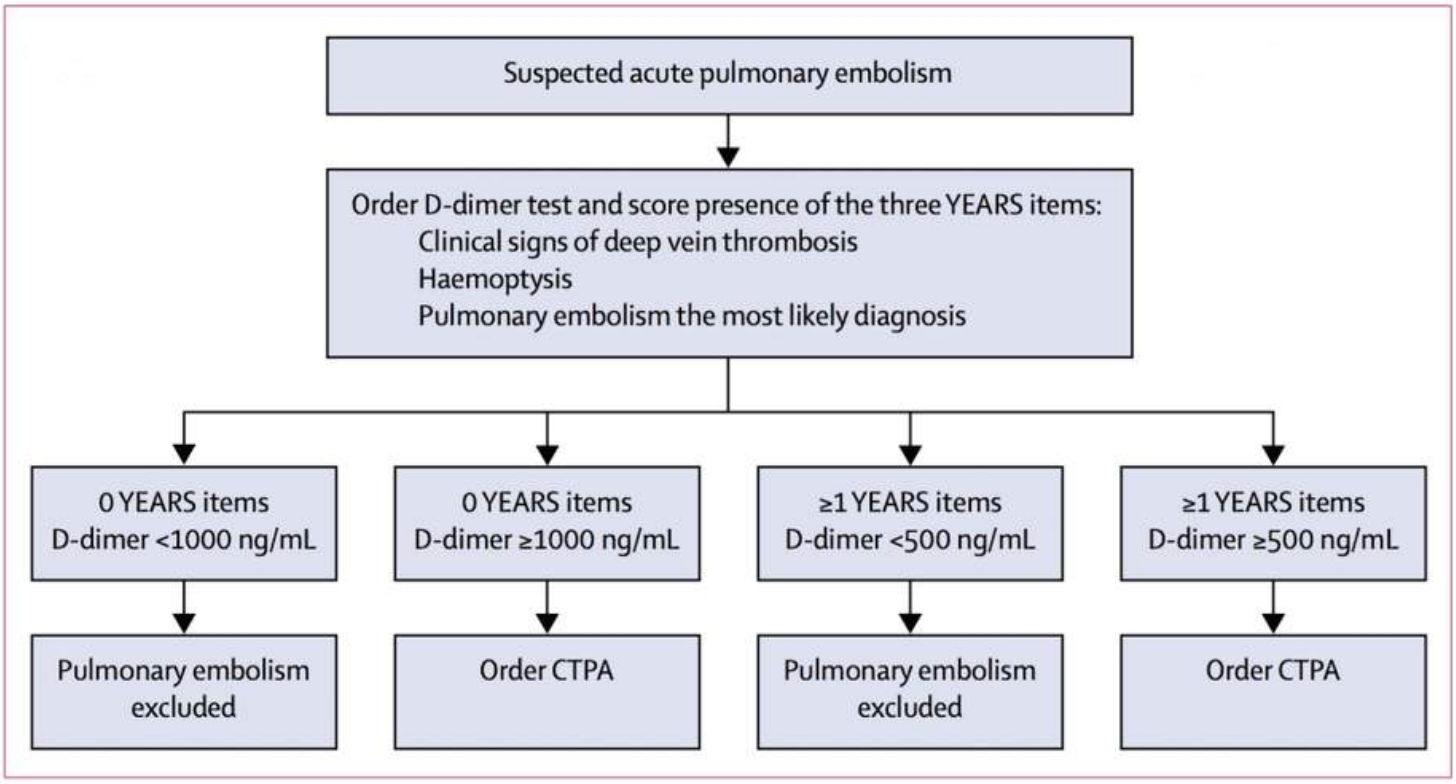


Figure 1: **YEARS algorithm**
CTPA=computed tomography pulmonary angiography.

Population: Pregnant women, 18 years of age and older, with clinically suspected PE (defined as new onset or worsening dyspnea, +/- hemoptysis or tachycardia) referred to the ED or the obstetrical ward.

Intervention: Application of the pregnancy-adapted YEARS algorithm to rule out PE in pregnant women.

Exclusions: Treatment with a full-dose therapeutic anticoagulant agent, can't follow-up, allergy to the contrast dye, or a life expectancy of less than three.

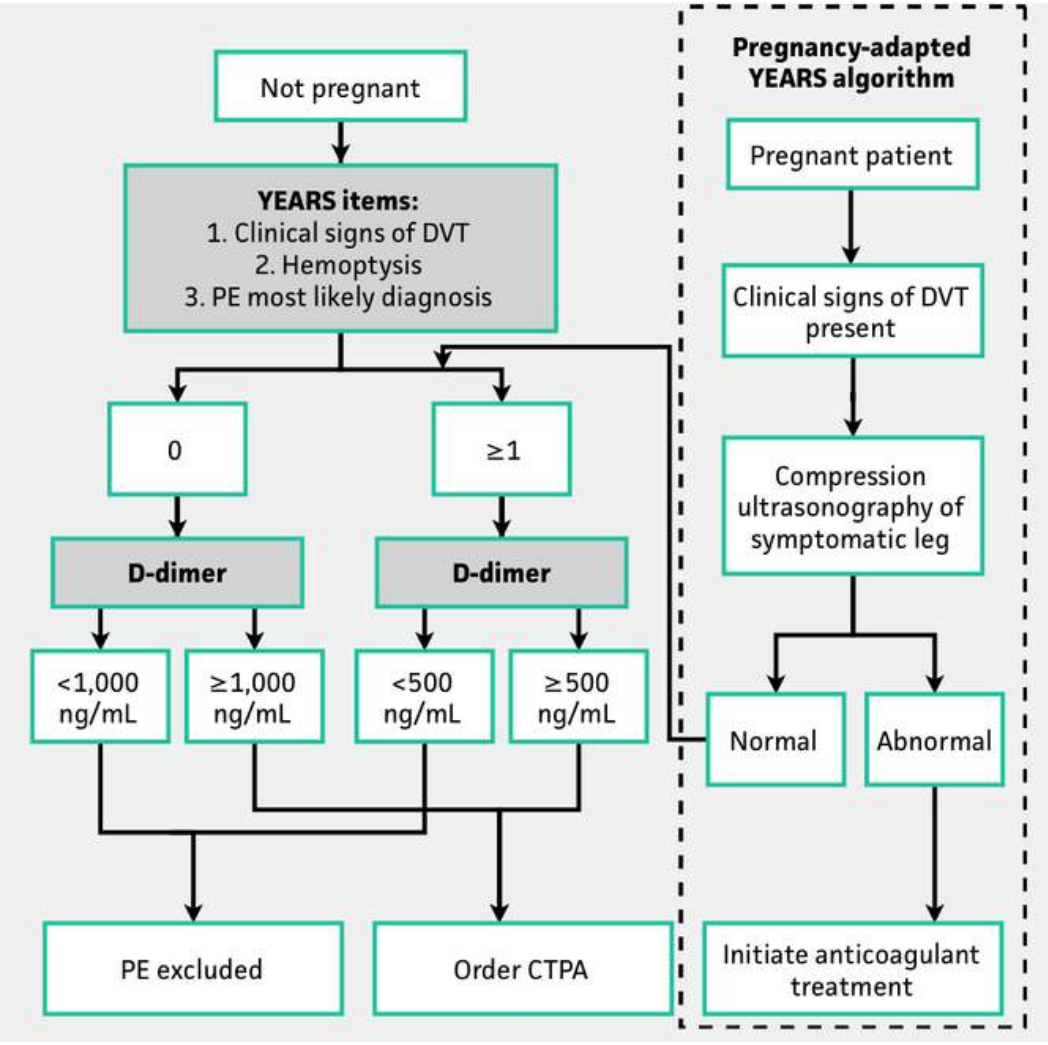
Comparison: Not using pregnancy-adapted YEARS (Hypothetical situation in which all patients undergo CTA or VQ scan)

Outcome:

- **Primary Outcome:** The cumulative incidence of symptomatic VTE, with confirmation by objective tests, during a 3-month follow-up period in the subgroup that anticoagulation treatment was withheld.

- **Secondary Outcomes:** Proportion of patients in whom CTPA was not indicated.

The pregnancy-adapted YEARS algorithm is the same as the YEARS algorithm but if the pregnant patient has signs of a DVT you get an ultrasound of the leg. If it shows a DVT you treat for VTE. If it does not show a DVT then you enter the regular YEARS algorithm.



Authors' Conclusions

"Pulmonary embolism was safely ruled out by the pregnancy-adapted YEARS diagnostic algorithm across all trimesters of pregnancy. CT pulmonary angiography was avoided in 32 to 65% of patients".

Quality Checklist for Clinical Decision Tools

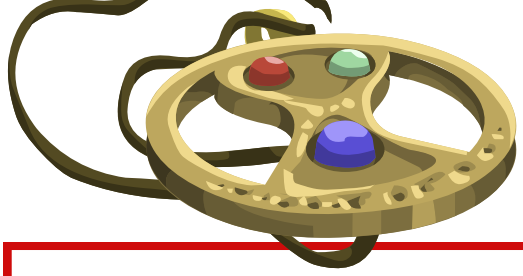
- [?] 1. The study population included or focused on those in the ED.
- [✓] 2. The patients were representative of those with the problem.
- [✓] 3. All important predictor variables and outcomes were explicitly specified.
- [✓] 4. This is a prospective, multicenter study including a broad spectrum of patients and clinicians (level II).
- [✗] 5. Clinicians interpret individual predictor variables and score the clinical decision rule reliably and accurately.
- [✗] 6. This is an impact analysis of a previously validated CDR (level I).
- [✗] 7. For Level I studies, impact on clinician behavior and patient-centric outcomes is reported.
- [✓] 8. The follow-up was sufficiently long and complete.
- [?] 9. The effect was large enough and precise enough to be clinically significant.

Case Outcomes

Key Results:
They recruited 498 consecutive pregnant women with clinically suspected PE into the study. The mean age was 30 years and almost half (46%) were in their third trimester. Half of the patients had no YEARS criteria and half had at least one of the three criteria (19% signs of DVT, 8% hemoptysis and 89% PEs were the most likely diagnosis).

- **Primary Outcome:** VTE at three months in the subgroup anticoagulation was withheld.
  - 477/498 (96%) VTE was ruled out at baseline
  - Only 1 DVT (0.21%)was identified during follow-up (95% CI; -0.04 to 1.2)

- **Secondary Outcomes:** Proportion of patients in whom CTPA was not indicated
  - 195 patients were ruled out based on the adapted YEARS algorithm
  - 12 (6.2%) patients had a CTPA even though not indicated (protocol violation). All 12 were negative for PE.
  - CTPA could safely be avoided in 39% of the patients (95% CI 35-44)



Time to Talk Nerdy

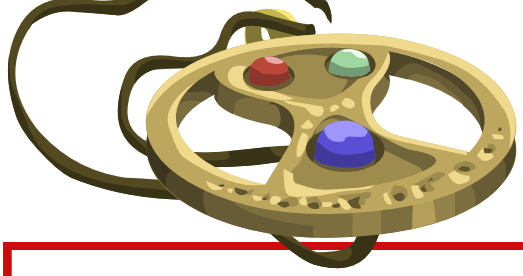
1. Incorporation Bias: This can occur when results of the test under study are actually used to make the final diagnosis. In this study the authors acknowledge that the physician may have been aware of the d-dimer results when assessing the YEARS criteria. This can make the test (diagnostic algorithm) appear more powerful by falsely raising the sensitivity and specificity.

2. Partial Verification Bias (Referral Bias or Work-Up Bias): This can happen when only a certain set of patients who underwent the index test is verified by the reference standard. In YEARS, only those with a positive d-dimer (>1,000 or >500 depending on zero or 1+ criteria) got the definitive test. This could increase sensitivity but decreases specificity.

3. Differential Verification Bias (Double Gold Standard): This is very similar to partial verification bias and could be part of incorporation bias. Differential verification bias can occur when the test results influence the choice of the reference standard. So, a positive index test gets an immediate/gold standard test (CTPA in this case) whereas the patients with a negative index test get clinical follow-up for disease. This can raise or lower sensitivity and specificity.

4. Subjectivity: One of the weaknesses of this study is that it includes the subjective part of the Well's criteria as part of the YEARS criteria. The part where the clinician needs to use clinical gestalt and decide if a PE is the most likely diagnosis.

5. Spectrum Bias: You made me think of one more potential bias, spectrum bias. Sensitivity depends on the spectrum of disease, while specificity depends on the spectrum of non-disease. So, you could falsely raise the specificity if the YEARS algorithm is used as a screening test. Just because a pregnant patient has some vague chest pain or shortness of breath does not



Time to Talk Nerdy

get them into the algorithm. The clinician had to have a clear suspicion of PE. The best paper on these biases was Understanding the Direction of Bias in Studies of Diagnostic Test Accuracy (Kohn et al AEM 2013).

Comment on Authors' Conclusion Compared to SGEM Conclusion:
We generally agree with the authors' conclusion.

Clinical Application: The data on the pregnancy-adapted YEARS algorithm is encouraging but should go through external validation prior to implementation.

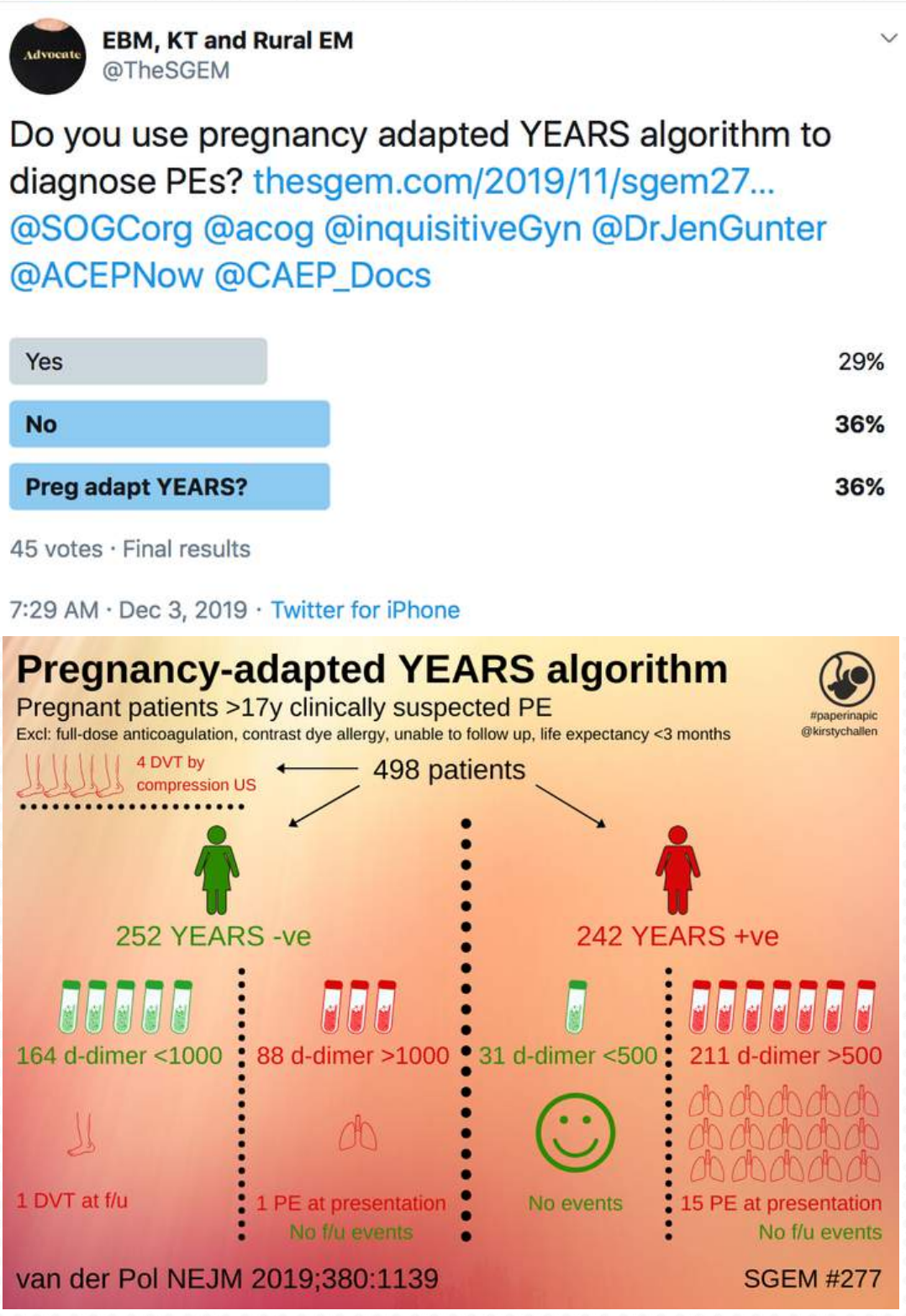
What Do I Tell the Patient? You tell her that based on over 20 years of experience you do not think she has a blood clot in her lung. You explain that the blood test she googled is called a d-dimer. While it is good for ruling out blood clots it can be falsely elevated. This can lead to unnecessary CT scans with radiation that she is terrified about being exposed to. You provide reassurance and tell her to return to the ED if she gets increasing shortness of breath, develops chest pain, starts cough up blood, one leg swells up or she is worried.

Case Resolution: Your clinical gestalt is she does not have a VTE and you do not work her up for a PE.

Episode End Notes

Other FOAMed resources:

- REBEL EM
- EM Literature of Note



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SEEN YOUR VIDEO FOR ACUTE OTITIS MEDIA DISCHARGE INSTRUCTIONS?

Clinical Question:

Are video discharge instructions superior to a paper handout with respect to the acute otitis media-symptom severity score (AOM-SOS_

Bottom Line:

Consider using video discharge instructions for parents of children with acute otitis media.

Guest:

Dr. Chris Bond is an emergency medicine physician and assistant Professor at the University of Calgary. He is also an avid FOAM supporter/producer through various online outlets including TheSGEM.

Case Overview

Case: An 18-month-old, previously healthy female presents to the emergency department with 24 hours of fever. The past few days the parents note there has been some rhinorrhea and cough. She looks well, immunizations are up to date and her examination reveals right sided acute otitis media (AOM). When discussing discharge instructions for her AOM, you wonder whether having the parents watch a video will be more beneficial for the child's symptoms, rather than giving the parents oral instructions with a paper handout.

Background: AOM is the second most commonly diagnosed illness in children and the most common indication for antibiotic prescription [1-2]. There are significant costs associated with AOM and parents often bring their children to health care providers for evaluation of pain and fever [3-4]. More than one third of children experience pain, fever or both three to seven days following treatment, and nearly seventy-five percent of parents identify pain and disturbed sleep as the most important sources of AOM related burden [5-6].

There is significant parental uncertainty regarding treatment of AOM and less than 30% of US parents receive instructions on appropriate analgesia for their children [7-8]. Discharge instruction complexity and inadequate comprehension is associated with medication errors, suboptimal post-discharge care and unnecessary recidivism [9-12]. Medication errors can be reduced using standardized discharge instructions, and parents prefer these to verbal summaries [13-15].

Video discharge instructions have been shown to be preferred over paper instructions in many pediatric presentations, however no study has explored the effectiveness of video instructions for AOM [16-17].

Reference: Belisle et al. Video discharge instructions for acute otitis media in children: a randomized controlled open-label trial. AEM December 2019

Population: Parents of children age 6 months to 17 years with a chief complaint of otalgia in the setting of URTI and where the treating physician was at least 50% certain of a clinical diagnosis if AOM. Diagnostic certainty was on a 100mm visual analog scale based on the physicians' rate of color photos of AOM.

Intervention: Video discharge instructions

Comparison: Paper-based discharge instructions identical to the video discharge instructions

Exclusions: Parents who were not the primary care provider, had poor English proficiency, lacked internet or telephone access, and whose children had: a pre-existing diagnosis of AOM (<72 hours old); other concomitant diagnoses (pneumonia, urinary tract infection, gastroenteritis, sinusitis, or any other condition requiring antibiotics and/or hospital admission); tympanostomy tubes; acute tympanic membrane perforation.

Outcome:

- **Primary Outcome:** AOM Severity of Symptom (AOM-SOS) score on day three post-discharge.
- **Secondary Outcomes:** Knowledge questionnaire scores, parental satisfaction with the intervention, number of days of missed school or daycare (child) and work (parent), proportion of children with at least one return visit to a healthcare provider, and proportion of children who received analgesia.

Authors' Conclusions

"Children of parents with AOM who watched a five-minute video in the ED detailing the identification and management of pain and fever experienced a clinically important and statistically significant decrease in symptomatology compared to a paper handout."

Quality Checklist for Randomized Control Trials

- ☑ 1. The study population included or focused on those in the emergency department.
- ☑ 2. The teams were adequately randomized.
- ☑ 3. The randomization process was concealed.
- ☑ 4. The teams were analyzed in the groups to which they were randomized.
- ☒ 5. The study teams were recruited consecutively (i.e. no selection bias).
- ? 6. The teams in both groups were similar with respect to prognostic factors.
- ☒ 7. All participants (patients, clinicians, outcome assessors) were unaware of group allocation.
- ☑ 8. All groups were treated equally except for the intervention.
- ☒ 9. Follow-up was complete (i.e. at least 80% for both groups).
- ☑ 10. All (team) patient-important outcomes were considered.
- ☑ 11. The treatment effect was large enough and precise enough to be clinically significant.

Case Outcomes

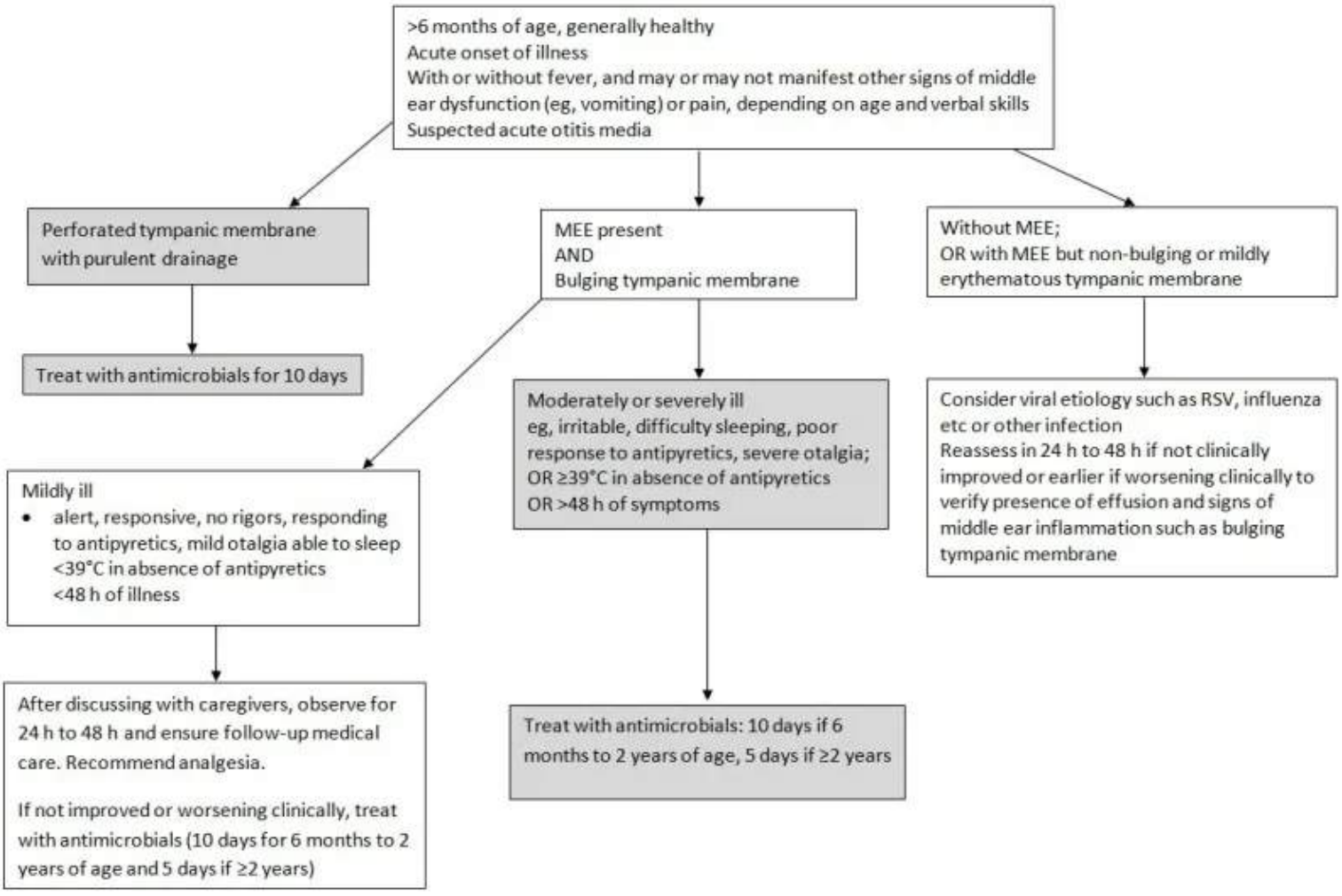
Key Results:
Overall, 5334 parents were screened for eligibility, 219 were randomized and analyzed and 149 completed the primary outcome (77 video; 72 paper instructions). Children included 107/219 (49%) females with an overall mean age of 2.9 years and 41/219 (18.7%) were not offered analgesia prior to arrival. There were no crossovers in the trial.

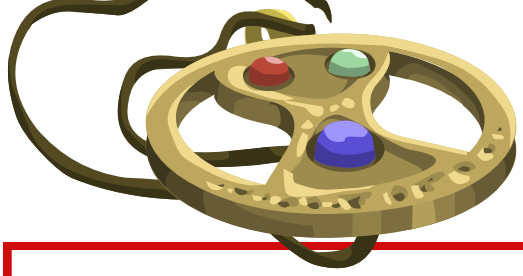
- **Primary Outcome:** AOM-SOS score on day three (0 to 14 with higher scores indicative of greater symptom severity)
  - 1 video group vs. 3 paper group (p=0.004) even after adjusting for pre-intervention AOM-SOS and medication use (analgesics and antibiotics)
  -

- **Secondary Outcomes:**
  - There were no significant differences in secondary outcomes, including knowledge gain, functional outcomes or the number of children receiving antibiotics or analgesics following discharge.

This is an SGEMHOP episode which means we have the lead author on the show. Dr. Naveen Poonai is a Paediatric Emergency Medicine physician at the Children's Hospital, London Health Sciences Centre, Associate Professor of Paediatrics and Internal Medicineat Western University, Canadian Association of Paediatric Health Centres (CAPHC) project lead for Paediatric Pain Assessment, and has a cross-appointment with the Department of Epidemiology and Biostatistics. He was previously on SGEM#177 discussing POCUS for diagnosing pediatric fractures.

This episode we are going to be talking about acute otitis media. There are a number of different guidelines out there for acute otitis media (Canadian Pediatric Society, American Academy of Pediatrics, American Association of Family Physicians, United Kingdom, and Australia) Naveen prefers the Canadian Pediatric Society guidelines.





Time to Talk Nerdy

1. Children: You included children age 6 months to 17 years of age. There is a big difference between an infant and a teenage. Why not just limit it to children under 5 years old? The mean age was 2.9 years with a SD of 2.8 years.

It is true that a young child is quite different from a teenager. We decided to cast a wide net to be more instead of less inclusive. Older children suffer from AOM as well and inclusion of these individuals extends the generalizability of our findings.

2. Diagnosis of AOM: The diagnosis of AOM can be a bit tricky. You included patients that the physician was 50% certain of a clinical diagnosis of AOM using a 100mm visual analog scale. That was based on color photos of AOM from published diagnostic criteria. Why not use a more objective criteria like tympanometry or acoustic reflectometry to increase diagnostic certainty?

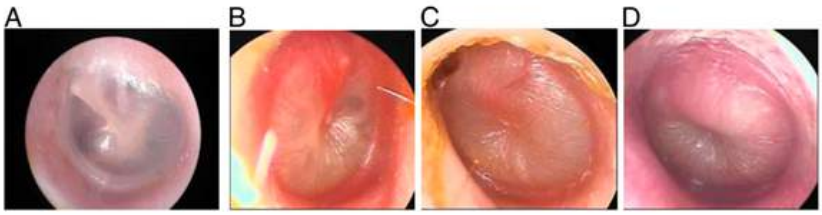
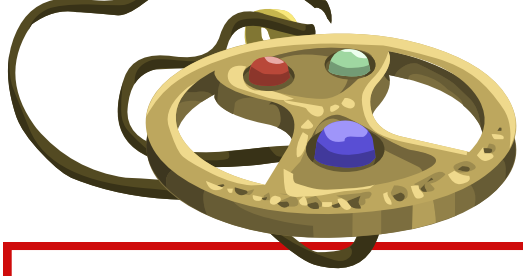


FIGURE 2
A, Normal TM. B, TM with mild bulging. C, TM with moderate bulging. D, TM with severe bulging. Courtesy of Alejandro Hoberman, MD.

In an ideal world we would have been able to use tympanometry or acoustic reflectometry, however these tools are unfortunately not available in our emergency department.

3. Convenience Sample: Recruitment was done seven days a week from 10am to 10pm. We understand the realities of conducting research and having someone available 24 hours a day. However, do you think parents that present overnight with sick children a different than those who present during the day?



Time to Talk Nerdy

It is possible that children that present in the middle of the night are experiencing more pain than those that present during daytime or evening hours. But is more likely that the pain they are experiencing is disruptive to their sleep and perhaps more so, their parents' sleep. Parents that present with their child overnight may process discharge information quite differently from daytime hours.

4. Single Tertiary Pediatric Centre: This was a single centre study done at a pediatric emergency department. Do you think this data can be extrapolated to other pediatric emergency departments in Canada or internationally?

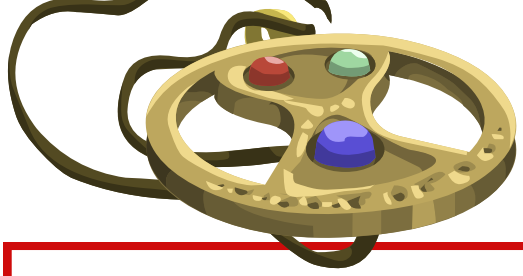
I *think that this data can certainly be extrapolated to other Canadian pediatric emergency departments as other tertiary care pediatric centres are likely to have populations similar to ours. However further study would have to be undertaken to determine if the data would be applicable to international populations of differing languages and cultures. We excluded non-English speaking populations for feasibility purposes and so this study would have to be repeated including those speaking other languages to be able to confidently say the data apply more broadly.*

In addition, I work in a rural community emergency department. We see adults and children. Do you think these results would apply to non-pediatric emergency departments?

I think these results would definitely apply to rural community emergency department pediatric patients of English speaking families.

5. Education Level: The parents in your study were well educated. More than 70% had at least a college education. How do think this could have impacted your results?

I think this may have contributed to the reason we saw no difference in knowledge



Time to Talk Nerdy

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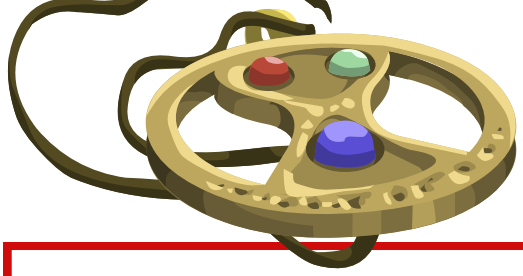


Time to Talk Nerdy

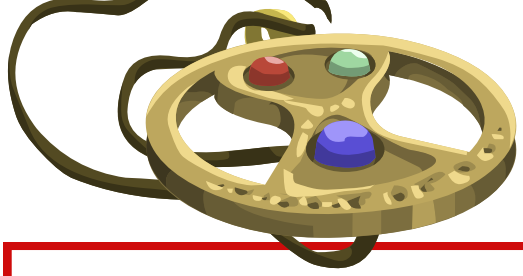
acquisition between groups. If we had demonstrated greater knowledge acquisition in the video group, we may have postulated that the significant difference in symptomatology between groups could be related to great knowledge acquisition and therefore more appropriate care of the children randomized to the video group.

6. Health Literacy: You used a grade 8 level for literacy. Less than 5% of your population reported elementary school only. I conducted some research looking at rural populations and found 40% of adults attending a number of rural emergency departments had limited health literacy defined as below Grade 9 level. This has me concerned that the video and paper discharge instructions may not be understandable to a significant part of rural emergency department patients.

This is a valid concern. I would wonder what is provided for discharge instructions in these rural emergency departments. It may be possible that much like many emergency departments almost 30% of patients with AOM are not provided any instruction on pain management and potentially providing a video even if it is slightly above the educational level of individual, it may be better than what is currently done. The best-case scenario would be to develop a video targeting caregiver with minimal or no education.

7. Exclusion of Non-English: You screened over 5,300 patients and almost 5,000 did not meet inclusion criteria. How many were because of non-English speaking parents? Did they have different demographics than the English-speaking parents? If they had lower health literacy, this cohort could be the group to benefit more from improved discharge instructions than English speaking highly educated parents.

The vast majority of patients screened were excluded because they did not have a diagnosis of AOM. A small percentage were excluded because of non-English



Time to Talk Nerdy

speaking parents. However, we didn't collect demographic data on non-eligible patients.

8. AOM-SOS Score: Could you explain this score to the SGEMers? You state that it has been validated and provide a reference (Hoberman et al NEJM 2011). This study was done in children under the age of two years. Your mean age was 2.9 years. Has the AOM-SOS score been validated in children over the age of two years?

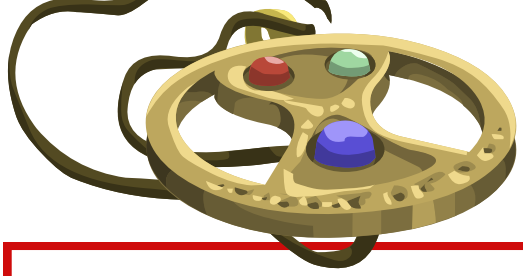
The acute otitis media severity of symptoms score is a 7-question survey that assesses the child's symptoms over the last 24 hours as reported by the caregiver, thereby reflecting their perception of the child's symptomatology. A score of 0 reflects no symptoms and a score of 13 reflects maximal symptoms. The questions enquire about things such as crying, ability to sleep, appetite, activity level.

The AOM SOS has been validated for use in children two years and under. So, a noteworthy limitation of our study is that we extrapolated the use of this tool to older children. However, the AOM-SOS was the best tool we had given there is no tool validated for use in older children.

You state in the conclusions that this is both a statistically significant and a clinically significant change in AOM-SOS scores on day three. However, if patients were just eating a less on day three, the scores would be one versus two in the groups. Would this really be a clinically significant impact?

I would argue that a difference in any one of the AOM-SOS survey questions is a clinically significant change given the impact these of these behavioural changes on the family, the level of stress experienced by the caregiver and the comfort of the child.

You had the parents complete the AOM-SOS Score only on the first three days



Time to Talk Nerdy

with the primary outcome being the score at day three. Why did you pick day three and why not score for the duration of the suggested length of treatment, five to ten days?

We chose day three as our primary outcome because the AOM symptomatology generally undergoes the greatest change over the first three days of illness.

Additionally, one of the biggest challenges with conducting studies such as this is loss to follow up – we anticipated loss to follow up would be too great if we attempted to follow participants for longer than three days.

Appendix S3

Acute Otitis Media Severity of Symptom Score

TABLE 4. AOM-SOS (Version 3.0)*

We are interested in finding out how your child has been doing. For each question, please place a check mark in the box corresponding to your child's symptoms. Please answer all questions.

	No	A Little	A Lot
Over the past 12 h, has your child been tugging, rubbing, or holding the ear(s) more than usual?	☐	☐	☐
Over the past 12 h, has your child been crying more than usual?	☐	☐	☐
Over the past 12 h, has your child been more irritable or fussy than usual?	☐	☐	☐
Over the past 12 h, has your child been having more difficulty sleeping than usual?	☐	☐	☐
Over the past 12 h, has your child been less playful or active than usual?	☐	☐	☐
Over the past 12 h, has your child been eating less than usual?	☐	☐	☐
Over the past 12 h, has your child been having fever or feeling warm to touch?	☐	☐	☐

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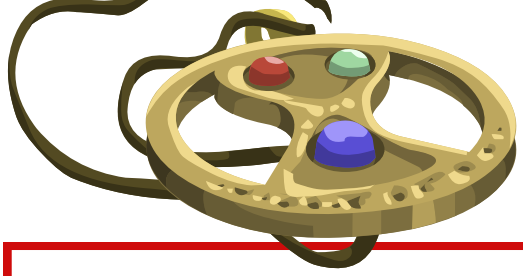
Shaikh N, Hoberman A, Paradise JL, et al. Responsiveness and construct validity of a symptom scale for acute otitis media. Pediatr Infect Dis J. 2009;28:9 –12.

9. Loss to Follow-up. We typically like to see at least 80% of patients included in the analysis. In other words, less than 20% loss to follow-up. You anticipated a high loss to follow-up in your power calculation and were correct with only 68% of patients in the trial completed the primary outcome (follow-up at 3 days). How do you think losing 1/3 of patients could impact the results and their interpretation?



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Well it's entirely possible that parents who followed up were more satisfied with their care and may have been more likely to report lower symptoms scores, biasing us away from the null hypothesis.

10. Gift Card: You offered parents a $5 gift card as compensation for study participation. Both Chris and I were wondering if this was a Tim Horton's Card?

They were actually Starbucks (greater flexibility of emailing gift cards).

Is there anything else you want to say about your HOP publication?

Sure. The findings of this study indirectly speak to the need to address children's pain both in the ED and post-discharge. We've done our best to translate what is already known about the distress of AOM into what we hope is practice-changing discharge instructions.

Comment on Authors' Conclusion Compared to SGEM Conclusion: We generally agree with the authors' conclusions and would add in this single tertiary pediatric emergency department.

Clinical Application: This study provides support for use of video discharge instructions for AOM.

What Do I Tell the Parents? Your child has an ear infection. It has been shown that your child's pain and symptoms will be better managed 3 days after discharge if we have you watch a 5-minute video about ear infection treatment before you leave. We'll also give the video link so you can watch it again at home and I'll answer any questions you have after watching prior to your discharge.

Case Resolution: After a brief discussion with the parent, you have them watch a video of discharge instructions for their child. You then return and answer their questions prior to discharge.

Episode End Notes

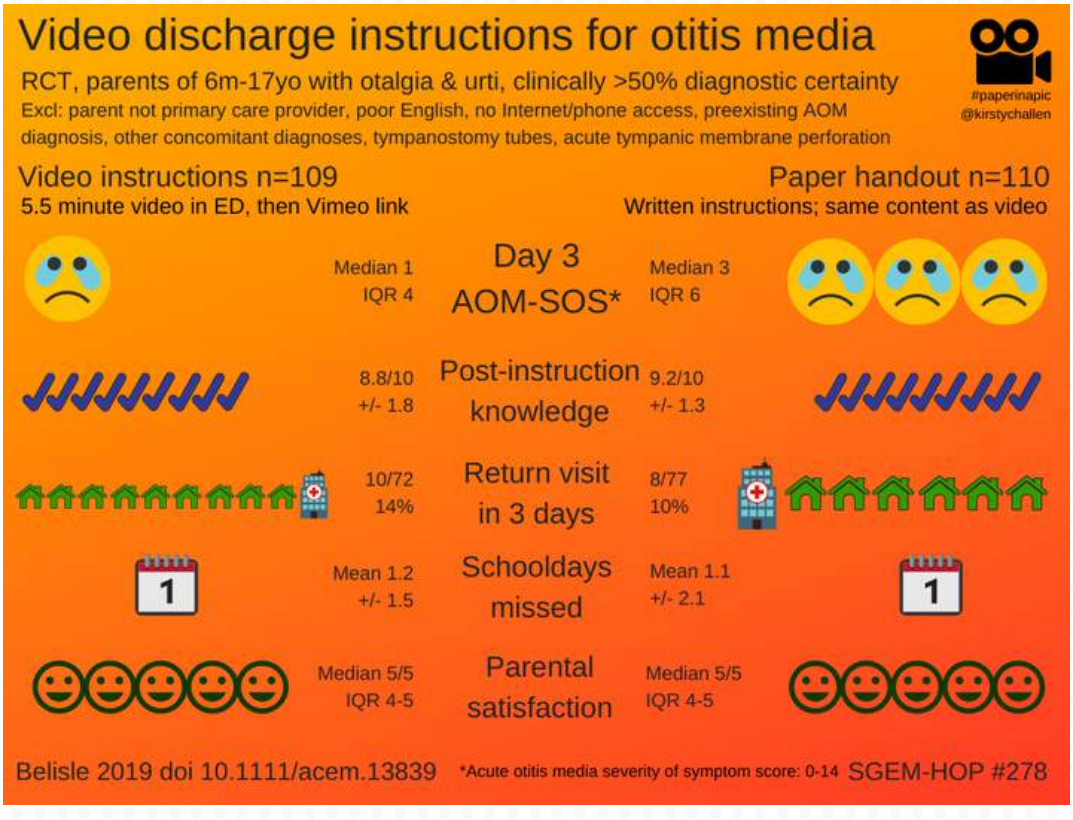
Ken Milne - EBM and Rural
@TheSGEM

What type of discharge instructions do you usually give to parents of children with acute otitis media? #SGEMHOP onlinelibrary.wiley.com/doi/full/10.11... @SAEMonline @AcademicEmerMed @AAPNews @CanPaedSociety @SRPCanada @CHEOhospital @SickKidsNews

Oral	39%
Printed	11%
Video	0%
Oral + Printed	**50%**

44 votes · Final results

9:14 AM · Dec 17, 2019 · Twitter for iPhone



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DO YOU REALLY WANT TO HURT ME AND USE A PLACEBO CONTROL FOR A MIGRAINE TRIAL?

Clinical Question:

Does ubrogepant increase the percentage of patients who were free from pain and absent of the most bothersome migraine-associated symptom at two hours from initial dose in comparison to placebo?

Bottom Line:

Ubrogepant and the other CGRP antagonists are not ready for widespread use in the emergency department for patients who present with a migraine headache.

Guest:

Dr. Anand Swaminathan is an Assistant Professor of Emergency Medicine at St. Joseph's Hospital in Paterson, NJ. He is also the managing editor of EM:RAP and associate editor at REBEL EM.

Case Overview

Case: A 23-year-old man with a history of migraines presents with two days of headache, nausea and photo-photophobia typical of his prior migraines. He's tried a number of medications at home including ibuprofen, acetaminophen, aspirin and sumatriptan without any considerable improvement in symptoms. You start to offer him your standard medications like metoclopramide and haloperidol when he asks about a new drug he heard about called ubrogepant.

Background: Migraine headaches are a chronic neurologic disease characterized by throbbing, often unilateral headaches that are often associated with nausea, vomiting, photophobia and phonophobia. It is a common disease and can be severe enough to impede on people's lives.

Headaches themselves are not only a common emergency department presentation but one that is filled with potential dangers. There are a number of causes of headache that are life and limb threatening – subarachnoid hemorrhage (SGEM#201), meningitis, encephalitis, cerebral venous thrombosis, vertebral artery dissection among other things but, most headaches are benign in nature.

There is an international classification system of headaches (IHS 2018). The current system classifies them into primary and secondary headaches. An important part of our job as emergency physicians is to differentiate the lethal headache from the benign headache.

Though we rarely make a de novo diagnose of migraines in the emergency department, many patients with migraines present to us for symptom management. The pathophysiology of migraines is both complicated and poorly understood but there are a number of potential treatments including NSAIDs, acetaminophen, aspirin, neuroleptics, triptans and even propofol.

More recently, calcitonin gene-related peptide antagonists (CGRPs) have emerged as a new potential treatment. The first big study that came out on these drugs was published in the NEJM in 2019 and was entitled Rimegepant, an Oral Calcitonin Gene-Related Peptide Receptor Antagonist for Migraine (Lipton et al).

Now, we have a second study published in the NEJM on a related drug, ubrogepant.

Reference: Dodick DW et al. Ubrogepant for the Treatment of Migraine. NEJM 2019

Population: Adult patients (18-75 years of age) with at least a one-year history of migraine with or without aura that met criteria from the International classification of headache disorders and had migraine onset before the age of 50. Patients had to have a history of migraines between 4-72 hours and a history of migraine attacks separated by at least 48 hours of freedom from headache. Additionally, they had to have suffered from two to eight migraines per month over the last three months.

Intervention: Ubrogepant 50 mg or 100 mg

Comparison: Placebo

Exclusions: Patients with 15 or more headaches/month on average in the previous six months. Hard to distinguish the type of headache. Use of acute migraine treatment on ten or more days in the previous three months. Participated in a trial involving CGRP. Had clinically significant cardiovascular or cerebrovascular disease. History of hepatitis in the last six months or laboratory findings of liver disease (elevated AST, AST, Bilirubin or low serum albumin).

Additional Exclusions from ClinicalTrials.gov:

- Has a history of migraine aura with diplopia or impairment of level of consciousness, hemiplegic migraine, or retinal migraine
- Has a current diagnosis of new persistent daily headache, trigeminal autonomic cephalgia (eg, cluster headache), or painful cranial neuropathy
- Required hospital treatment of a migraine attack 3 or more times in the previous 6 months
- Has a chronic non-headache pain condition requiring daily pain medication
- Has a history of malignancy in the prior 5 years, except for adequately treated basal cell or squamous cell skin cancer, or in situ cervical cancer
- Has a history of any prior gastrointestinal conditions (eg, diarrhea syndromes, inflammatory bowel disease) that may affect the absorption or metabolism of investigational product; participants with prior gastric bariatric interventions which have been reversed are not excluded

Outcomes:

- **Co-Primary Outcome:** Freedom from pain at two hours from initial dose of medication. Absence of the most bothersome symptom associated with migraine two hours from initial dose of medication.

- **Secondary Outcomes:** Change in severity of headache at two hours, sustained pain relief, sustained freedom from pain, absence of photophobia, absence of photophobia and absence of nausea at two hours from initial dose. Adverse events were also collected.

Authors' Conclusions

"A higher percentage of participants who received ubrogepant than of those who received placebo had freedom from pain and absence of the most bothersome symptom at 2 hours after the dose. The most commonly reported adverse events were nausea, somnolence, and dry mouth. Further trials are needed to determine the durability and safety of ubrogepant for acute migraine treatment and to compare it with other drugs for migraine."

Quality Checklist for Randomized Control Trials

- ☒ 1. The study population included or focused on those in the emergency department.
- ☑ 2. The teams were adequately randomized.
- ☑ 3. The randomization process was concealed.
- ☒ 4. The teams were analyzed in the groups to which they were randomized.
- ? 5. The study teams were recruited consecutively (i.e. no selection bias).
- ? 6. The teams in both groups were similar with respect to prognostic factors.
- ☑ 7. All participants (patients, clinicians, outcome assessors) were unaware of group allocation.
- ☑ 8. All groups were treated equally except for the intervention.
- ☒ 9. Follow-up was complete (i.e. at least 80% for both groups).
- ☒ 10. All (team) patient-important outcomes were considered.
- ? 11. The treatment effect was large enough and precise enough to be clinically significant.

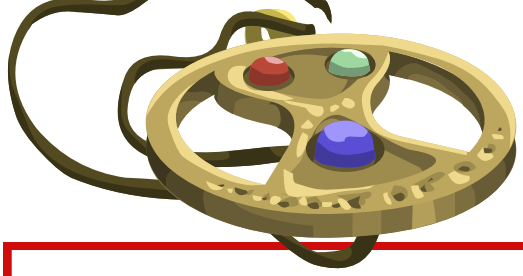
Case Outcomes

Key Results:
They enrolled 1,672 patients with roughly equal numbers allocated to each of the three groups. The mean age was around 40 years and almost 90% were female. The modified ITT analysis excluded 345 (21%) of participants.

Ubrogepant was superior to placebo in treating migraine headaches.

- **Primary Outcome:** (100mg/50mg/placebo)
  - Freedom from pain at two hours: 21%/19%/12% (both doses statistically better than placebo but, not better than the other). That gives an absolute difference of about 8% and Number Needed to Treat for Benefit (NNTB) of 13
  - Absence of most bothersome symptom at two hours: 38%/39%/28%. This is an absolute difference of 10% with a NNTB of 10.

- **Secondary Outcomes:**
  - Pain relief at two hours (61%/61%/49%) and sustained pain relief (38%/36%/21%) was better with ubrogepant compared to placebo.
  - **Serious Adverse Events:** There were five SAE with all of them being in the intervention group (two appendicitis, pericardial effusion, spontaneous abortion and seizure). Only the seizure was considered related to the trial drug. Six patients had ALT levels three times the upper limit of normal (one in the placebo group and five in the treatment group). Only one of the treatment group was considered possibly related to the trial regimen. Details are in the supplemental appendix.



Time to Talk Nerdy

1. Patients: We had a few issues with the patients included in this study. First, these were not emergency department patients but rather those recruited from outpatient clinic. Whether or not these are the same patients that present to the emergency department is unknown.

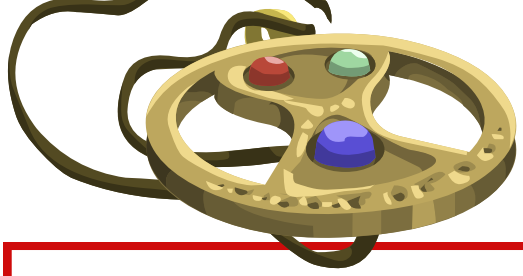
We are also unsure if the patients were recruited consecutively. This is an important aspect to avoid potential selection bias. Remember that when we use the term “bias” we are not talking about random noise in the data but something that systematically moves us away from the “truth”.

The third question we had about the included patients was whether or not both groups were similar with respect to prognostic factors. Baseline demographics are reported in Table 1. However, things like number of headaches/month, refractory headaches in the past, and other things are not reported. This could impact the results and therefore the conclusions.

2. Comparison to Placebo: Randomized control trials (RCTs) are considered an ideal study design to establish causality and effect of a medication. Drug intervention RCT design requires that the intervention be compared to something (active drug, standard treatment, no treatment or placebo).

It is widely agreed upon that comparison to placebo is acceptable when no proven intervention exists (Millum and Grady 2013). In contrast, placebo comparison is not considered acceptable in life-threatening conditions if there is an available treatment that is known to prolong life. The use of placebo for comparison in non-life-threatening conditions has been hotly debated for decades, particularly when an accepted treatment exists.

The argument against the use of placebos in these circumstances is guided by the Declaration of Helsinki. This documents state:



Time to Talk Nerdy

"In any medical study, every patient — including those of a control group, if any — should be assured of the best proven diagnostic and therapeutic methods."

Thus, if an effective treatment exists, it should be prescribed to patients (Simon 2000).

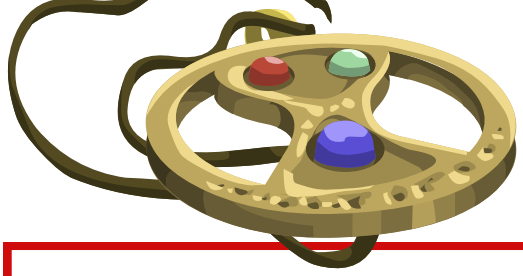
Those researchers arguing for use of a placebo comparator counter that even in the presence of effective treatment, placebo control may be necessary when:

"there are compelling and scientifically sound methodological reasons for its use and the participants in the study will not face additional risks of serious or irreversible harm from exposure to placebo" (Keranen et al 2015).

Even when a widely accepted treatment exists, some researchers argue that informed consent can be used to justify the use of placebo.

However, research participants are likely to believe that participation in a trial will lead to benefit and this therapeutic misconception may not be resolved simply by informed consent (Chiodo et al 2000). Patients randomized to the placebo group, when accepted active treatment exists, must not be subjected to additional risks or harms but in the absence of harm, placebo-control would be reasonable (Temple and Ellenberg 2000). The problem becomes what definition of harm to use.

Despite the ethical issues surrounding placebo-control studies, there are numerous prior studies that violate the tenets of the Declaration of Helsinki as well as the ideal of *"prima no nocere."* Examples include research into the treatment of onchocerciasis with ivermectin, ondansetron in chemotherapy-induced emesis, ACE inhibitors in congestive heart failure and antihypertensive agents (Rothman and Michels 1994). If a placebo-control



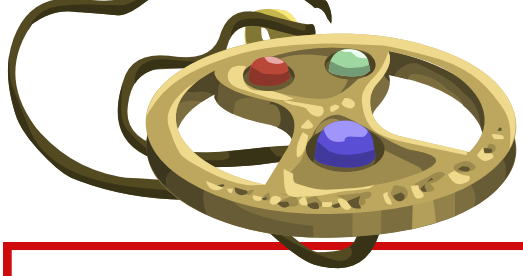
Time to Talk Nerdy

approach is used, rationale for this design is necessary. However, Keranen et al found that only about one-third (35%) of RCTs actually do this while the risk of placebo is often (83%) and not explained to patients (Keranen et al 2015).

With regards to abortive migraine treatment, there are a number of options with established efficacy. Three options that are considered first line include: antidopaminergics, triptans and nonsteroidal anti-inflammatory drugs (NSAIDs) (Friedman 2016, AHS Statement 2019). Lipton et al state that up to 66% of patients respond to triptans based on prior work (Lipton et al 2019). Lipton et al do not provide justification for the placebo-control methodology in the manuscript which is particularly important in the setting of effective alternative treatment.

While an argument can be made that treating migraine headaches with placebo does not lead to long-term harm, patients suffering from migraines often experience severe, debilitating pain often resulting in an inability to work or perform typical daily activities. I have suffered from migraines in the past and would be very upset to have received a placebo when effective treatments were available. Thus, a placebo-control study exhibits, at best, questionable ethical standards and subjects patients to possibly unnecessary harm.

So why would researchers choose to compare their drug to placebo as opposed to comparing to standard therapy? There may be a number of possible explanations for this choice. Comparing a new drug to placebo is easier to establish efficacy than to a known effective therapy. However, a non-inferiority study design could be used to compare the new drug to established treatment if the new drug had benefits over the prior treatment i.e. ease of use, cost, reduced side effects.



Time to Talk Nerdy

Some argue that historically, the Food and Drug Administration (FDA) has withheld drug approval when placebo-controls were not used in establishing efficacy. However, these concerns are likely exaggerated (Chiodo et al 2000, Orentlicher 2001).

The most obvious reason for using a placebo-control methodology is that pharmaceutical companies may believe:

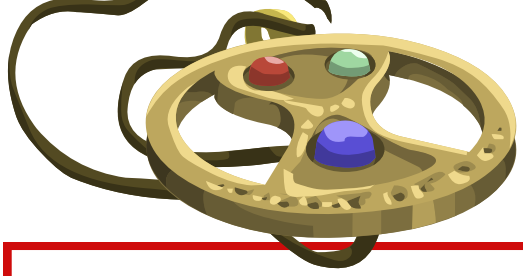
"it is their interest to compare new drugs with placebo rather than existing therapy, even when better information for patients and physicians would be provided by an active control" (Orentlicher 2001).

Demonstrating superiority to placebo is easier than demonstrating superiority to an effective therapy and is more likely to result in positive findings for the drug and the pharmaceutical company. This comes at the harm of patients and, adds little to our understanding of treatment for the disease.

If you want to dive into the ethics of using placebos in clinical trials you can check out Time to Talk a Little Nerdy (TTLN) as part of the EMRAP family of shows.

3. Co-Primary Outcomes: How many times will I have to use this great quote from the movie Highlander 1986..."there can be only one", primary outcome? I might have to start using the best 80's movie every (The Princess Bride 1987) quote: "You keep using that word (primary), I do not think it means what you think it means".

The term primary according to Merriam-Webster's dictionary means first rank, importance, or value. So, decide on what is the most important outcome, design your study accordioning, and report this finding. Everything



Time to Talk Nerdy

else can be secondary. By having more than one primary outcome (co-primary or composite outcome) you make the target larger (statistical significance) and therefore easier to claim a positive trial and get published.

4. Modified Intention-To-Treat (mITT) Analysis: A pure ITT is to take all the patients immediately after randomization and analyses them in the groups to which they were allocated. This is the conservative way to look at the data and is the preferred method for superiority trials.

A per-protocol approach analyses participants not by group allocation but by whether or not they received the intervention. This is a quality indicator for non-inferiority studies.

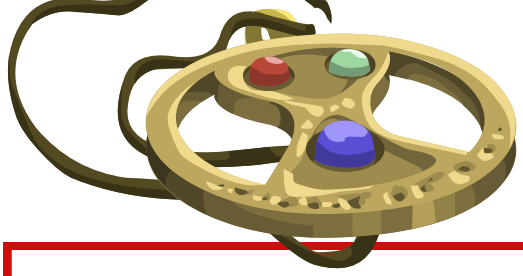
Between these dichotomous extremes is the mITT. These authors used a mITT analysis to report their data. Rather than analyzing patients allocated to each group they excluded a number of patients.

Patients were only included if they:

"took an initial dose of ubrogepant or placebo, recorded a baseline rating for the severity of the migraine headache, and recorded at least one rating for the severity of the migraine headache after the initial dose or recorded the presence or absence of at least one migraine- associated symptom at or before the 2-hour time point after the initial dose."

If this did not happen, patients were excluded from the efficacy analysis.

A mITT analysis can nudge the results (bias) towards finding efficacy. This may over-estimates the effect size for efficacy of ubrogepant and makes us less confident in the results.



Time to Talk Nerdy

5. Industry Funding: This was an industry supported trial. The publication says:

"Confidentiality agreements were in place between the sponsor (Allergan) and the authors. The sponsor developed the trial protocol in collaboration with external consultants, provided the trial drug and placebo, and gathered and analyzed the data. The manuscript was prepared by the sponsor, with contributions from all authors and with assistance from a professional medical writer employed by the sponsor."

This does not make the data wrong, but it should make us more skeptical.

Doing research is expensive and the funding needs to come from somewhere. Our current model includes industry involvement in studies that can take many forms. This introduces potential biases and it would be better if our system had no industry involvement.

If and until that ever happens, SGEMers need to keep their skeptical radar turned on when they see that industry has played a role in the design, analysis, writing, publication and dissemination of studies.

Comment on Authors' Conclusion Compared to SGEM Conclusion: While it appears that ubrogepant is superior to placebo, this isn't the question we should be asking. Rather, we should be asking if ubrogepant is better than standard therapy for migraine headaches.

Clinical Application: We do not know if ubrogepant is better, worse or the same efficacy as existing treatments for migraine headaches. Until data on patients presenting to the ED with migraine is reported that includes a comparison to standard active treatment and safety data, this drug doesn't belong in our armamentarium.

What Do I Tell the Patient? There is a new class of drug that have been approved to treat migraine headaches. The research was not done on patients like you in the emergency department. The studies also did not compare the new drugs to our existing treatments. We do not know if it is more or less effective than what we already use. The good news is the treatments we do have is very effective. We can also offer you a dose of steroids (SGEM#28) to prevent you suffering a rebound headache (NNT 9).

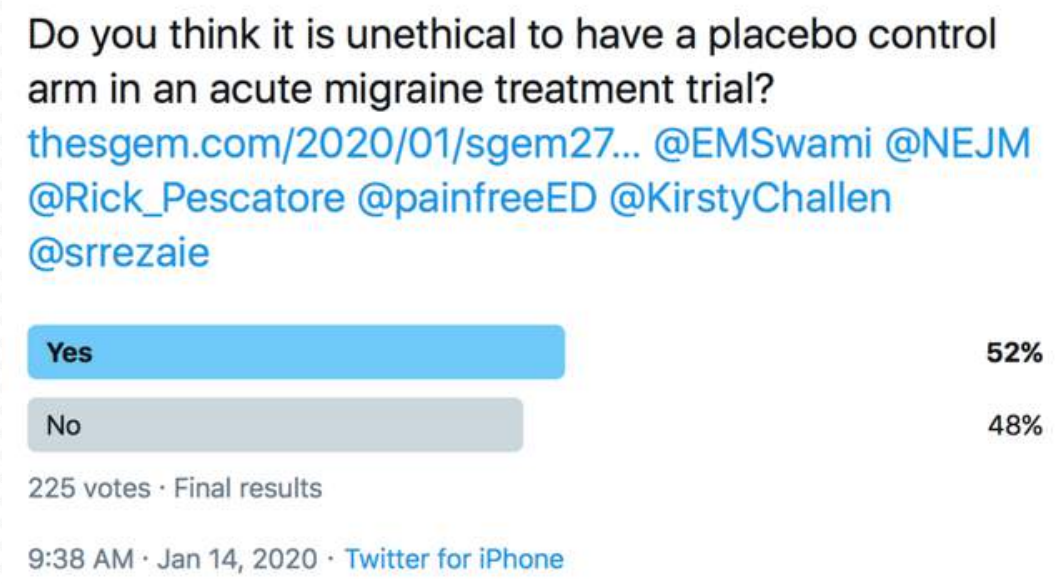
Case Resolution: You discuss with the patient that the novel CGRP receptor antagonists have potential to benefit patients with moderate to severe migraines but, that there's limited evidence for their use in the emergency department and that we have no idea if these drugs are more effective or safer than our standard medications .

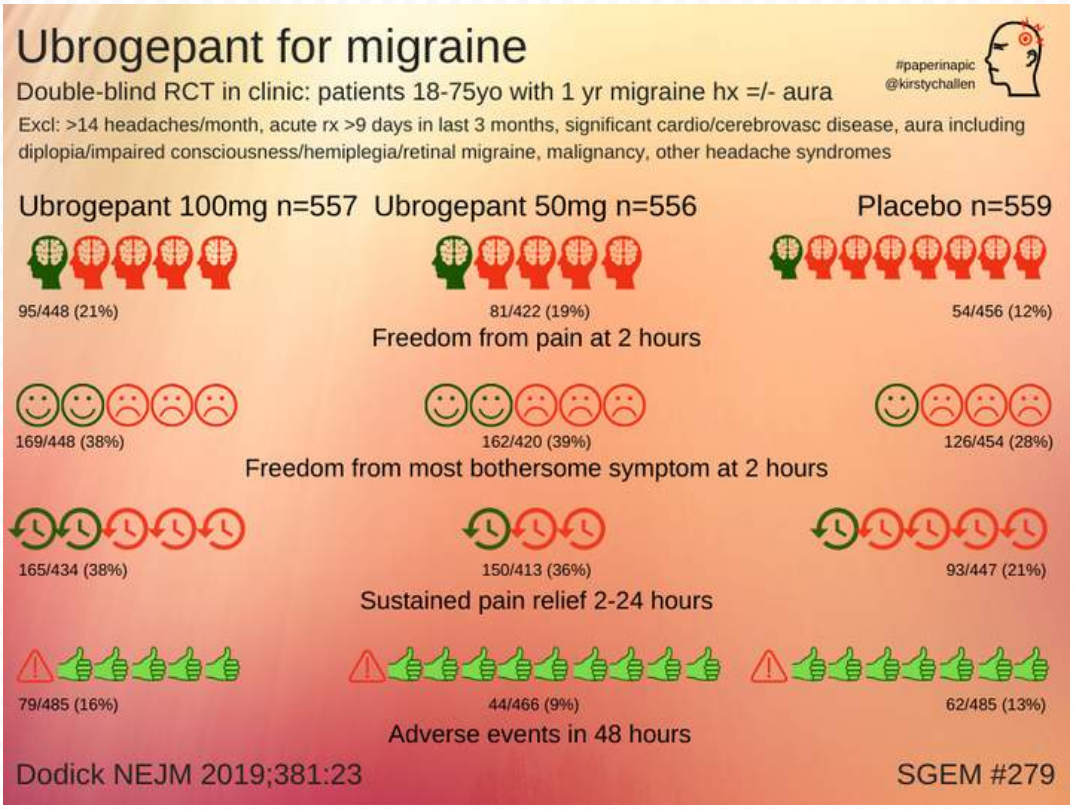
You decide instead to treat the patient with 10 mg of metoclopramide which has a modest reduction in pain. You follow this with 2.5 mg of haloperidol which results in the patient's pain reaching a level of 2 out of 10 and resolution of his nausea and photo-phonophobia. He is improved enough to go home and states he will follow up with his neurologist in the next week or so.

Episode End Notes

Other FOAMed:

- REBEL EM: Rimegepant and Inflammatory Neuropeptide Antagonism in Migraine
- EM Lit of Note: The New Cutting Edge Treatment for Migraines
- EM Lit of Note: Deja Vu – The New Cutting Edge Treatment for Migraines

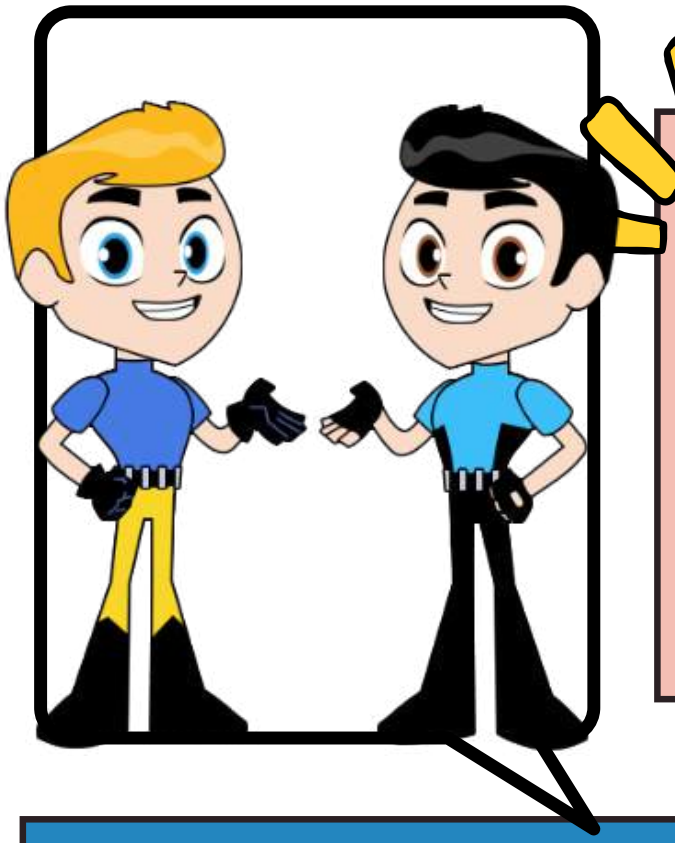




280 THIS OLD HEART OF MINE AND TROPONIN TESTING

Clinical Question:

What is the frequency of ACS in elderly patients presenting to the ED with nonspecific complaints, and what is the utility of troponin testing in this population?



Bottom Line:

In this retrospective study of elderly patients presenting to the emergency department with nonspecific complaints, the diagnosis fo ACS was rare, and troponin testing had limited value.

Guests:

Dr. James VandenBerg has a master's degree in clinical investigation from Washington University in St. Louis, and is currently the Chief Resident at Detroit Receiving Hospital.

Dr. Andrew Huang is the Chief Resident at Sinai-Grace Hospital.

Case Overview

Case: As the resident, you have just finished seeing a 78-year-old male who has been brought in by his family over the holidays. The triage nurse has put the reason for the visit as “multiple complaints”. Despite spending 30 minutes in the room, you still are not sure exactly why the patient is here.

Your attending says that if you take a good geriatric history that you can always determine what’s going on. However, 15 minutes later your attending leaves the room defeated. The patient’s complaints are just so nonspecific.

The attending ends up ordering the “geriatrogram” – ticking off every blood test on the form, including the troponin. You turn to the attending and ask, “do you really think this could be acute coronary syndrome (ACS)?”

Background: Patients 65 years and older account for about 15% of emergency department visits in the United States. Their presentations are often complicated as they present with nonspecific symptoms, and there is often obscuring co-morbid conditions, polypharmacy, and cognitive/functional impairment.

Nonspecific symptoms in the elderly usually yield a broad differential and there are no recommended diagnostic algorithms, leading to extensive testing. ACS is usually amongst this differential, as cardiovascular disease is a leading cause of morbidity and mortality in this population.

Additionally, the elderly population with ACS more commonly presents without chest pain compared to younger patients (up to 20% of elderly patients with MI present with “weakness” as part of their chief complaint). While cardiovascular disease is the leading cause of mortality and morbidity in the elderly, the frequency of ACS amongst this population presenting with nonspecific symptoms is unknown.

Reference: Wang et al. Troponin Testing and Coronary Syndrome in Geriatric Patients With Nonspecific Complaints: Are We Overtesting? AEM January 2020

Population: Patients aged 65 years and older presenting to the emergency department with nonspecific chief complaints who underwent troponin testing. “Nonspecific” was designed a priori as including weak or weakness, dizzy or dizziness, fatigue, lethargy, altered mental status, light-headedness, medical problem, examination requested, failure to thrive, or “multiple complaints.”

Intervention: Troponin testing

Comparison: None

Exclusions: If they had a focal chief complaint (ex. focal pain, injury complaint, shortness of breath, vomiting, diaphoresis, syncope, fever, cough, focal neurologic deficit)or fever of at least 38C at triage.

Outcomes:

- There were multiple outcomes of interest:
  - The proportion of patients with nonspecific complaints who underwent troponin testing.
  - The proportion of such patients who had elevated troponin.
  - The proportion of patients with ACS at the index visit or within 30 days.
  - The utility of troponin testing to diagnose or exclude ACS.
  - The frequency of other causes of troponin elevation in this population.

Authors' Conclusions

"While consideration for ACS is prudent in selected elderly patients with nonspecific complaints, ACS was rare and no patients received reperfusion therapy. Given the false-positive rate in our study, our results may not support routine troponin testing for ACS in this population."

Quality Checklist for a Chart Review

- [x] 1. Were the abstractors trained before the data collection?
- [x] 2. Were the inclusion and exclusion
- [x] 3. Were the variables defined?
- [x] 4. Did the abstractors use data abstraction forms?
- [x] 5. Was the abstractors' performance monitored?
- [x] 6. Were the abstractors aware of the hypothesis/study objectives?
- [x] 7. Was the interobserver reliability discussed?
- [x] 8. Was the interobserver reliability tested or measured?
- [x] 9. Was the medical record database identified or described?
- [x] 10. Was the method of sampling described?
- [x] 11. Was the statistical management of missing data described?
- [ ] 12. Was the study approved by the institutional or ethics review board?

Quality Checklist for Observational Study

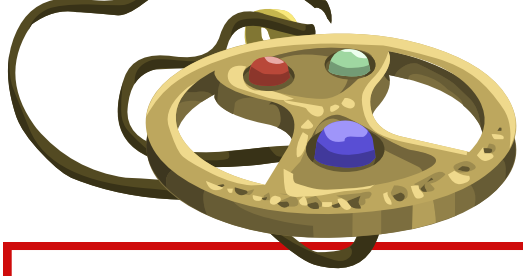
- ☑ 1. Did the study address a clearly focused issue?
- ☑ 2. Did the authors use an appropriate method to answer their question?
- ☑ 3. Was the cohort recruited in an acceptable way?
- ? 4. Was the exposure accurately measured to minimize bias?
- ☑ 5. Was the outcome accurately measured to minimize bias?
- ? 6. Have the authors identified all-important confounding factors?
- ☒ 7. Was the follow up of subjects complete enough?
- ☒ 8. How precise are the results? Fairly precise given the small sample size
- ☑ 9. Do you believe the results?
- ? 10. Can the results be applied to the local population?
- ? 11. Do the results of this study fit with other available evidence?

Case Outcomes

Key Results:
They initially identified 1,146 potentially eligible patients. After excluding the patients who had a specific complaint listed and those with documented fever, they were left with a total of 594 patients. Of those, 69% had troponins ordered.

The average age of the cohort was 78 years old, 58% were female, and 75% were admitted. The most common chief complaints were altered mental status (43%), weakness/fatigue (33%), and dizziness (21%).

1. The proportion of patients with nonspecific complaints who underwent troponin testing: 412/594 (69%)
2. The proportion who had an elevated troponin in the ED: 52/412 (12.6%) (Another 30 patients had an elevated troponin at some point during their hospital stay)
3. The proportion of patients with ACS at the index visit or within 30 days: 5/412 (1.2%) All occurred during the index admission.
4. The utility of troponin testing to diagnose or exclude ACS. Looking only at the first troponin in the ED, it was 80% sensitive and 88% specific (NPV = 99.7%, PPV = 7.7%) for ACS. The LR+ was 6.67, and LR– was 0.23. Considering all troponins, the sensitivity was 100% (95% CI = 48%–100%), the specificity was 81% (95% CI = 77%–85%), the NPV was 100%, and the PPV was 6.1%.
5. The frequency of other causes of troponin elevation in this population. There was a long list of non-ACS causes of troponin elevation. The top 3 causes were: dehydration, heart failure, and atrial fibrillation.



Time to Talk Nerdy

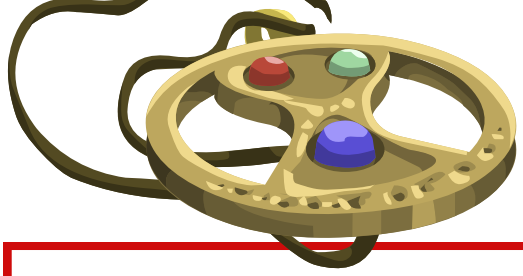
We asked Dr. Wang ten questions to get a greater understand of his publication. Listen to the SGEMHOP podcast to hear all of Dr. Wang's answers.

1. Defining *"Non-Specific"***:** The definition of "non-specific" symptoms is problematic while at the same time being pragmatic. For instance, "dizzy" could be construed as non-specific, but what if the patient had supporting focalized neurologic complaints? Additionally, some physicians list the chief complaint as the leading sentence a patient provides. This is problematic if a patient initially cites a "non-specific" complaint, but then describes suggestive ACS symptoms in their HPI. Conversely, "focal" chief complaints such as "shortness of breath" can be construed as non-specific in real practice based on the patient's HPI, but due to the paper's inclusion criteria, if any triage nurse or physician labeled a chief complaint as "focal" they would be excluded.

2. Chief Complaints Not Equal: Definitions of nonspecific included a spectrum of complaints, from altered mental status to failure to thrive. I imagine the yield of testing is much higher in altered mental status than it is in failure to thrive. Would there be a benefit of considering these chief complaints separately?

3. Retrospective Charting: You excluded patients who had nonspecific complaints at triage, but had a focal complaint listed in the ED physician note. The ED physician note might have been written after the troponin result was known. In the presence of a positive troponin, focal complaints might have been emphasized, despite being originally nonspecific.

4. Definition of ACS: You did a good job prospectively defining what would count as ACS based on objective measures.



Time to Talk Nerdy

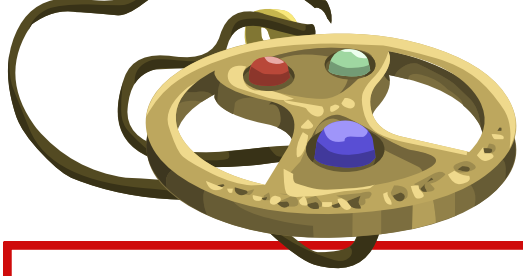
However, neither the decision to take a patient for revascularization nor stress testing are perfectly associated with ACS. The result is a possible over call of patients with ACS. On the other hand, based on the information provided, I don't think we can be 100% certain that the 5 patients diagnosed with ACS truly had ACS.

5. Use of A Single Troponin: Even before the use of high sensitivity troponins, troponin testing has never been binary. There have always been a large number of patients in a grey area, where clinician judgement or repeat testing is required. Here, you judge the value of troponin testing based on a single test. Do you think that troponin testing would have been more accurate if multiple values or the physicians' interpretation were considered?

6. Troponin Assays: The study also utilized two different troponin assays: A troponin I point of care whole blood assay (istat, Abbott) with cutoff of 0.08, based on 99th percentile, was primarily used in the ED. Inpatient troponin testing was performed with a troponin I fourth generation (Access, Beckman Coulter). The cutoff was 0.04, also based on 99th percentile. It is unclear whether these two measurements were of equal accuracy.

7. Rise and Fall in Troponin: You describe 30 patients who had a negative troponin in the ED and a positive troponin later during their hospital stay. Part of the definition of MI is a rise and fall in troponin, so these patients seem to fit that definition. What criteria was used to exclude ACS in these patients despite the objective evidence of cardiac ischemia?

8. Selection Bias: Rather than looking at all patients with non-specific complaints, you only looked at the patients in whom a clinician decided to send a troponin. Presumably, as compared to the patients with the same chief complaints without a troponin drawn, these are higher risk patients.



Time to Talk Nerdy

9. Positive Predictive Value: Although the sensitivity and specificity numbers look reasonably good, there were more than 10 false positives for every true positive. That results in a positive predictive value of only 6-7%.

10. Deaths: There were 32 deaths during the 30 day follow up period, as compared to only 5 diagnoses of ACS. Considering the inaccuracy in determining cause of death, might some of these patients actually have been missed ACS, and if so, how would have that altered your results?

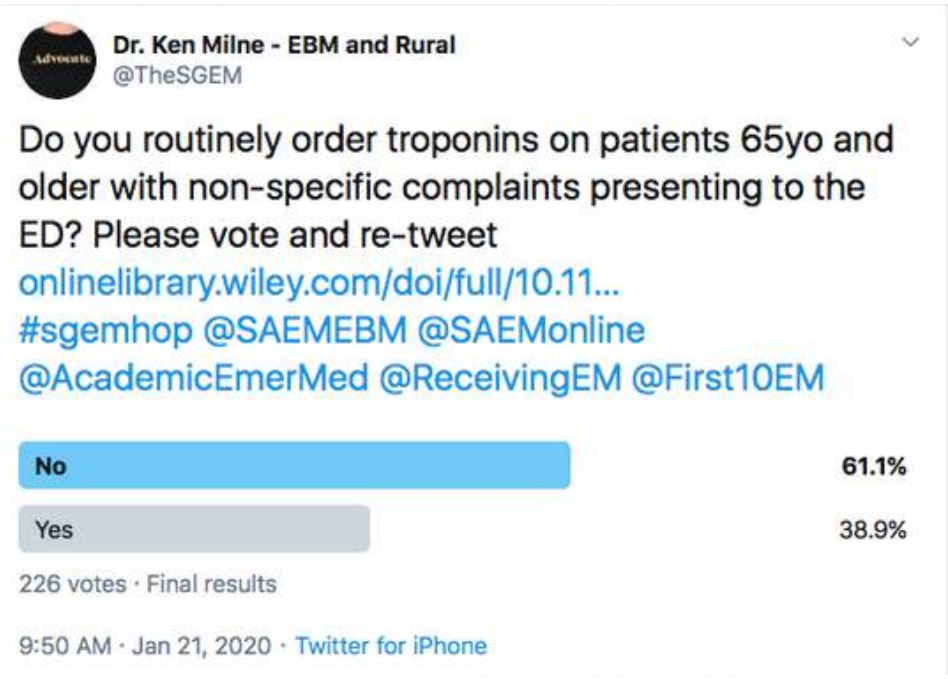
Comment on Authors' Conclusion Compared to SGEM Conclusion: We agree that, although ACS can have atypical presentations in elderly populations, the results don't support routine troponin testing for all patients with nonspecific complaints.

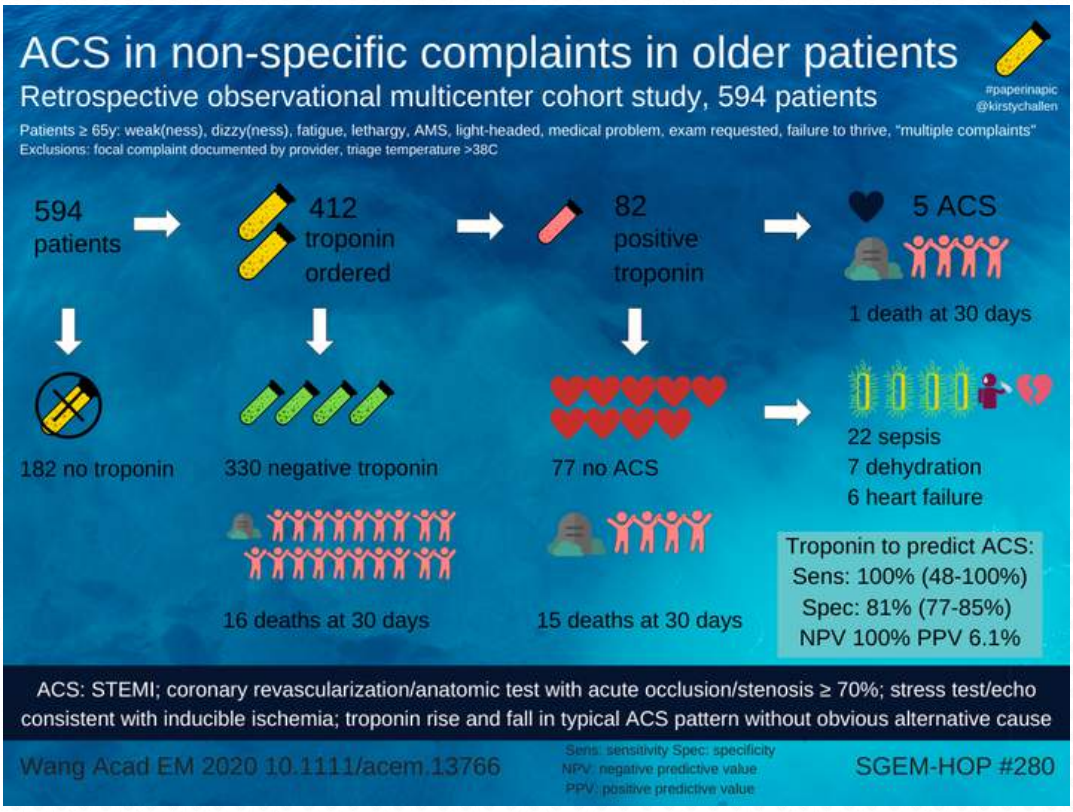
Clinical Application: The yield of troponin testing was low in this single centre retrospective cohort. However, the troponin testing may have led physicians to change the chief complaint from something non-specific to something focal, eliminating patients from this trial. It is therefore difficult to recommend any practice changes based on these results.

What Do I Tell the Patient? Based on the symptoms you are describing to me, it is very unclear what is causing your symptoms, but I think that a heart attack is very unlikely. We could send a blood test to help check on your heart, but with your symptoms the tests are wrong more often than they are right, so we might end up having to do even more tests. The other option would be to observe you over the next day, and only add the heart tests if we can't figure out what is going on or you develop new symptoms"

Case Resolution: Despite the resident's concern, you decided to order a troponin anyway, and you are relieved you did when it comes back positive. However, 3 weeks later when reviewing the patient's course, you notice that he had a significant bleed during an angiogram and the cardiologist ultimately determined that the troponin was a false positive.

Episode End Notes





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EM DOCS GOT AN AMBUBAG - THE PREVENT TRIAL

Clinical Question:

Is a bag-mask ventilation (BMV) performed during the apneic period of RSI (defined as the time between administration of RSI medicaitons and intubation) in critically ill adults safe and effective?

Bottom Line:

It is unclear if bag-mask ventilation in critically ill adult patients requiring intubation provides a clinically important benefit or is safe.

Guest:

Andrew Merelman is a critical care paramedic and second year medical student at Rocky Vista University in Colorado. His primary interests are resuscitation, critical care, airway management, and point-of-care ultrasound.

Case Overview

Case: A 60-year-old male is in your emergency department with sepsis from pneumonia. He has worsening work of breathing and a decreasing level of consciousness. You decide based on his clinical presentation that he needs to be intubated. Due to his already poor oxygenation, you are concerned about him desaturating during intubation and wonder if there is anything you can do to help prevent it**.**

Background: Emergency medicine is often referred to as the ABC (Airway, Breathing and Circulation) specialty. We have covered airway a few times on the SGEM:

- SGEM#75: Video Killed Direct Laryngoscopy?
- SGEM#96: Machine Head – NIPPV for Out of Hospital Respiratory Distress
- SGEM#247:Supraglottic Airways Gonna Save You for an OHCA?
- SGEM#249: Ace in the Hole – Confirming Endotracheal Tube Placement with POCUS
- SGEM#271: Bougie Wonderland for First Pass Success

Rapid Sequence Intubation (RSI) has been a mainstay of emergency airway management for years. However, there are aspects of the procedure that have been debated, one of which is how best to oxygenate the patient during the apneic period while not increasing rates of aspiration.

Reference: Casey et al. Bag-Mask Ventilation during Tracheal Intubation of Critically Ill Adults. NEJM February 2019

Population: Adults patients (older than 17 years of age) undergoing induction and tracheal intubation in the intensive care unit.

Exclusions: Patients who were pregnant, incarcerated, had immediate need for intubation or if the treating clinicians felt that ventilation was indicated or contraindicated between induction and laryngoscopy.

Intervention: Bag-mask ventilation (BMV) during the time between administration of sedation/paralysis and insertion of the laryngoscope into the mouth for intubation.

Comparison: Apnea with or without nasal cannula oxygen during the time between administration of sedation/paralysis and insertion of the laryngoscope into the mouth for intubation.

Outcomes:

- **Primary Outcome:** The lowest oxygen saturation observed during the interval between induction and two minutes after tracheal intubation.
- **Secondary Outcome:** The incidence of severe hypoxemia (oxygen saturation of less than 80%).

Authors' Conclusions

"Among critically ill adults undergoing tracheal intubation, patients receiving bag-mask ventilation had higher oxygen saturations and a lower incidence of severe hypoxemia than those receiving no ventilation."

Quality Checklist for Randomized Control Trials

- ☒ 1. The study population included or focused on those in the emergency department.
- ☑ 2. The teams were adequately randomized.
- ☑ 3. The randomization process was concealed.
- ☑ 4. The teams were analyzed in the groups to which they were randomized.
- ? 5. The study teams were recruited consecutively (i.e. no selection bias).
- ☒ 6. The teams in both groups were similar with respect to prognostic factors.
- ☒ 7. All participants (patients, clinicians, outcome assessors) were unaware of group allocation.
- ☒ 8. All groups were treated equally except for the intervention.
- ☑ 9. Follow-up was complete (i.e. at least 80% for both groups).
- ☒ 10. All (team) patient-important outcomes were considered.
- ? 11. The treatment effect was large enough and precise enough to be clinically significant.

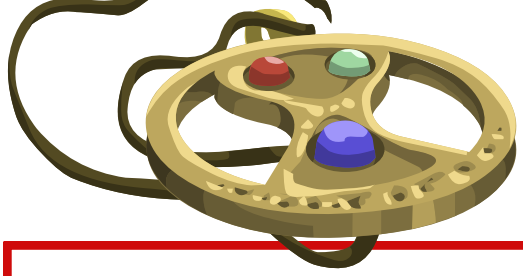
Case Outcomes

Key Results:
They screened 667 patients and enrolled 401. The median age was 60 years, 56% were male and half the patients had sepsis or septic shock.

Bag-mask ventilation group had higher oxygen saturations and less severe hypoxemia compared to the control group.

- **Primary Outcome:** Lowest oxygen saturation
  - 96% (interquartile range, 87% to 99%) in the BMV group vs. 93% (interquartile range, 81% to 99%) in the no-ventilation group (P = 0.01).

- **Secondary Outcome:**
  - 21 patients (11%) in the BMV group had severe hypoxemia vs. 45 patients (23%) in the no-ventilation group (relative risk, 0.48; 95% CI: 0.30 to 0.77).



Time to Talk Nerdy

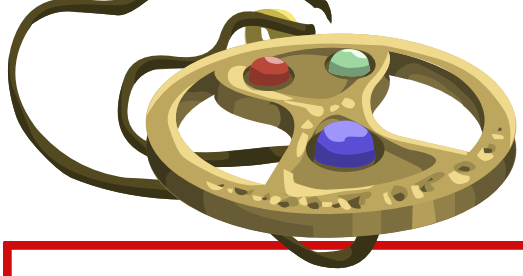
1. Patients: Patients in this study were recruited from seven academic intensive care units (ICUs) in the United States. Eighty percent of the patients were intubated for respiratory failure. While many adult patients in the emergency department are intubated for the same reason many others are intubated of cardiac arrest and trauma depending on your place of practice. It is unclear if this study population has external validity outside the ICU and to the emergency department.

Another thing about the patients who were excluded. The study did not enroll those patients judged to be a very high risk of desaturation or aspiration, had hypoxemia, or had acidemia. These patients are ones that we potentially care more about when it comes to peri-intubation oxygenation and ventilation, so it is difficult to say if these results are generalizable to this population.

2. Consecutive Patients: They claim that patients were recruited consecutively. However, selection bias could have been introduced. Patients could be excluded if they required immediate intub ation or if the treating clinicians felt that ventilation was indicated or contraindicated between induction and laryngoscopy.

This is pragmatic but it does introduce subjectivity into the process and could have resulted in bias. It is unclear if this would have any meaningful impact on the results.

3. Prognostic Factors: A quality indicator for an RCT is that both the intervention group and control group are similar with regards to prognostic factors. There were statistical differences between the two groups with 10% more patients having pneumonia and 6% less having a gastrointestinal bleeding in the control group.



Time to Talk Nerdy

4. Treated Equally: Another quality indicator is that both groups are treated equally except for the intervention. That was not the case in this trial. The BMV group was more likely to be preoxygenated with a BMV (40% vs 11%) while the no ventilation group was more likely to be preoxygenated with NiPPV (24% vs 16%). Preoxygenation can have an impact on likelihood of desaturation during intubation.

- Note: The BMV ventilation in this trial was extremely well done. The providers in the trial were trained to provide appropriate rates, volumes, and adequate mask seal. This is not typical in most emergency departments.

5. DOOs, MOO and POO: Their primary and secondary outcomes were disease-oriented outcomes (DOOs) or monitor-oriented outcomes (MOOs). The median lowest oxygen saturation and incidence of severe hypoxia are surrogate markers and do not represent a patient-oriented outcome (POO).

They did look at a number of exploratory-oriented outcomes (EOO) for safety (ex. aspiration, new opacity on chest x-ray and cardiac arrest) and efficacy (ex. mortality, days in ICU and ventilator-free days). However, they did not include what could be considered the most important POO, survival with good neurologic outcome.

Comment on Authors' Conclusion Compared to SGEM Conclusion: We generally agree with the authors' conclusions but would also add that a statistical difference in a DOO does not necessarily translate into a clinically important POO.

Clinical Application: Due to the multiple limitations identified in this trial it is difficult to know how to clinically apply this data.This is a common problem faced by clinicians practicing evidence-based medicine. The literature informs and guides our care but should not dictate our care. When we do not have definitive literature for efficacy or safety we must rely more upon our clinical judgement. In addition, we do not know if BMV will result in a clinically important outcome (survival with good neurologic outcome). This does not mean we should not perform very good preoxygenation prior to intubation.

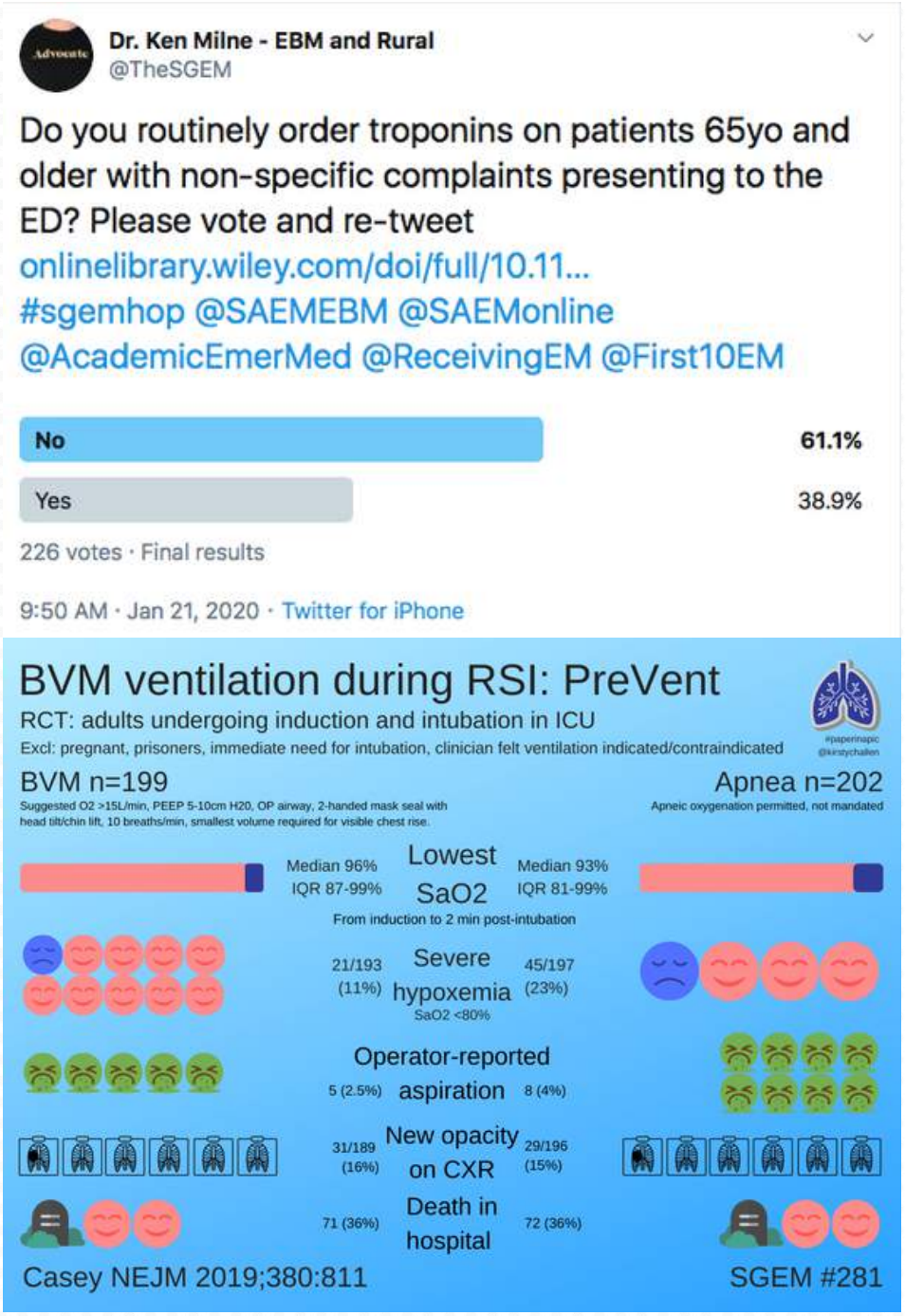
What Do I Tell the Patient? You have pneumonia and it is making it difficult for you to breath. We can help by putting a tube in your throat. This will make it easier to breath and give time for the antibiotics to work. This can be scary. Before we would put the tube down your throat you would get some extra oxygen. Then, if you say OK to the tube, you will get some medicine to relax you and so you will not remember the experience. We will do everything possible to make sure this is successful and there are no complications.

Case Resolution: Because the patient is at high risk of desaturation during intubation, you make a plan that optimizes preoxygenation. You use your clinical judgment and provide gentle, controlled bag-mask ventilation during the apneic period to prevent desaturation.

Episode End Notes

Other FOAMed:

- First10EM: PreVent Trial
- EM Nerd: The Case of the Conspicuous Conclusion
- REBEL EM: PreVent BMV Prior to Intubation
- The Resus Room: Managing the Apneic Period – The PreVent Trial
- St. Emlyn's: Ventilation During RS
- The Bottom Line: PreVent2



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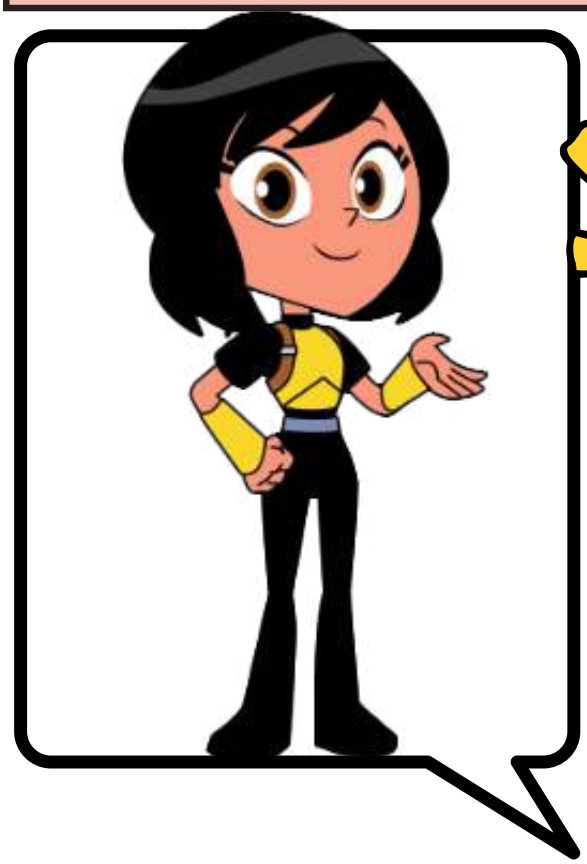
IT'S ALL 'BOUT THAT BAYES, 'BOUT THAT BAYES- NO TROUBLE - IN DIAGNOSING PULMONARY EMBOLISM

Clinical Question:

Can a clinical pretest probability-based D-dimer safely rule out the diagnossi of pulmonary embolism without imaging?

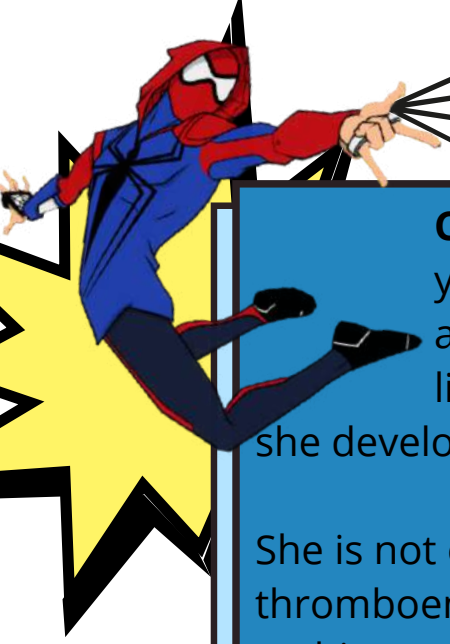


Bottom Line:

It is reasonable to use the PEGed strategy to safely rule out PE in low risk patients.

Guest:

Dr. Nour Khatib is an emergency physician at Lakeridge Health and Sunnybrook Hospital. She is also one of the organizers of the EM Vision 2020 conference.



Case Overview

Case: You are caring for a 33-year-old female who comes to your emergency department with chest pain. She was attending the incredible EM Vision 2020 conference and while listening to Dr. Alan Drummond talk about over over-crowding, she developed sudden onset of pleuritic chest pain.

She is not on any hormone replacement therapy, no history of venous thromboembolism, has not been immobile, has no hemoptysis and has no history of malignancy. Her vital signs are as follows: heart rate 105 beats/minute, blood pressure 110/70, respiratory rate 18 breaths/minute, oxygen saturation 96% on room air. You order a d-dimer test to rule out pulmonary embolism (PE) and it comes back at 850 and your first reaction is DOH!!

You think to yourself, “well my hands are tied” and you are about to order the CT angiogram when you remember hearing about a PEGeD study. She is Well’s score low, but how are you going to handle that elevated d-dimer?

Background: There is a reason why pulmonary embolism is covered so often on The SGEM and other podcasts (SGEM#51, #126, #163, and #219); it’s a diagnosis we are appropriately trained to always think of but it presents itself with symptoms that are common in a variety of other conditions.

Of course, how can we forget the DDD threat – the Dreaded D-Dimer. It is a highly sensitive test but with low specificity. For the longest time we treated it like a binary test. If the DDD is positive (>500ng/ml), then further imaging (CTA or VQ). If the DDD is negative (<500ng/ml) we do are happy dance and no further testing.

We need to talk a little bit about Bayesian thinking. Thomas Bayes was an English statistician, philosopher and Presbyterian minister, a real renaissance man. He is best known for a theorem that he never published.

Bayes was trying to mathematically prove divinity but kept finding that observed miracles could be explained by random chance. It was Richard Price who went through his notes and published the theorem after his death. The main thing about Bayesian thinking is that posterior probability is dependent on prior probability. It is really how we think as clinicians. We take a look at some information (history, physical examination and tests) and we interpret it, based on our clinical experience (pre-test probability). All information needs to be interpreted. Bayes can help us with that part.

There have been a few changes to the DDD over the last few years. One thing that has changed my practice is the ADJUST PE Study (Righini et al JAMA 2014). That is where you take the patient's age over 50 and times it by 10. The result is the new upper limit for the DDD. If the patient is 68 years of age, a d-dimer less than 680 is considered negative or rules out a PE. It is still binary but the cut-off is variable.

We the ADJUST PE Study with Dr. Kirsten de Witt out of McMaster University on SGEM#112. She is one of the authors on this study we are reviewing today.

Another change is using the YEARS criteria in diagnosing PE. Just to remind everyone about the three items of the YEARS criteria are:

1. Clinical signs of DVT
2. Hemoptysis
3. PE most likely diagnosis

If your YEARS score is zero you can use a d-dimer cut-off of 1,000ng/ml which is double the usual cut-off of 500ng/ml. If the YEARS score is 1 or greater than you use the traditional d-dimer of 500ng/ml.

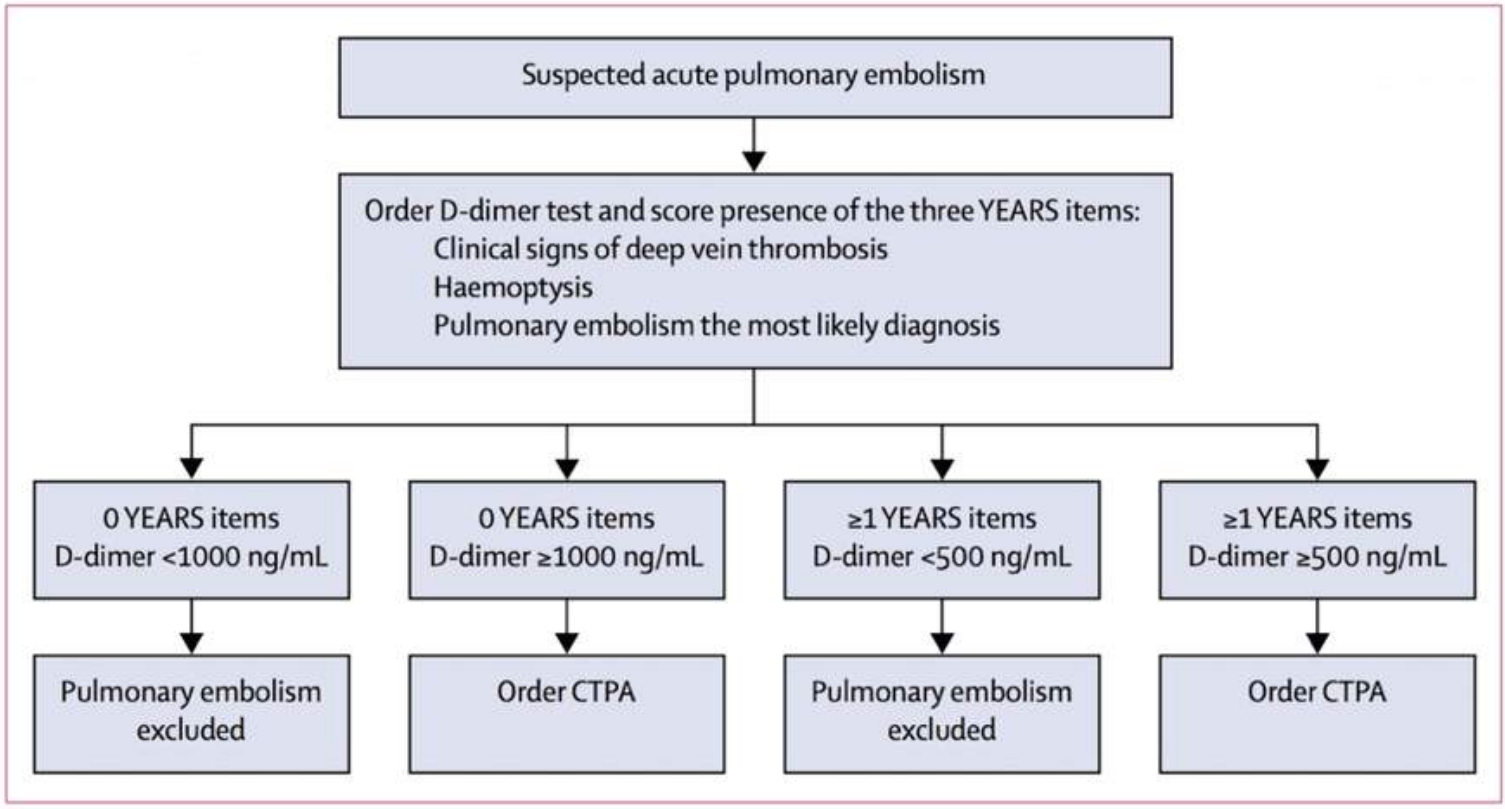


Figure 1: **YEARS algorithm**
CTPA=computed tomography pulmonary angiography.

We recently covered the study looking at pregnancy-adapting the YEARS algorithm on SGEM#277. That was another LIVE episode that was recorded at the Kewartha EM conference in Peterborough with the wonderful Dr. Theresa Robertson. We felt this new algorithm was not ready for prime time until externally validated.

Now there is the PEGed study or the Pulmonary Embolism Graduated D-dimer study looking at clinical pre-test probability (C-PTP).

Reference: Kearon C et al. Diagnosis of Pulmonary Embolism with D-dimer Adjusted to Clinical Probability. NEJM 2019.

Population: Adults (18 years of age or older) from the emergency department or outpatient clinic with signs or symptoms of possible pulmonary embolism

Exclusions:

- < 18 years of age
- Received full-dose anticoagulant therapy for 24 hours
- Undergone major surgery in the past 21 days
- had a D-dimer level that was known before the C-PTP was assessed
- had undergone chest imaging contrary to the protocol (i.e., before the C-PTP was documented, or despite having a D-dimer level of <1,000 ng/ml for a low C-PTP or <500 ng/ml for a moderate C-PTP)
- had undergone contrast-enhanced CT of the chest for another reason
- had an ongoing need for anticoagulant therapy (example diagnosed with A fib)
- had a life expectancy of less than 3 months,
- Pregnant
- geographically inaccessible for follow-up

Intervention: This was a diagnostic accuracy study of the risk of PEusing the Well's criteria to assess clinical pre-test probability

- Low Risk: Well's score 0 to 4 (d-dimer of <1,000 ng/ml was used to rule out patients with low C-PTP)
- Moderate Risk: Well's Score 4.5 to 6 (d-dimer of <500 ng/ml was used to rule out patients with moderate risk)
- High risk: Well's Score 6.5 or greater and would receive diagnostic imaging (generally, CTPA) with no d-dimer testing

Comparison: Standard strategy where d-dimer cut-off is 500 ng/ml, YEARS protocol and an age-adjusted D-dimer

Outcomes:

- **Primary Outcome:** The incidence of venous thromboembolism (VTE) at three-month follow up among the low and moderate clinical pre-test probability groups who had negative (adjusted) d-dimers and did not receive any anticoagulation.

- **Secondary Outcome:** The percentage of patients with VTE in predefined subgroups, bleeding events and deaths and the percentage of patients who avoided diagnostic imaging and had a low C-PTP and a d-dimer under 1,000 ng/ml or those with moderate C-PTP and a d-dimer less than 500 ng/ml.

Authors' Conclusions

"A combination of a low C-PTP and a D-dimer level of less than 1000 ng per milliliter identified a group of patients at low risk for pulmonary embolism during follow-up"

Quality Checklist for Observational Study

- [x] 1. Did the study address a clearly focused issue?
- [x] 2. Did the authors use an appropriate method to answer their question?
- [ ] 3. Was the cohort recruited in an acceptable way?
- [x] 4. Was the exposure accurately measured to minimize bias?
- [x] 5. Was the outcome accurately measured to minimize bias?
- [x] 6. Have the authors identified all-important confounding factors?
- [x] 7. Was the follow up of subjects complete enough?
- [x] 8. How precise are the results? Fairly precise given the small sample size
- [x] 9. Do you believe the results?
- [x] 10. Can the results be applied to the local population?
- [x] 11. Do the results of this study fit with other available evidence?

Case Outcomes

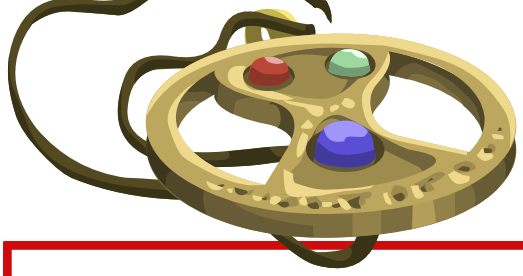
Key Results:
They enrolled a total of 2,017 patients in the study (1,752 low risk C-PTP, 218 moderate risk C-PTP and 47 high risk C-PTP). The mean age was 52 years and two-thirds were female.

- **Primary Outcome:** VTE in low or moderate C-PTP patients at 3 months was 0% (95% CI; 0% to 0.29%). There was one patient in the low-risk group had a + d-dimer test of 1,200ng/ml and a negative CT PE, was found to have a PE at follow up.

- **Secondary Outcome:**
  - Percentage of patients with VTE in predefined subgroups after initial testing and anticoagulant therapy: Low 1.15%, Moderate 0% and High 0%.
  - Bleeding Events: Seven major and 23 minor bleeding episodes
  - Deaths: None of the 34 deaths were attributed to PE
  - Avoiding Diagnostic Imaging: Reduced by 17.6% (51.9% with YEARS and 34.3% with PEGeD).

Table 3. Number of D-Dimer Tests and Chest Imaging Examinations with the PEGeD Strategy as Compared with Other Diagnostic Strategies.*

Diagnostic Strategy	Low C-PTP (N=1752)		Moderate C-PTP (N=218)		High C-PTP (N=47)		All Patients (N=2017)	
	D-Dimer Test	Chest Imaging†	D-Dimer Test	Chest Imaging†	D-Dimer Test	Chest Imaging†	D-Dimer Test	Chest Imaging†
PEGeD	1752	467	218	178	0	47	1970	692
Standard‡	1752	782	0	218	0	47	1752	1047
Difference: PEGeD – standard	0	–315	218	–40	—	0	218	–355
Age-adjusted§	1752	654	218	164	0	47	1970	865
Difference: PEGeD – age-adjusted	0	187	0	14	—	0	0	–173
YEARS¶	1752	520	218	176	47	37	2017	733
Difference: PEGeD – YEARS	0	–53	0	2	–47	10	–47	–41



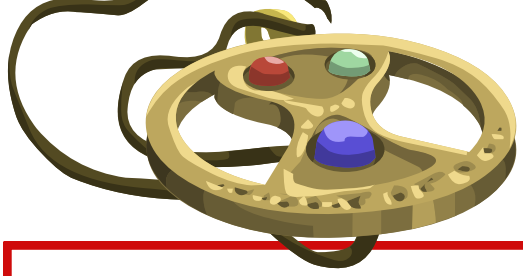
Time to Talk Nerdy

1. Patients: Most of the patients included in the study were considered low risk (87%). There were only 11% (218/2017) moderate risk patients and 2% (47,2017) high risk patients. Then when you look at those who were stratified as low risk, only 5% of those patients had a PE. If you look back at some of the original studies on diagnosing PE (PIOPED 1990) the low risk group had about more than double that rule-in rate around 12%. This suggests that these were not low risk but very low risk patients. This can increase the diagnostic strategy given the low prevalence of disease. Even the moderate risk patients had a rule in rate of 20% compared to PIOPED that was 33%.

2. Selection Bias: It is important to always look at who was included and excluded from the study. The authors lay out a clear exclusion criterion. However, some of the exclusion criteria were subjective (ex: life expectancy < 3 months). This could lead to some section bias in excluding patients. With regards to inclusion criteria, it is unclear how these patients were specifically recruited. They did not explicitly state in the manuscript that it was consecutive patients presenting to the clinic or emergency department. The methods section says the study population included those patients with signs or symptoms suggestive of pulmonary embolism. This is pragmatic, uses clinical judgment/gestalt but is also subjective. That lack of clear objective inclusion criteria also could introduce some selection bias.

3. Comparison: No direct comparison between this study and current practice (age-adjusted and YEARS algorithm), the secondary analysis was done in retrospect.

4. Confirms YEARS: The study provides more evidence for what we have already suspected with the YEARS study. That is where we learned that we can apply a <1,000ng/ml d-dimer limit for patients with low pretest probability. Furthermore, the YEARS algorithm was validated in pregnant patients which this study excluded. The results from the moderate pretest



Time to Talk Nerdy

probability group where they tried to rule out PE based on a value of 500ng/ml are inconclusive given the low number of moderate risk participants.

5. External Validity: They reported a potential 18% reduction in imaging using a PEGeD strategy comparted to YEARS. Less imaging results in less incidentalomas, over diagnosing, over treating, less harm and less cost. While it is very good to reduce imaging, we are wondering how persuasive this will be on some clinicians? This study was conducted in Canada. What would be the impact in other countries like the USA? They face much different medical legal pressure and patient expectations. It would be great to see an impact analysis done in different practice environments.

Comment on Authors' Conclusion Compared to SGEM Conclusion: We generally agree with the authors' conclusions.

Clinical Application: Adjusting d-dimer threshold to less than 1,000 ng/ml for low risk clinical pre-test probability patients can reduce imaging and appears safe.

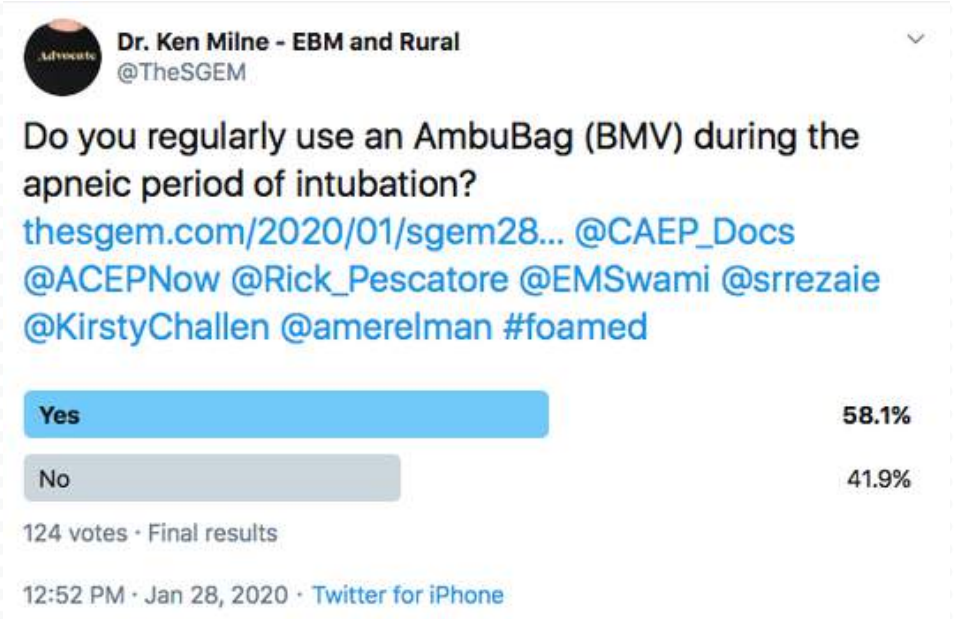
What Do I Tell the Patient? We were concerned you might have had a blood clot in your lung. This can be very serious and even deadly problem. We ran some blood tests and they were normal. It's very unlikely you have a blood clot. Now we need to look for other causes of your chest pain.

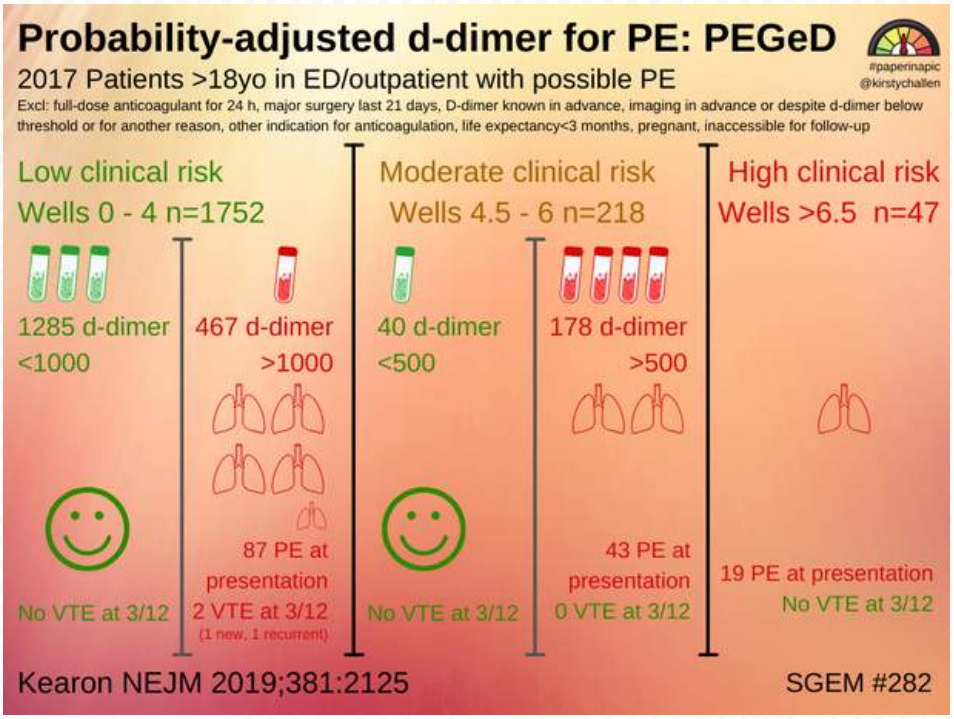
Case Resolution: With our patient who is low risk C-PTP and a d-dimer under 1,000 ng/ml, it is reasonable to rule out PE and forgo any further chest imaging in our Canadian practice environment.

Episode End Notes

Other FOAMed:

- REBEL EM
- EM Literature of Note
- The Bottom Line





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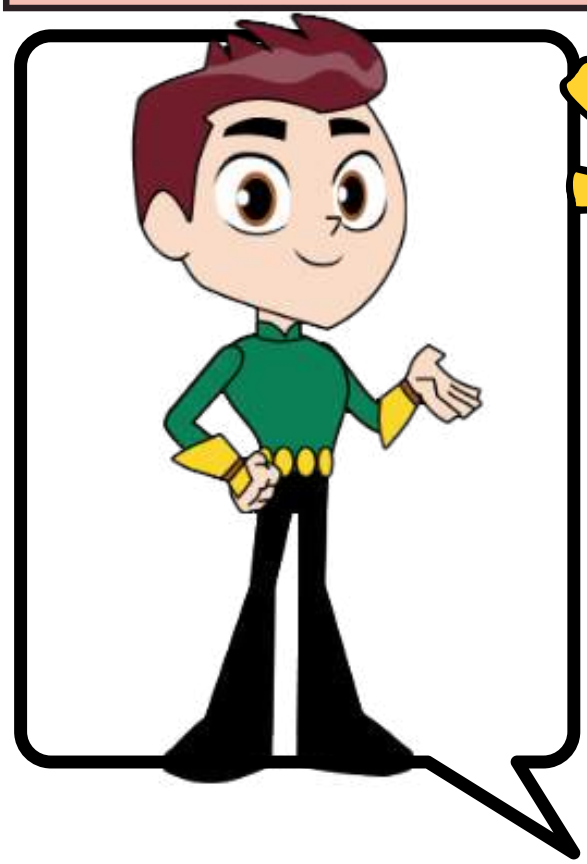
CAN YOU BE ABSOLUTELY RIGHT IN DIAGNOSING A SAH USING A CLINICAL DECISION INSTRUMENT?

Clinical Question:

What is the clinical impact of the Ottawa SAH rule and the 6-hour CT rule compared to standard care when implemented in six emergency departments across Camada?



Bottom Line:

The Ottawa SAH rule is hgihly sensitive but has very poor specificity. It is unclear how it performs against unstructured clinical judgement or in non-urban tertiary care teaching hospitals. WHile the 6-hr CT rule has a high sensitivity, it is not 100%

Guest:

Dr. Rory Spiegel is an EM/CC doctor who splits his time in the Emergency Department and Critical Care department. He also has this amazing #FOAMed blog called EM Nerd.

Case Overview

Case: A 48-year-old male presents to your emergency department with a sudden onset headache, which started about one-hour prior to arrival. The headache is severe is quality and the patient does not have a history of similar headaches in the past. It is associated with nausea, vomiting and photophobia.

Background: Headaches are a common complaint presenting to the emergency department. Subarachnoid hemorrhage represents one of the most serious underlying causes of headaches and we have covered it a number of times on the SGEM:

- SGEM#48: Thunderstruck – Subarachnoid Hemorrhage
- SGEM#134: Listen, to what the British Doctors Say about LPs post CT for SAH
- SGEM#140: CT Scans to Rule Out Subarachnoid Hemorrhages in A Non-Academic Setting
- SGEM#201: It's in the Way That You Use It – Ottawa SAH Tool

In patients who present neurologically intact making the diagnosis early is key to preventing subsequent more life-threatening bleeding. A number of controversies surround the diagnosis of SAH in the emergency department. Two of the more provocative are the use of the Ottawa SAH Rule and whether a lumbar puncture (LP) is required following a negative CT if the scan is performed within 6-hours of symptom onset.

The Ottawa SAH Rule (tool) was covered on SGEM#201. The bottom line from that study was that the clinical decision instrument needed external validation, a meaningful impact analysis performed and patient acceptability of incorporating this rule into a shared decision-making instrument before being widely adopted.

We were surprised that in their background/introduction material they did not include the excellent SRMA on this topic by Carpenter et al. AEM 2016.

Reference: Perry et al. Prospective Implementation of the Ottawa Subarachnoid Hemorrhage Rule and 6-Hour Computed Tomography Rule. Stroke 2019

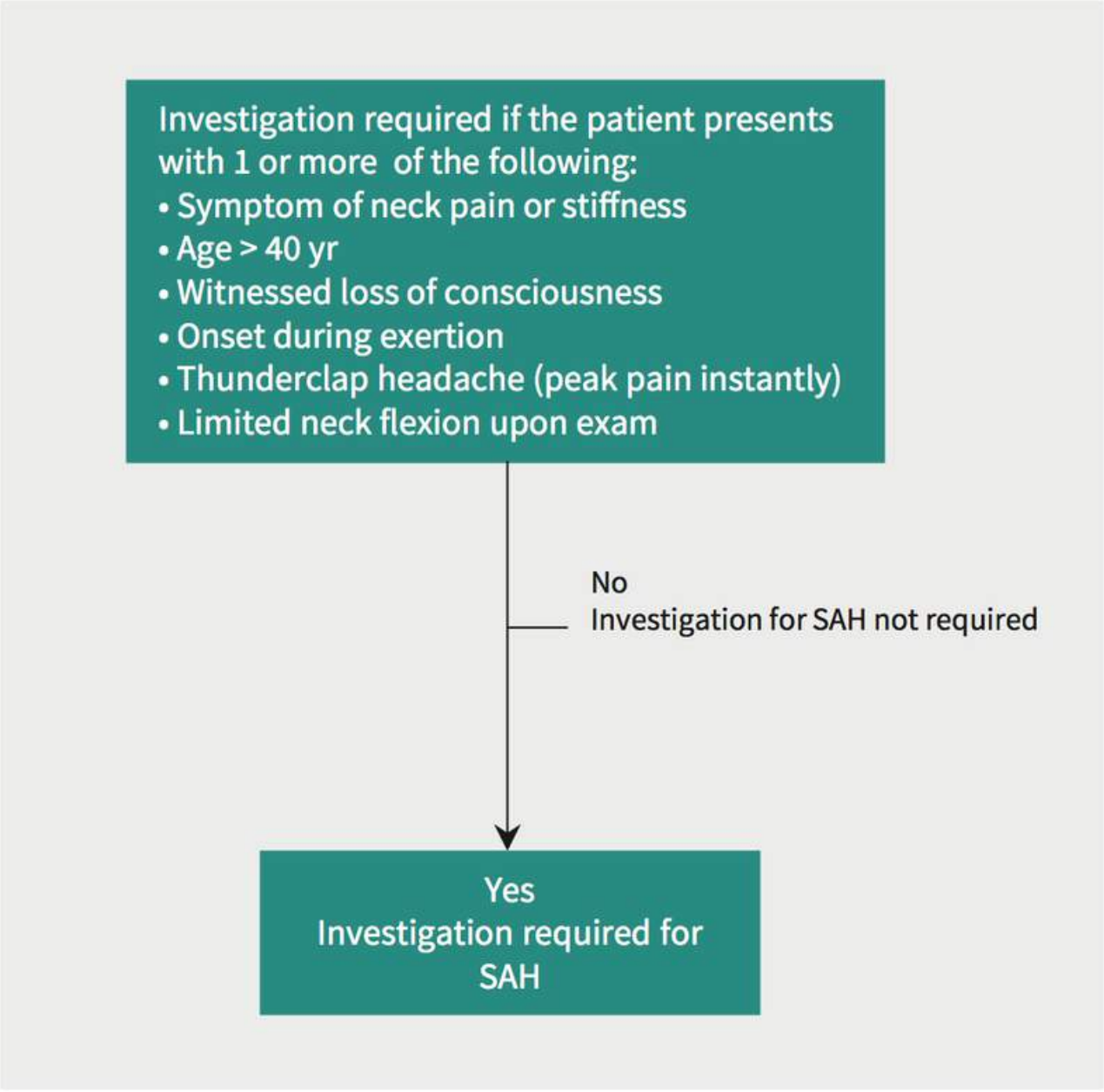


Figure 1: The Ottawa Subarachnoid Hemorrhage (SAH) Rule. Used in alert patients > 15 yr of age with new acute severe nontraumatic headache that reaches maximum intensity within 1 h of onset. Not to be used in patients with new neurological deficits, previous aneurysms, SAH or brain tumors, or a history of similar headaches (≥ 3 episodes over ≥ 6 mo).[10]

Population: Neurologically intact adult presenting to the ED with a chief complaint of a nontraumatic, acute headache, or syncope associated with a headache.

Exclusions: Patients with any of the following:

- 3 or more previous similar headaches (ie, same intensity/character as their current headache) over a period of >6 months (eg, established migraines)
- confirmed SAH before arrival at study ED
- previously investigated with CT and LP for the same headache
- papilledema
- new focal neurological deficit
- previous diagnosis of intracranial aneurysm or SAH
- known brain neoplasm
- cerebroventricular shunt
- headache within 72 hours following a LP
- headache described as gradual or peak intensity beyond 1 hour.

Intervention: Physicians were actively encouraged to use the Ottawa SAH Rule and the 6-hour-CT Ruleto determine when to undergoing diagnostic workups for SAH and when a CT alone with an appropriate workup. Clinicians had the option to override the proposed rules.

Comparison: The control phase was standard care. Clinicians were encouraged to not use any clinical decision instrument and make the decision to pursue diagnostic studies based on their own clinical discretion.

Outcomes: The primary outcome was the clinical impact of the Ottawa SAH Rule and 6-hr CT Rule for making the diagnosis of a SAH compared to usual care. SAH was defined as:

1. Subarachnoid blood on CT
2. Xanthochromia in the cerebrospinal fluid
3. Red blood cells in the final tube of cerebrospinal fluid with an aneurysm demonstrated on cerebral angiography, CTA, or magnetic resonance imaging angiography.

Authors' Conclusions

""This implementation study validates the accuracy of the Ottawa SAH rule and 6-hour-CT rule for SAH. Both the Ottawa SAH rule and the 6-hour-CT rule are now fully validated and ready to use clinically. Using the Ottawa SAH rule did not increase or decrease the number of investigations performed. The 6-hour-CT rule resulted in a modest decrease in testing following a normal early CT. Utilizing the Ottawa SAH rule and the 6-hour-CT rule allows clinicians in ED to safely standardize care for alert, patients with acute headache."

Quality Checklist for a Diagnostic Study

- [x] 1. The clinical problem is well defined.
- [x] 2. The study population represents the target population that would normally be tested for the condition (ie no spectrum bias).
- [x] 3. The study population included or focused on those in the emergency department.
- [x] 4. The study patients were recruited consecutively (ie no selection bias).
- [x] 5. The diagnostic evaluation was sufficiently comprehensive and applied equally to all patients (ie no evidence of verification bias).
- [x] 6. All diagnostic criteria were explicit, valid and reproducible (ie no incorporation bias)
- [x] 7. The reference standard was appropriate (ie no imperfect gold-standard bias).
- [?] 8. All undiagnosed patients underwent sufficiently long and comprehensive follow-up (ie no double gold-standard bias).
- [x] 9. The likelihood ratio(s) of the test(s) in question is presented or can be calculated from the information provided.
- [x] 10. The precision of the measure of diagnostic performance is satisfactory.

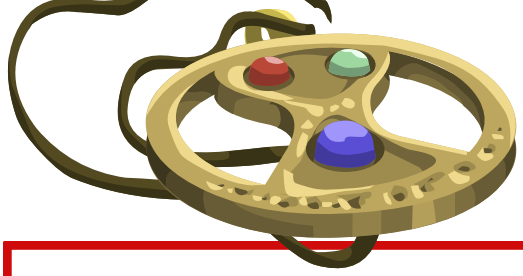
Case Outcomes

Key Results:
They had 3,672 patient that met inclusion criteria. There were 1,743 patients in the control phase of the study and 1,929 patients in the implementation phase of the study when. The mean age was 45 years and 60% were female. They identified 188 (5.1%) of patients had a SAH.

- **Ottawa SAH Rule:**
  - Sensitivity 100% (95% CI 98.1% to 100%)
  - Specificity 12.7% (95% CI: 11.7% to 13.9%)

- **6hr CT Rule:**
  - Sensitivity 95% (95% CI 89.8% to 98.5%)
  - Specificity 100% (95% CI: 99.7% to 100%)

	Usual Care vs. Ottawa SAH Rule
CT Utilization	88.0% vs. 87.5% (p=0.643)
Lumbar Puncture	38.9% vs. 25.9% (p<0.0001
Tests after CT (LP or CTA)	51.3% vs. 42.2% (p<0.0001)
Admissions	9.8% vs. 7.4% (p=0.011)
Mean LOS	6.3hrs vs 6.4hrs (p=0.685)



Time to Talk Nerdy

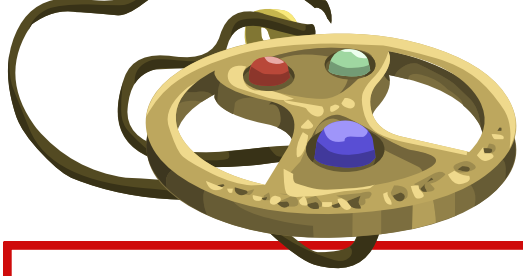
1. Patient Population: This was a pretty wide group of patients which were considered for this study. A rule like Ottawa SAH Rule where the specificity is so low you would ideally like to apply it in a population at high risk for the disease state. So, in patients in whom I am already considering a workup for SAH and if the Ottawa SAH Rule is negative, I can stop the work up. This would be similar to the PERC rule. Applying the Ottawa SAH Rule in a more generalized group of patients may lead to an increase in downstream testing.

In contrast this may have helped the 6-hr CT Rule as not a lot of these patients (5%) ended up having a SAH. Now it did go up to 9% when only the subset of patients presenting within 6-hrs of symptom onset where included.

2. Gold Standard: The gold standard here is a bit complicated. Ideally what you would like is a measure the accurately diagnoses SAH and it would be preferable if the investigators used this same measure on all patients included in the study. But that is not always practical in real world studies. So, in this case you would ideally like if everyone received an LP and then some form of angiography to assess for aneurysm if the LP was positive. Obviously, it's impractical and ethically questionable to perform an LP and angiography on all the patients in this study so the authors had to use different gold standards depending on what was found on the initial CT scan. This can lead to a number if forms of bias.

Incorporation bias occurs when results of the test under study are actually used to make the final diagnosis. This makes the test appear more powerful by falsely raising the sensitivity and specificity.

In this case, subarachnoid blood seen on the CT scan was included in the gold standard definition of SAH. Obviously, this will make the specificity of the CT scan appear really good and, in this case, it was 100%



Time to Talk Nerdy

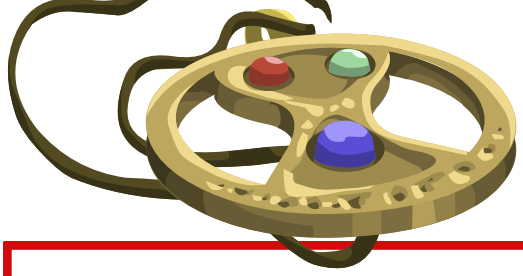
Partial verification bias is a type of measurement bias in which the results of a diagnostic test affect whether the gold standard procedure is used to verify the test result. This type of bias is also known as “work-up bias”or “referral bias”.

In this case, patients with a negative CT did not always undergo an LP. Since not all patients underwent the gold standard testing this can influence the diagnostic accurate of the test in question. In this case the 6-hr CT may appear more accurate than it is reality because if some SAH are missed on CT and having not undergone the LP there is the potential they will be counted as a true negative result.

3. Proxy Outcome Measure: In cases when a consistent gold standard cannot be used on all subjects a proxy measure can be used in its place. In this case the authors used the proxy outcome of alive and well at 6-months as a surrogate as not having an SAH. This seems like a reasonable surrogate. If you had a headache and did not receive any intervention for an aneurysm and did not have a SAH the likelihood that your initial headache was a herald bleed is minimal.

This is known as differential verification bias (double gold standard). This occurs when the test results influence the choice of the reference standard. So, a positive index test gets an immediate/gold standard test whereas the patients with a negative index test get clinical follow-up for disease. This can raise or lower sensitivity/specificity.

The question is what is an adequate definition of not having a SAH on 6-month follow up? The authors used a review the medical records of the hospital which they initially presented as well as every hospital with neurosurgical capacity in the same city as the index ED visit.



Time to Talk Nerdy

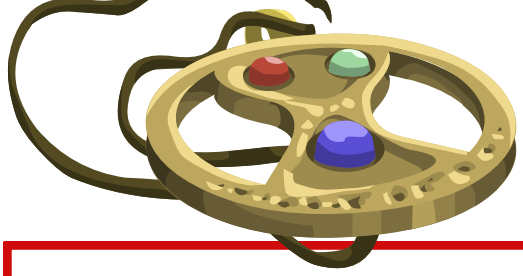
Is this adequate follow up? In previous studies the authors also performed telephone follow-up to further exclude a subsequent SAH, but in that case it had a yield of zero. So, because of resource issues they chose not to include it as a part of the proxy outcome in this study. Could they have included death records at 6-month as well to ensure no patients had died in their follow up period?

4. Majority of Both Groups Used the Ottawa SAH Rule: In the control period clinicians followed the Ottawa SAH Rule 78% of the time. Compared to 86% of the time in the intervention period. The difference in utilization of the rule was minimal. So, was this study really comparing standard care vs. the Ottawa SAH Rule? This could be considered contamination bias and has the potential of making the two groups appear more similar then reality.

One other point about those clinicians in the study. These were staff physicians certified in emergency medicine or supervised residents. Does this have external validly for others using the tool in a community or rural setting. The majority of emergency medicine in Canada is not provided by board certified emergency physicians. It would be nice to see this tool validated in those environments.

5. Sensitivity of the 6-hour CT Rule: The sensitivity of the 6-hour-CT rule was only 95% for subarachnoid hemorrhage. This is lower than the 100% initially reported in the original Perry et al study (JAMA 2013).

The confidence intervals were wide. The lower end of the 95% CI was 89.8% suggesting up to 10% of SAH could be missed. This may not be acceptable in some medical legal environments.



Time to Talk Nerdy

There were five patients with an early CT scan that had SAH with the CT reported as normal: Two unruptured aneurysms on CTA and presumed traumatic LP (as deemed by the treating neurosurgeon); One missed by the radiologist on the initial interpretation; one dural vein fistula (ie, non-aneurysmal); and one patient with sickle cell anemia with profound anemia (Hgb, 63 g/L) with a 3 mm aneurysm.

If you exclude two out of the five patients with traumatic LPs than the sensitivity is 97%. Certainly not perfect and still may not be good enough for some zero miss cultures.

We talked a lot about diagnostic biases in this nerdy section. If you want to know more about these issues an outstanding paper is by Kohn et al Understanding the Direction of Bias in Studies of Diagnostic Test Accuracy (AEM 2013).

Comment on Authors' Conclusion Compared to SGEM Conclusion: We think the authors' conclusions are for the most part reasonable. Given the extent the Ottawa SAH Rule was used by clinicians in the control period I don't think we can confidently conclude that the Ottawa SAH Rule has been compared to standard care or that it does not increase downstream testing.

As far as the 6-hr CT Rule it is no surprise it decreased downstream LPs. It is important to know that it increased the rate of CTA by a lesser extent. Whether this decrease in overall testing is appropriate it's hard to tell from this data as the authors did not publish any of the clinical outcomes of the patients.

Clinical Application: The Ottawa SAH Rule and 6-hr CT Rule can be incorporated into the current diagnostic pathways for the workup of SAH as long as their respective weakness are well understood and taken into account when utilizing them.

What Do I Tell the Patient? We were concerned your headache could have been from a bleed in your brain. This is called a subarachnoid hemorrhage. It can be due to an aneurysm from a weakness in an artery. The scan of your head and the spinal tap showed no evidence of a bleed. The risk that your headache is due to an aneurysm in your brain is essentially zero. We will make sure you have adequate pain control and then send you home to follow up with your primary care physician.

Case Resolution: The patient underwent a non-contrast head CT was negative for a SAH. The patient presented with 6-hrs of symptom onset and in this case the non-contrast CT is highly sensitive but not perfect for ruling out SAH.

A shared decision-making discussion was had with the patient and his wife and it was determined given the high-risk nature of his symptoms he would undergo an LP. The LP was negative for red blood cells or xanthochromia, ruling out a SAH as the cause of his headache.

Episode End Notes

Dr. Ken Milne - EBM and Rural
@TheSGEM

Do you use the Ottawa SAH rule?

thesgem.com/2020/02/sgem28...

@CAEP_Docs @ACEPNow @acemonline

Yes	45.2%
No	41.5%
I don't know this rule	13.3%

135 votes · Final results

1:27 PM · Feb 11, 2020 · Twitter Web App

Ottawa SAH rule & 6 hour CT implementation

#paperinapic @kirstychallen

Neurologically intact ED pt >16y, chief complaint nontraumatic acute headache/syncope+headache

Excl: >2 prev similar headaches >6 months, SAH confirmed pre arrival, prev CT/LP for same headache, papilledema, prev intracranial aneurysm/SAH, known brain neoplasm, cerebroventricular shunt, headache within 72h of LP, gradual headache/peak intensity >1 h.

Intervention 2013-6 n=1929, 88 SAH Ottawa SAH/6 hour CT rule encouraged but override possible		Control 2011-3 n=1734, 100 SAH Physician discretion for CT/LP/CTA
1688 (87.5%)	CT performed	1534 (88%)
500 (26%)	LP performed	678 (39%)
419 (22%)	CTA performed	328 (19%)
813 (42%)	Either LP or CTA	894 (51%)
143 (7%)	Hospital admission	170 (10%)

Ottawa SAH rule
Sensitivity 100% (95% CI 98.1–100)
Specificity 12.7% (95% CI 11.7–13.9)

6 hour CT rule
Sensitivity 95.5% (95% CI 89.8–98.5)
Specificity 100% (95% CI 99.7–100)

Perry Stroke 2019 10.1161/STROKEAHA.119.026969 SGEM #283

284

MIGHT AS WELL JUMP, BUT WE WOULD RECOMMEND A PARACHUTE

Clinical Question:

Do parachutes reduce death or major injury when jumping from aircraft?

Bottom Line:

Wear a parachute if jumping out of a moving aircraft in the air to prevent morbidity and mortality.

Guest:

Marcus Prescott is a nurse in Norway. He is also now a third-year medical student.

Case Overview

Case: A 32-year-old woman with no previous medical history calls you while a passenger on a crashing plane. She has been offered a parachute by the flight attendant but is unsure whether jumping from the plane is wise. You quickly scour the literature for evidence to inform her decision.

Background: The parachute– an umbrella term for devices to slow the motion of an object through an atmosphere by creating drag – was first deployed in China roughly 4,000 years age. The modern versions reached widespread use with the invention of heavier than air flight early last century.

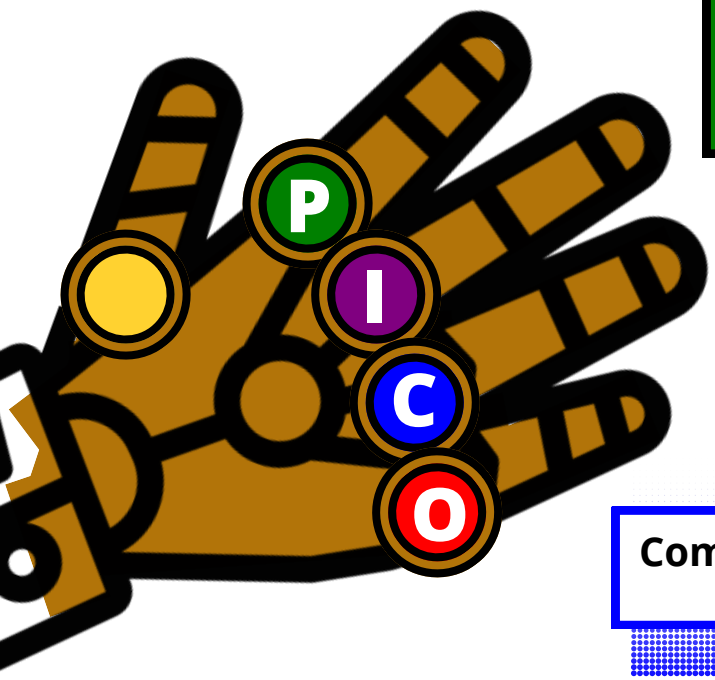
Different variants of parachutes have been used both for recreational and safety purposes; in either case aiming to avoid death in people falling from heights presumed to be lethal. Despite the near universal application, a systematic review from 2003 (Smith and Pell, BMJ) found no RCTs of parachute intervention.

That systematic review published in the BMJ is a classic paper and part of their annual holiday edition. It stated that there was observational data showing parachutes failed at times to prevent morbidity and mortality. There are also case reports of free falls that did not result in 100% mortality.

The authors suggested taking evidence-based medicine advocates up in a plane for a double blinded randomized control trial. The intervention would be a parachute and the control arm would be a sham parachute (backpack). To make it more rigorous, anyone who survived the first jump would cross over into the other arm of the study and jump again. Only then would we have definitive evidence that a parachute was effective in preventing death and major trauma related to gravitational challenges.

After years of trying to organize a trial, researchers were finally able to recruit some volunteers to jump out of a plane with a parachute or backpack.

Reference: Yeh et al. Parachute use to prevent death and major trauma when jumping from aircraft: randomized controlled trial. BMJ 2018.



Population: Adults 18 years of age and older, seated on aircraft and deemed rational decision makers.

Intervention: Jumping from aircraft with parachute

Comparison: Jumping from aircraft with backpack

Outcomes:

- **Primary Outcome:** Composite of death and major traumatic injury (ISS>15) within five minutes of impact or at 30 days.
- **Secondary Outcomes:** Health status and subgroup analysis based on type of aircraft or previous parachute use.

Authors' Conclusions

"Parachute use did not significantly reduce death or major injury when jumping from aircraft in the first randomized evaluation of this intervention. However, the trial was only able to enroll participants on small stationary aircraft on the ground, suggestion cautious extrapolation to high altitude jumps. When beliefs regarding the effectiveness of an intervention exists in the community, randomized trials might selectively enroll individuals with a lower perceived likelihood of benefit, thus diminishing the applicability of the results to clinical practice."

Quality Checklist for Randomized Control Trials

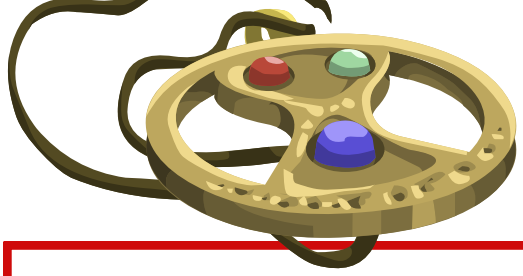
- ☒ 1. The study population included or focused on those in the emergency department.
- ☑ 2. The teams were adequately randomized.
- ☑ 3. The randomization process was concealed.
- ☑ 4. The teams were analyzed in the groups to which they were randomized.
- ☒ 5. The study teams were recruited consecutively (i.e. no selection bias).
- ? 6. The teams in both groups were similar with respect to prognostic factors.
- ☒ 7. All participants (patients, clinicians, outcome assessors) were unaware of group allocation.
- ☑ 8. All groups were treated equally except for the intervention.
- ☑ 9. Follow-up was complete (i.e. at least 80% for both groups).
- ☑ 10. All (team) patient-important outcomes were considered.
- ☒ 11. The treatment effect was large enough and precise enough to be clinically significant.

Case Outcomes

Key Results:
They screened 92 adults with only 23 agreeing to be in the trial. The median age was 38 years and 43% were female.

Parachutes did not reduce death or major injury.

- **Primary Outcome:**
  - Composite of death and major traumatic injury (ISS>15) within five minutes of impact was 0% vs. 0% with p>0.9
  - Composite of death and major traumatic injury (ISS>15) within 30 days was 0% vs. 0% with p>0.9
- **Secondary Outcomes:**
  - No statistical difference in health status
  - No statistical differences when stratified by type of aircraft or previous parachute use.



Time to Talk Nerdy

There were many limitations to this study including a composite outcome for the primary outcome. However, we will only discuss five things that threaten the validity and interpretation of this trial.

1. Convenience Sample: These were not consecutive adults sitting on an airplane. Participants were selected from those seated next to the recruiter. This could have introduced some selection bias into the study population. When we use the term “bias” we are not talking about random noise in the data but rather something that systematically moves us away from the true point estimate.

2. Lack of Blinding: Allocation to parachute or backpack was not concealed to the investigator who assigned the treatment. This too could have led to some selection bias. The groups were unbalanced with more frequent fliers in the control (backpack) group. This may or may not have impacted the results.

3. Ikea Bias: Most of the participants who were randomized were study investigators. They would be unblinded to the study hypothesis and could be more invested in the results because they helped design the study. Whether or not this would have a significant impact on the results is unclear.

4. Lack of Deployment: In the intervention arm none of the12 participants had their parachute open. This makes the trial very difficult to interpret. If the parachute did deploy properly would it have provided a benefit? However, none of the 12 participants died or were injured because the parachute did not open during the jump.

5. Fatal Flaw: There was a difference between participants and non-participants. Participants jumped from a mean altitude of 0.6m traveling at a velocity of 0km/hr. This is in comparison to the non-participants who were at a mean altitude of 9,000m and traveling at a velocity of 800km/hr.

Comment on Authors' Conclusion Compared to SGEM Conclusion:
We generally agree with the authors' conclusions.

Clinical Application: Based on your understanding of physics and reality, you would recommend people use parachutes if jumping out of an aircraft that is flying. While it does not guarantee you will not be injured or die it is the best evidence we have on the topic. In addition, more research is not needed to determine if parachutes prevent morbidity or mortality due to gravitational challenges.

What Do I Tell the Patient? Accept the parachute being provided by the flight attendant.

Case Resolution: Despite the lack of high-quality evidence demonstrating the efficacy of parachutes, you advise your friend to use the parachute being offered by the flight attendant.

Episode End Notes

Other FOAMed:

- Hayes et al. Most medical practices are not parachutes: a citation analysis of practices felt by biomedical authors to be analogous to parachutes. CMAJ 2018
- Potts and Grossman. Parachute approach to evidence based medicine. BMJ 2006
- Mamas. What a Parachute Study Tells Us About RCTs. Medscape 2018
- First10EM: Finally, an RCT of parachutes

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AND I SEE YOUR TRUE COLOURS CALMING YOU - FROM YOUR ANXIETY

Clinical Question:

Can colouring decrease anxiety in adult patients presenting to the Emergency Department?

Bottom Line:

Art therapy in the form of coloring may be a useful non-pharmacologic alternative treatment for ED patients with anxiety

Guest:

Dr. Corey Heitz is an emergency physician in Roanoke, Virginia. He is also the CME editor for Academic Emergency Medicine.

Case Overview

Case: One night during an overnight shift, you are taking care of a patient who presented to the emergency department (ED) due to anxiety and vague suicidal ideation. The process for medical clearance and psychiatric evaluation can take quite a while, and you notice that this patient seems stressed and anxious. You wonder if there's a way to assist them during the prolonged wait without resorting to sedative medication.

Background: Psychological disorders are a common reason for presenting to the ED. Anxiety disorders are the most common (Marchesi et al EMJ 2004). However, we have only covered mental health issues a few times on the SGEM:

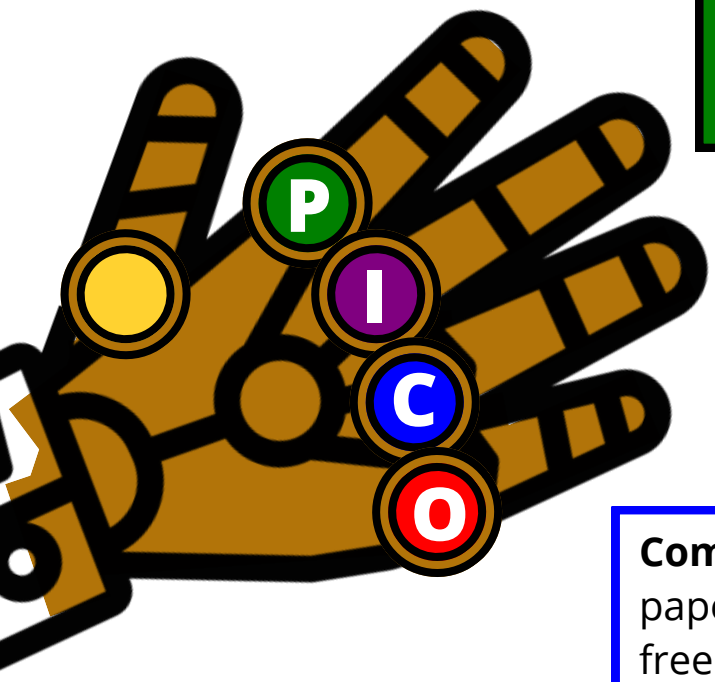
- SGEM#45: Vitamin H (Haloperidol for Psychosis)
- SGEM#178: Mindfulness – It's not Better to Burnout than it is to Rust
- SGEM#218: Excited Delirium Syndrome
- SGEM#237: Screening Tool for Child Sex Trafficking
- SGEM#252: Blue Monday- Screening Adult ED Patients for Risk of Future Suicidality

Patients with psychological disorders are often kept in the ED for a prolonged period of time. The ED itself can be a stressful environment and exacerbate anxiety.

Emergency physicians have pharmaceutical options to treat anxiety. One of the most common medications to use is a benzodiazepine like lorazepam or diazepam.

There is a need for non-pharmacological therapies to treat anxiety, and in some settings, art therapy has been studied. Specifically, adult coloring books have been used in the community and seem to function through cognitive easing (Rigby et al BMJ 2016 and Curry et al Art There 2005).

Reference: Rajendran et al. Randomised control trial of adult therapeutic colouring for the management of significant anxiety in the Emergency Department. AEM February 2020



Population: Patients >15 years old with a score of >6 on the Hospital Anxiety and Depression Scale Anxiety (HADS-A). A score of >6 is considered moderate to severe anxiety.

Intervention: Colouring pack (10 adult colouring pages and 36 pencil colours)

Comparison: Placebo pack (10 plain sheets of paper, a Bic pen and instructions to draw or write freely)

Outcomes:

- **Primary Outcome:** Within-patient change in HADS-A score from baseline after two hours of therapy.
- **Secondary Outcomes:** Survey questions regarding value of therapy and level of engagement with treatment packs (length of time)

This is an SGEMHOP episode which means we have the lead author on the show. Dr. Naveen Rajendran is an intern at the Westmead Hospital in Sydney with a keen interest in emergency medicine and the investigation of novel therapies that could aid in alleviating the growing stress on modern emergency departments. This study was conducted when he was a medical student at the University of Sydney with Dr. Coggins (@coggi33) who was his research supervisor.

Authors' Conclusions

"Among ED patients, exposure to adult colouring books resulted in lower self-reported levels of anxiety at 2-hours compared to placebo."

Quality Checklist for Randomized Clinical Trials

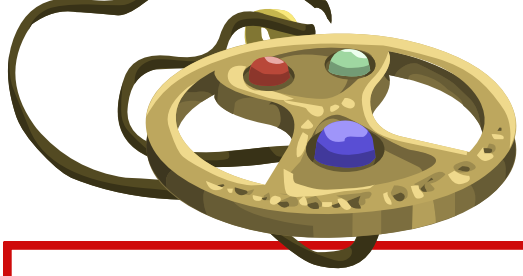
- ☑ 1. The study population included or focused on those in the emergency department.
- ? 2. The teams were adequately randomized.
- ☑ 3. The randomization process was concealed.
- ☑ 4. The teams were analyzed in the groups to which they were randomized.
- ? 5. The study teams were recruited consecutively (i.e. no selection bias).
- ☑ 6. The teams in both groups were similar with respect to prognostic factors.
- ☒ 7. All participants (patients, clinicians, outcome assessors) were unaware of group allocation.
- ☑ 8. All groups were treated equally except for the intervention.
- ☑ 9. Follow-up was complete (i.e. at least 80% for both groups).
- ☑ 10. All (team) patient-important outcomes were considered.
- ☑ 11. The treatment effect was large enough and precise enough to be clinically significant.

Case Outcomes

Key Results:
They screened 179 patients that were flagged as being anxious. The cohort included 53 participants with a mean age of 33 years and 73% were female.

- **Primary Outcome:**
  - Intervention Group: Mean HADS-A decrease at two hours was 3.7 (95%CI 2.4 to 5.1, p<0.001)
  - Control Group: Mean HADS-A decrease at two hours: 0.3 (95%CI -0.6 to 1.2, p=0.51)
- **Secondary Outcomes:**
  - For the question “would you recommend colouring” on a Likert Scale (1-5) the average satisfaction score was 4.2.

Minutes Using Resource	Intervention	Control
<5	0	10 (37%)
5-60	14 (53.8%)	13 (48.1%)
60-120	12 (46.2%)	4 (14.8%)



Time to Talk Nerdy

We asked Naveen ten questions to get a greater understand of his publication. Listen to the SGEMHOP podcast to hear all of his answers.

1. Single Centre: This was a relatively small sample size of 53 patients. However, you did recruit enough to meet your power calculation of 48 participants to find a 2.5-point decrease with 80% power. We were more concerned that this was conducted in a single center and raises question of external validity to other populations.

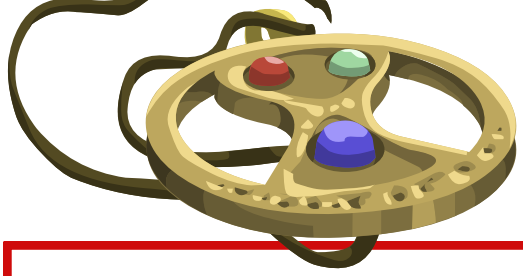
2. Consecutive Patients: We are unsure if this was a consecutive sample. The methods section says; “all patients in the ED were potentially eligible for the study.” However, patients needed to be flagged by residents, consultants, triage nurses or social workers as being “anxious”. People have unconscious biases and this method could have introduced some selection bias. Why not just ask patients if they were feeling anxious and then ask them to be included in the trial?

3. **Exclusions:** A significant number of patients were excluded after initial screening. Can you discuss how this might affect real-world utility of something like this?

4. Lack of Blinding: The patients would know if they were in the colouring pack vs. placebo pack. Could this have impacted the results?

5. Blinding to Hypothesis: Were the patients, clinicians, and outcome assessors blinded to the research hypothesis?

6. HADS-A Scoring: The HADS-A has been validated in various languages and groups of patients. You say this anxiety scoring system has been validated in the ED setting. We pulled that study and it was done in Saudi Arabia (Al Aseri et al BMC Emerg Med 2015). Has it been validated in any other countries like the USA or Canada?



Time to Talk Nerdy

7. Placebo Control: There is a difference between a placebo control and an active control. Can you discuss how your placebo control group is a true placebo? It seemed to us more like an active control group. How is the activity such as coloring so different from having a pen and paper and being told to occupy yourself with them?

8. Medication: You compared the colouring activity to the placebo pack (Bic Pen, plain paper and encouragement to draw). Why not comparing it to usual care such as a benzodiazepine?

9. Magnitude of Effect: The intervention decreased the HADS-A score by 3.4 more than the control. While it was statistically significant is this observed decrease clinically significant.

10. Duration of Effect: Your primary outcome was at two hours. Did you measure any anxiety outcomes after the activity has ended? Do we know how long it takes someone to return to a high anxiety level once art therapy is removed?

11. Conflicts of Interest: Did you receive any funding or support from the adult colouring book industry?

Comment on Authors' Conclusion Compared to SGEM Conclusion: We agree with the authors' conclusions.

Clinical Application: Adult coloring books are a low risk and potentially rewarding non-pharmacologic way to treat anxiety in the ED.

What Do I Tell the Patient? You seem anxious, and this visit may take some time. Some people have found that being able to spend some time colouring can help them cope with the stress of an ED visit. Would you like some supplies and try doing some colouring?

Case Resolution: You provide your patient with an adult coloring book and coloring pencils. Two hours later, they seem calmer, and their ED visit is almost over. They thank you for providing them something to ease their mind during their stay.

Episode End Notes

Dr. Ken Milne - EBM and Rural
@TheSGEM

Would you use art therapy (colouring) to treat patients with anxiety in the emergency department?
#SGEMHOP

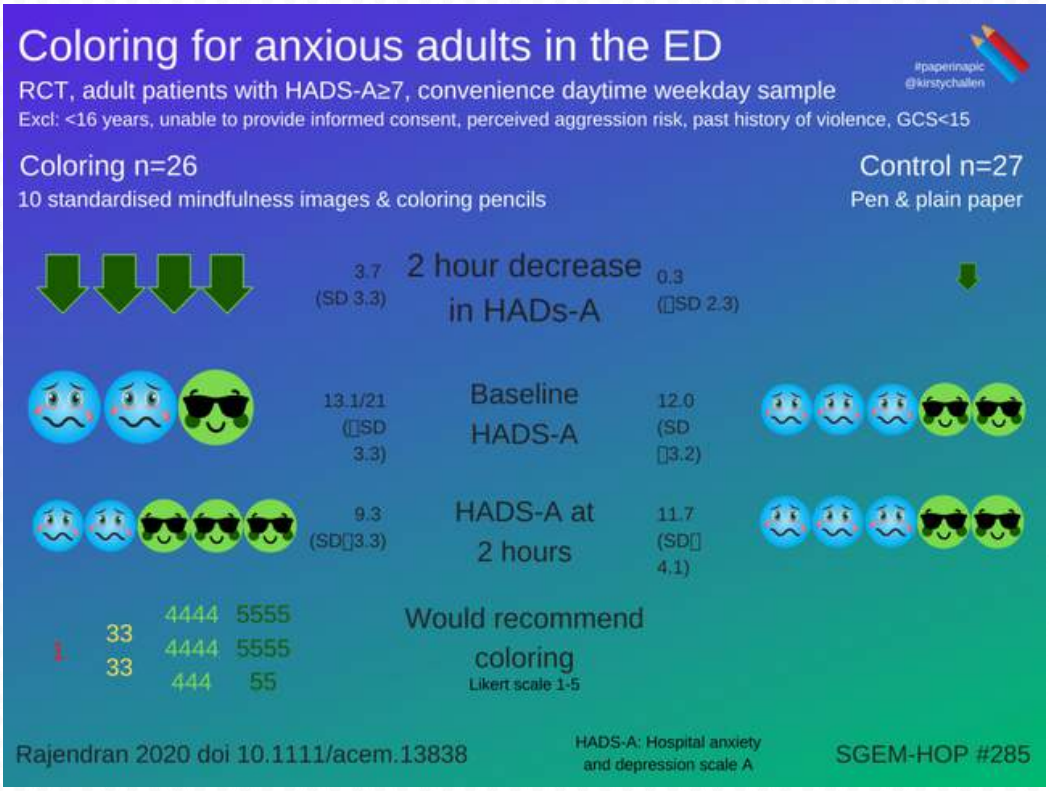
onlinelibrary.wiley.com/doi/abs/10.111...

@SAEMonline @AcademicEmerMed @CHeitzMD

Yes	58.4%
No	41.6%

137 votes · Final results

9:39 AM · Mar 3, 2020 · Twitter Web App



286 BEHIND THE MASK - DOES IT NEED TO BE AN N95 MASK?

Clinical Question:

Are N95 masks superior in preventing flu or flu-like illnesses in hospital workers compared to medical masks?

Bottom Line:

There appears to be no statistical advantage to the N95 respiratory mask over surgical or medical mask for hosptial employees in preventing flu or flu like illnesses.

Guests:

Dr. Christopher Patey is an Assistant Professor with Memorial University Medical School in St. John's, Newfoundland Canada. Over the past seventeen years he has practiced as a rural emergency and family physician and Clinical Chief of Emergency at Carbonear Hospital.

Paul Norman is a registered nurse working as a frontline emergency nurse in Eastern Health, Newfoundland, Canada. Paul has greater than ten years of experience working in Emergency Nursing and Critical Care. His focus is implementation of LEAN strategies, quality and process improvement. Paul's work has been extended to reach emergency services throughout Canada and he has contributed on many platforms including local, regional, provincial and national speaking engagements.

DISCLAIMERS: THIS EPISODE IS ABOUT INFLUENZA NOT CORONAVIRUS (COVID-19)

Dr. Patey's Disclaimer: I am not an expert on PPE (Personal Protective Equipment), Influenza/HINI/Coronavirus, Journal Reviews or Emergency Department management of pandemics.

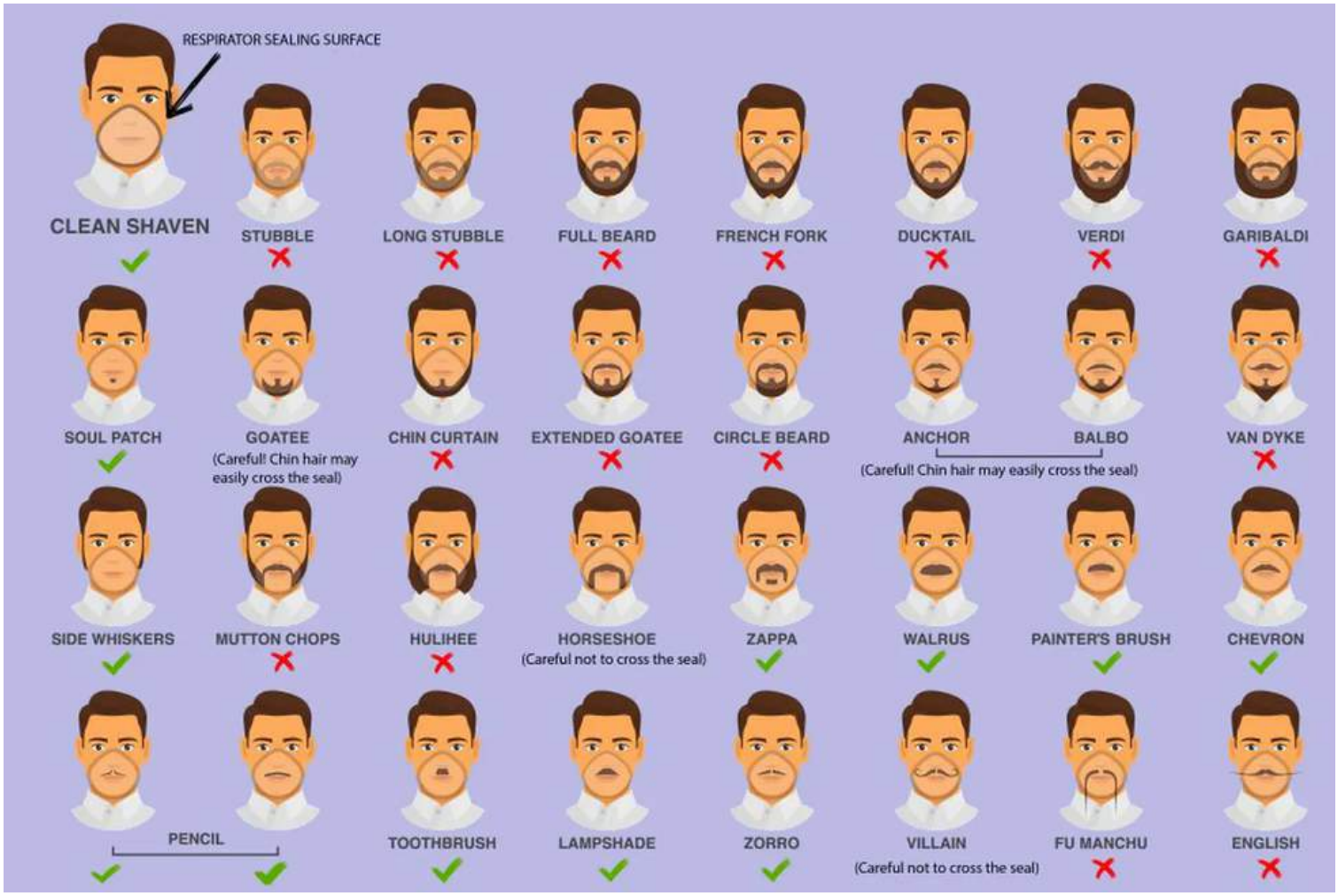
Paul Norman's Disclaimer: We (Dr. Patey and I) are experts on asking questions on the frontline of a Rural Emergency Department to ensure quality, and most importantly, effective patient care.

Dr. Ken Milne's Disclaimer: I am an expert on critical appraisal but do not know what mask (if any) is best for preventing the Covid-19 virus.

I think we can all agree on a few general recommendation: Get a flu shot if possible, wash your hands well (at least 20 seconds with soap and water), try not to touch your face, avoid people who are sick, stay home if you are feeling ill, cough into a tissue and throw it out immediately or cough into your elbow, disinfect objects or surfaces with a regular household cleaning wipe or spray, people who are well do not need to wear a facemask, people who are feeling ill should wear a facemask, and reach out to your local health authority if you think you might have the COVID-19.

Case Overview

Case: With the potential global impact of the coronavirus (COVID-19) and our rural emergency departments (ED) having an extremely low compliance rate for N95 mask fit testing, our ED administration sends an urgent request for everyone to have N95 mask testing as soon as possible (ASAP). The urgent email also request shaving facial hair. You wonder about the evidence supporting the initiative and if there is any recent evidence surrounding N95 masks usage for preventing health care workers getting acute respiratory illnesses.



Background: Many hospitals had their health care workers fitted with N95 masks in response to the 2009 H1N1 pandemic. The N95 masks were known to prevent small particles and therefore thought to be more effective. What was not known is whether or not this better effectiveness would translate into less viral respiratory infections acquired in hospital compared to regular disposable surgical medical masks. In other words, would N95 masks have a healthcare provider-oriented outcome.

When it appeared that the transmission of the pandemic H1N1 was not different from seasonal influenza the recommendation for medical masks in most settings was reinstated.

With the potential for an epidemic/pandemic outbreak of coronovirus, there is the demand for increased vigilance in preventive measures to prevent and contain the outbreak of this communicable disease.
There have been a number of other studies discussing masks in preventing influenza spread:

- Loeb et al 2009 did a non-inferiority trial of surgical masks vs. N95 respirator masks for preventing flu in Ontario nurses working at tertiary care hospitals. They concluded surgical masks were non-inferior.
- MacIntyre et al 2009 did a cluster RCT on the use of face masks to control for respiratory virus transmission in households. They found face masks were unlikely to be an effective policy for seasonal respiratory diseases. This was in part because <50% of participants had mask adherence. Those who wore the mask did have a statistically significant reduction in clinical infection.
- MacIntyre et al 2011 published another study in the same year comparing efficacy non-face masks to fit tested and non-fit tested N95 respiratory mask in preventing respiratory infections in hospital workers in China. The results showed a significant decrease in respiratory illnesses including influenza. The authors did cautioned readers that the trial may have been underpowered.

Background:

- Smith et al CMAJ 2016 did a systematic review and meta-analysis on this topic. The authors concluded: “Although N95 respirators appeared to have a protective advantage over surgical masks in laboratory settings, our meta-analysis showed that there were insufficient data to determine definitively whether N95 respirators are superior to surgical masks in protecting health care workers against transmissible acute respiratory infections in clinical settings.”

Reference: Radonovich et al. N95 Respirators vs Medical Masks for Preventing Influenza Among Health Care Personnel. A Randomized Clinical Trial. JAMA 2019 The Respiratory Protection Effectiveness Clinical Trial (ResPECT)

Population: Full-time hospital employees defined as providing at least 24hrs of direct patient care a week. Participants were instructed to wear their assigned protective devices during a 12-week period (intervention period) during which the incidence of viral respiratory illness was expected to be highest that year developed by the ALERT algorithm. This was for 48 weeks of intervention spanning four consecutive viral respiratory seasons.

Intervention: N95 respirator mask. Employees were told to wear their masks when six feet (two meters) from a person suspected or confirmed of having a respiratory illness.

Control: Medical mask

Outcomes:

- **Primary Outcome:** Incidence of laboratory-confirmed influenza.
- **Secondary Outcomes:** Incidence of acute respiratory illness, laboratory-detected respiratory infections, laboratory-confirmed respiratory illness, and influenza like illness. Adherence to interventions was also assessed.

Authors' Conclusions

"Among outpatient healthcare personnel, N95 respirators vs medical masks as worn by participants in this trial resulted in no significant difference in the incidence of laboratory-confirmed influenza."

Quality Checklist for Randomized Clinical Trials

- [x] 1. The study population included or focused on those in the emergency department.
- [x] 2. The teams were adequately randomized.
- [x] 3. The randomization process was concealed.
- [x] 4. The teams were analyzed in the groups to which they were randomized.
- [x] 5. The study teams were recruited consecutively (i.e. no selection bias).
- [x] 6. The teams in both groups were similar with respect to prognostic factors.
- [x] 7. All participants (patients, clinicians, outcome assessors) were unaware of group allocation.
- [x] 8. All groups were treated equally except for the intervention.
- [x] 9. Follow-up was complete (i.e. at least 80% for both groups).
- [?] 10. All (team) patient-important outcomes were considered.
- [x] 11. The treatment effect was large enough and precise enough to be clinically significant.

Case Outcomes

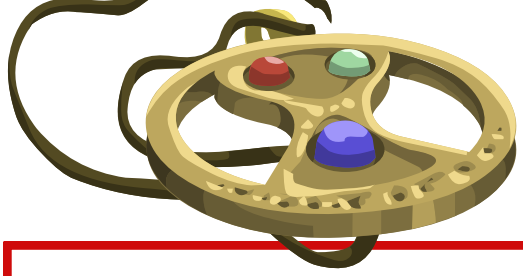
Key Results:
This study was conducted at seven medical centers and 137 outpatient sites over four years (2011-2015) during the 3-month flu season. They enrolled 2,862 full time employees with a mean age of 43 years and 84% female. Nurses made up 41% of the cohort and less than 10% were physicians.

- **Primary Outcome:** Laboratory-confirmed influenza
  - 8.2% N95 respirator group and 7.2% medical mask group (difference, 1.0%, [95% CI: −0.5% to 2.5%]; P = 0.18)
  - Adjusted odds ratio (OR) was 1.18 (95% CI: 0.95 to 1.45)

- **Secondary Outcomes:** No statistical difference in any of the secondary outcomes using an intention-to-treat (ITT) or per-protocol (PP) analysis.

Self-reported wearing of the mask “always” or “sometimes” was about 90% in both groups.

Incidence	N95 Mask	Med Mask	Incidence rate (95%CI)
Acute Resp Illness	1556/2512	1771/2668	0.99 (0.92-1.06)
Lab Detected Resp Disease	679/2512	745/2668	0.99 (0.89-1.09)
Lab Confirmed Resp Illness	371/2512	471/2668	0.96 (0.83-1.11)
Influenza Like Illness	128/2512	166/2668	0.86 (0.68-1.10)



Time to Talk Nerdy

1. Self-Reporting: Health care workers self-reported any illness. This could have resulted in under or over reporting of being sick. Adherence to mask use was also self-reported. Of those reporting, 90% said they wore the mask always or sometimes. However, almost one-third in each group did not even report adherence. This further limits the interpretation of the results.

2. Lack of Physicians: Less than 10% of the cohort were physicians. This means we have much less data on this group of individuals. I also suspect physicians were less likely to follow mask recommendations. Unfortunately, the supplemental material did not break down how many physicians were in the physician, physician trainees or advanced practitioners' cohort.

3. Outside of Work: Participants were not required to use the masks outside of their work setting. Employees had to have at least 24 hours/week of direct patient care to be included in the study. However, more time would have been spent out of the hospital/clinic setting. These outside influences/exposures could have an impact on the results.

4. Patient-Oriented Outcome: This study was focused on the employees. While there was no significant difference in the health care worker getting ill it would have been great to know if it had any impact on the patients' well-being.

5. Cost: N95 respiratory masks are more expensive than medical masks. First, we must determine if the intervention works. This study does not support a benefit for hospital employees. If it did show a benefit to them or more importantly the patients, then we could decide if the cost was worth any efficacy. Without good evidence of benefit, we should consider putting resources towards things that do have evidence of efficacy like vaccination programs and hand washing initiatives.

Comment on Authors' Conclusion Compared to SGEM Conclusion: We generally agree with the authors' conclusions.

Clinical Application: This study will increase my use of a mask (medical mask or N95) with all suspected patients arriving to an ED or outpatient setting. We should also focus on things that have been demonstrated to have a benefit like vaccination and good hand washing.

What Do I Tell the Staff? Get immunized against influenza, wash your hands well and often, try not to touch your face and wear a mask when around patients who have suspected or confirmed respiratory illness.

Case Resolution: You respond to the email from the nursing administration to follow hospital guidelines, continue N95 mask testing and to follow hospital policies. However, I think it is important to stress to all staff to get their flu shot, consistently wash their hands, stop touching their face and wear a mask if a patient has suspected or confirmed respiratory illness.

Episode End Notes

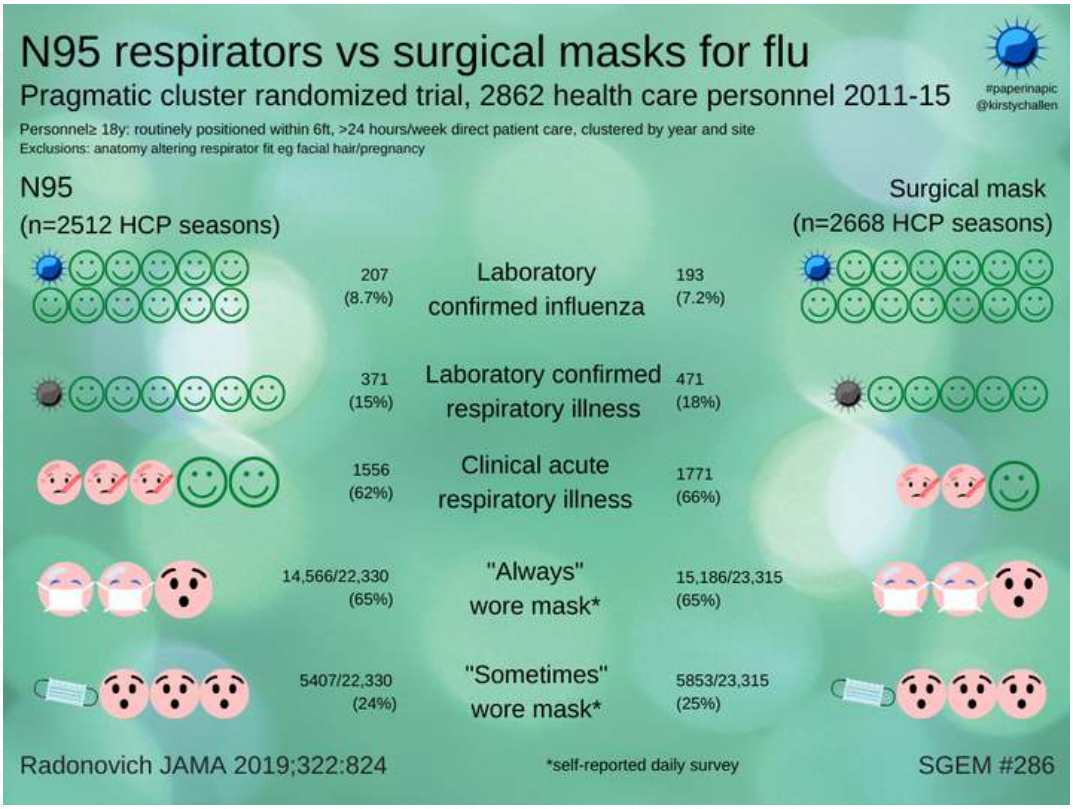
What's the best mask to prevent influenza transmission to healthcare workers?

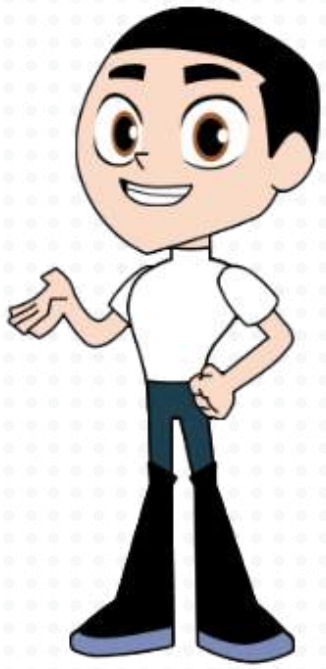
thesgem.com/2020/03/sgem28...
#foamed #ebm

@CAEP_Docs @meganranney
@ACEPNow @AliRaja_MD
@Rick_Pescatore @KirstyChallen
@DFTBubbles @ALiEMteam
@ketaminh @LITFLblog

Medical/surgical mask	20%
N95 mask	**34%**
Both about the same	34%
I don't know	12%

208 votes · Final results





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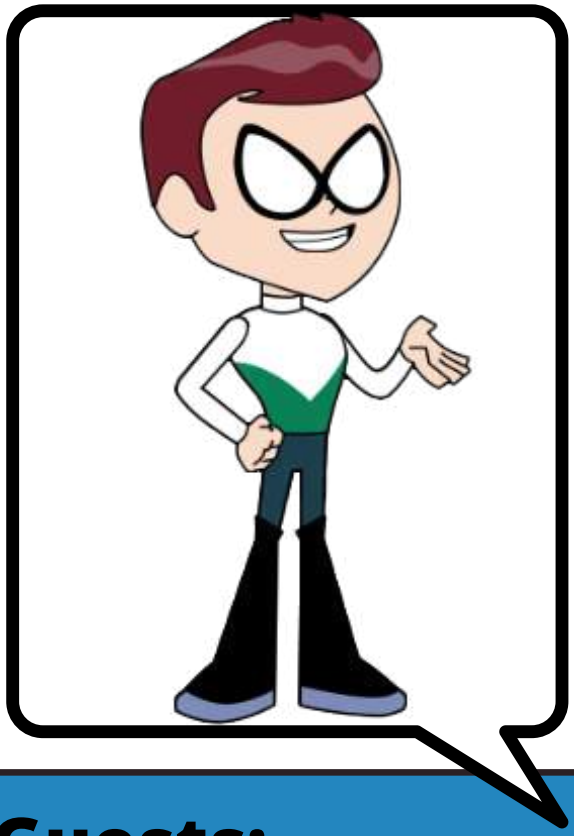
DIFFICULT TO BREATHE - IT COULD BE PNEUMONIA

Clinical Question:

What is the accuracy of biomarkers for the diagnosis of community acquired pneumonia?



Bottom Line:

Do not rely only upon a biomarker in the emergency department to rule in or rule out community acquired pneumonia.

Guests:

Dr. Chris Bond is an emergency medicine physician and assistant Professor at the University of Calgary. He is also an avid FOAM supporter/producer through various online outlets including TheSGEM.

DISCLAIMER: THIS EPISODE IS NOT ABOUT CORONAVIRUS (COVID-19)

Case Overview

Case: A 47-year-old healthy, non-smoker, presents to the emergency department (ED) with a productive cough, fever and says it has been difficult to breathe for the past four days. He appears well, with a temperature of 38.7 Celsius, heart rate of 90 beats per minute, respiratory rate of 20 breaths per minute and room air oxygen saturation of 91%. On auscultation you hear some fine crackles at the bases. You wonder if there is value in ordering any bloodwork, particularly a biomarker such as C-reactive protein (CRP), procalcitonin (PCT) or a complete blood count for white blood cell count (WBC) in addition to doing a chest x-ray (CXR).

Background: Community-acquired pneumonia (CAP) is a significant source of morbidity and mortality in adults (1,2). We have covered this issue a couple of times on the SGEM. One episode looked at β-Lactam monotherapy vs. β-Lactam plus macrolide combination therapy in adult patients admitted to hospital with moderately severe CAP (SGEM#120). This study supported the combination therapy in these patients.

More recently, we looked at the question of whether steroids improve morbidity and mortality in patients admitted to hospital with CAP (SGEM#216). The bottom line was that corticosteroids appear to improve mortality and/or morbidity in patients admitted to hospital with CAP.

There is evidence that an accurate diagnosis of CAP may lead to earlier treatment while avoiding unnecessary antibiotics for patients who do not have CAP. Pervious research has demonstrated that individual signs and symptoms have limited accuracy in the diagnosis of CAP. The diagnosis of CAP is usually based on an abnormal chest x-ray in a patient with signs and symptoms of a lower respiratory tract infection (3,4).

Background: White blood cell count (WBC), C-reactive protein (CRP), and procalcitonin are biomarkers associated with an increased likelihood of CAP. There are also clinical prediction rules that include CRP for the diagnosis of CAP (5,6).

Procalcitonin is another potential biomarker that may help in the diagnosis of bacterial pneumonia (7). Guidelines such as the National Institute for Health and Care Excellence (NICE) recommend the use of CRP at the point of care to reduce inappropriate antibiotic when diagnosing CAP (8) These various biomarkers are readily available in the ED setting in the US, as well as in the primary care setting in other countries in Europe.

The study we are reviewing on this SGEM episode performs an updated systematic review and meta-analysis (SRMA) of the diagnostic accuracy of biomarkers for CAP.

Reference: Ebell et al. Accuracy of Biomarkers for the Diagnosis of Adult Community-Acquired Pneumonia: A Meta-analysis. AEM March 2020

Population: Adult patients presenting with symptoms of acute respiratory infection and patients with clinically suspected pneumonia based on physician order of a chest radiograph, reporting sufficient information to calculate sensitivity and specificity for the diagnosis of CAP for at least one biomarker.

Exclusions: Studies of dyspnea or sepsis rather than suspected CAP. Studies limited t patients with chronic lung disease, patients i skilled nursing facilities, or immunosuppressed/HIV patients. Ventilator or hospital acquired pneumonia. Studies of the diagnosis of a specific pathogen (i.e. mycoplasma or legionella). Studies that did not use a cohort design (i.e. recruited patien with known CAP and healthy controls)..

Comparison: Chest imaging with CXR or CT scan

Intervention: C-reactive protein (CRP), procalcitonin or white blood cell (WBC) count

Outcomes: Diagnosis accuracy of biomarkers for pneumonia

This is an SGEMHOP episode which means we have the lead author on the show. Dr. Mark Ebell is a Family Physician and Professor at the University of Georgia in Athens. He is a co-founder of POEMs, editor-in-chief of Essential Evidence, deputy editor of American Family Physician, and co-host of the podcast Primary Care Update.

Authors' Conclusions

Biomarkers can be useful for the diagnosis of community-acquired pneumonia. The cutoff chosen will determine whether the test is most useful for ruling out pneumonia (CRP < 10 or 20 mg/L) or for ruling in pneumonia (e.g., CRP > 50 or 100 mg/L). CRP is the most accurate of the three studied biomarkers that are currently being used to assist in the diagnosis of community acquired pneumonia. We note that CRP is inexpensive and readily available in many settings and may be easily integrated into the clinical workflow for diagnosis of community acquired pneumonia in appropriate patients.

Quality Checklist for Therapeutic Systematic Reviews

- ☑ 1. The clinical question is sensible and answerable.
- ☑ 2. The search for studies was detailed and exhaustive.
- ☑ 3. The primary studies were of high methodological quality.
- ☑ 4. The methodological quality of primary studies were assessed for bias.
- ☑ 5. The assessment of studies were reproducible.
- ☑ 6. The outcomes were clinically relevant.
- ☒ 7. There was low heterogeneity for estimates of sensitivity or specificity.
- ☒ 8. There was low statistical heterogeneity for the primary outcomes.
- ☑ 9. The treatment effect was large enough and precise enough to be clinically significant.

Case Outcomes

Key Results:
They screened 829 studies and found 14 that met inclusion and exclusion criteria with a total number of 6,599 patients. The study time periods ranged from 1986 to 2016, with 12 studies being performed in Europe, and one in each of the United States and Chile. Half of the studies were performed in ED patients and the other half in primary care settings.

CRP was studied in 13 of the 14 studies, PCT in seven and leukocytosis in five. One study used the combination of CRP and PCT.

Eight studies were felt to be at low risk of bias using the QUADAS-2 tool while six studies were felt to be at moderate risk of bias. None of the studies appeared to have been industry funded.

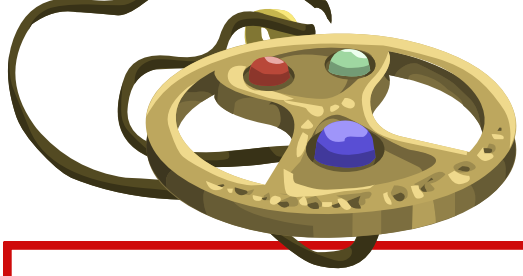
All of these biomarkers have a threshold effect, meaning that sensitivity increases as specificity decreases. As a result, summary estimates of sensitivity, specificity and likelihood ratio are shown for different cutoffs for each test.

Diagnostic accuracy for community acquired pneumonia was greatest with CRP.

Test & Cutoff	Sensitivity (95%CI)	Specificity (95%CI)	Likelihood Pos (95% CI)	Likelihood Neg (95% CI)
CRP>10mg/L	0.90 (0.52-0.99)	0.48 (0.27-0.70)	1.71	0.27
CRP>20 mg/L	0.80 (0.68-0.89)	0.62 (0.51-0.71)	2.08 (1.77-2.40)	0.32 (0.21-0.45)
CRP>50 mg/L	0.71 (0.56-0.82)	0.80 (0.70-0.88)	3.68 (2.70-4.92)	0.36 (0.25-0.50)
CRP>100 mg/L	0.58 (0.39-0.74)	0.90 (0.80-0.95)	5.79 (3.49-9.07)	0.48 (0.31-0.65)
CRP>200 mg/L	0.36(0.31-0.41)	0.96(0.92-0.98)	8.83 (4.42-18.47)	0.67 (0.62-0.73)
PCT>0.25 mcg/L	0.44 (0.21-0.70)	0.91 (0.76-0.97)	5.43 (2.29-10.80)	0.62 (0.38-0.83)
PCT>0.50 mcg/L	0.28 (0.11-0.53)	0.96 (0.80-0.99)	8.25 (1.85-28.20)	0.76 (0.54-0.91)
WBC>9.5-10.5 x 10^9 cells/L	0.55 (0.45-0.66)	0.82 (0.78-0.86)	3.15 (2.46-3.97)	0.54 (0.42-0.66)

Case Outcomes

- **Primary Outcome:** Diagnostic accuracy of community acquired pneumonia
  - C-Reactive Protein: A CRP cutoff of 10 mg/L had the highest sensitivity at 90% and lowest negative likelihood ratio of 0.27. CRP > 20 mg/L CRP > 50 mg/L and CRP > 100 mg/L had positive likelihood ratios of 2.08, 3.68 and 5.79 respectively, with poor negative likelihood ratios.
  - Procalcitonin: PCT > 0.25 mcg/L and PCT > 0.50 mcg/L had good positive likelihood ratios (5.43 and 8.25 respectively), negative likelihood ratios were worse than for CRP
  - Leukocytosis: This was defined as a white blood cell count (WBC) > 9.5 to 10.5 x 10^9 cells/L had modest accuracy (LR+ 3.15, LR- 0.54) with good homogeneity around this estimate.



Time to Talk Nerdy

We asked Mark five questions to get a greater understand of his publication. Listen to the SGEMHOP podcast to hear all of his answers.

1) External Validity: Less than 1/3 of patients came from the ED setting. This limits the application of these results to this clinical setting. The NICE guideline recommends the use of CRP in the primary care setting, presumably as a point of care test to help decide whether or not to order a CXR. Is this a rational use of resources in an ED setting where a CXR could be done as the initial test?

2) Point Estimates and 95% Confidence Intervals: There have been some conventional cut offs for likelihood ratios. None of the positive likelihood ratios were >10 to confidently rule in pneumonia and none of the negative likelihood rations were <0.1 to confidently rule out pneumonia. There were generally wide confidence intervals around the point estimates.

3) Post-Hoc Cut Offs: It is not clear in some of the studies used a post-hoc cutoff. We have discussed this before on the SGEM of potentially overfitting the data. How do you think this could affect your results and the interpretation?

4) Imperfect Gold Standard Bias (Copper Standard Bias): The biomarkers were compared to CXR in 13 of the 14 studies. We know that CXRs is less accurate in diagnosing CAP than a CT scan. How do you think that could have impacted the results?

5) Clinically Significant: A positive CXR does not mean a patient has a bacterial pneumonia. Prescribing antibiotics to patient with a viral pneumonia is unlikely to have a patient-oriented outcome (POO). Do you think this disease-oriented outcome (DOO) and not a POO is a problem?

Comment on Authors' Conclusion Compared to SGEM Conclusion: We agree that biomarkers "can" be useful for diagnosis of CAP in the outpatient setting but are skeptical of their impact on the diagnosis of ED patients.

Clinical Application: We are not going to use these biomarkers routinely to make the diagnosis of community acquired pneumonia in the emergency department.

What Do I Tell My Patient? It looks like you have a pneumonia in the base of your right lung on the CXR. Here is a prescription for an antibiotic. If it is a bacterial pneumonia the medicine should work. If it is a viral pneumonia the antibiotic is unlikely to help. Follow-up with your family physician next week. Return to the emergency department if you develop a rash, get increasing shortness of breath or are worried.

Case Resolution: You order CXR which is reported by the radiologist as a "right lower lobe infiltrated consistent with early pneumonia, clinical correlation required". You prescribe the antibiotic doxcycline and provide appropriate follow-up and discharge instructions.

Episode End Notes

@socmobem @markebell
@AcademicEmerMed
@SAEMonline @AliRaja_MD
#sgemhop #ebm #foamed

Always	4%
Sometimes	23%

Biomarkers in adult CAP: meta-analysis

#paperinapic
@kirstychallen

14 studies, 6599 patients.

Adults with symptoms of acute respiratory infection + adults with clinically suspected pneumonia based on physician order of CXR; CXR/CT as reference standard.

CRP
13 studies

AUROC 0.80
(95% CI 0.78 - 0.85)

Cutoff >10mg/ml
Sens 0.90 (0.52–0.99)
Spec 0.48 (0.27–0.70)
LR+ 1.71 LR- 0.27

Cutoff >50mg/ml
Sens 0.71 (0.56–0.82)
Spec 0.80 (0.70–0.88)
LR+ 3.68 (2.70–4.92)
LR- 0.36 (0.25–0.50)

Cutoff >200mg/ml
Sens 0.36 (0.31–0.41)
Spec 0.96 (0.92–0.98)
LR+ 8.83 (4.22–18.47)
LR- 0.67 (0.62–0.73)

Leukocytosis
7 studies

AUROC 0.78
(95% CI 0.74 - 0.81)

Cutoff >9.5-10.5
Sens 0.55 (0.45–0.66)
Spec 0.82 (0.78–0.86)
LR+ 3.15 (2.46–3.97)
LR- 0.54 (0.42–0.66)

Procalcitonin
5 studies

AUROC 0.77
(95% CI 0.74 - 0.81)

Cutoff >0.1 µg/L
Sens 0.74 (0.48–0.90)
Spec 0.69 (0.42–0.87)
LR+ 2.50 (1.50–4.31)
LR- 0.39 (0.20–0.63)

Cutoff >0.5 µg/L
Sens 0.28 (0.11–0.53)
Spec 0.96 (0.80–0.99)
LR+ 8.25 (1.85–28.20)
LR- 0.76 (0.54–0.91)

Cutoff >1.0 µg/L
Sens 0.43 (0.38–0.48)
Spec 0.96 (0.92–0.98)
LR+ 10.54 (5.05–21.98)
LR- 0.60 (0.54–0.65)

Ebell 2020 doi 10.1111/acem.13889

Sens: sensitivity, spec: specificity, LR+: positive likelihood ratio, LR-: negative likelihood ratio

SGEM-HOP #287

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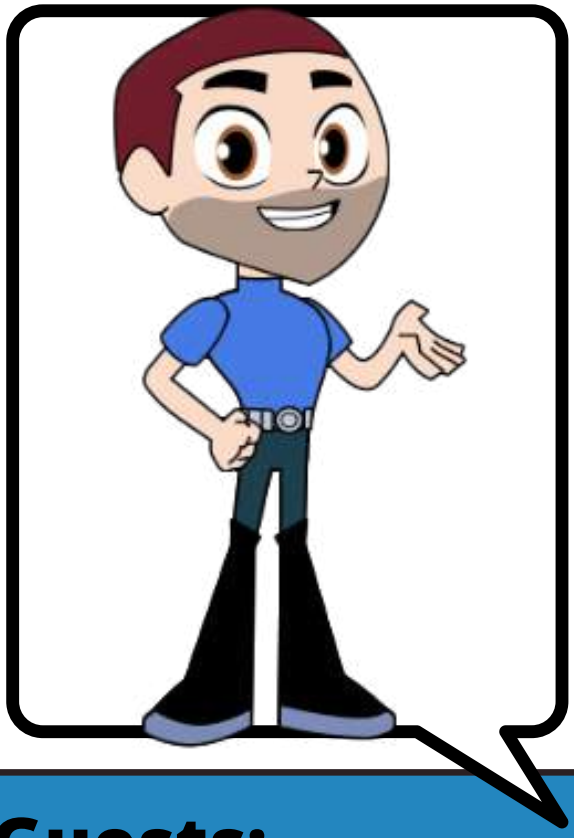
CRAZY GAME OF POCUS TO DIAGNOSE SHOULDER DISLOCATIONS

Clinical Question:

What is the diagnostic accuracy of point-of-care ultrasound for the diagnosis of shoulder dislocations as compared with x-ray?

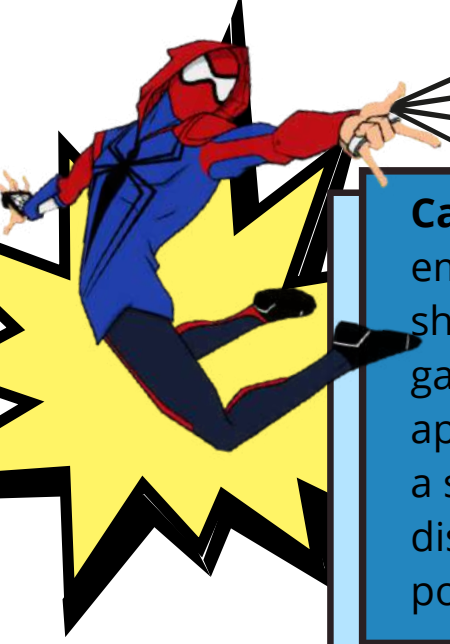


Bottom Line:

While POCUS has very good diagnostic accuracy, clinicians should keep using x-rays as their primary imaging study for patients with suspected shoulder dislocations.

Guests:

Dr. Tony Zitek is an Emergency Medicine physician in Miami, Florida. He is an Assistant Professor of Emergency Medicine for Florida International University and Nova Southeastern University, and Tony is the Research Director for the Emergency Medicine residency program at Kendall Regional Medical Center.



Case Overview

Case: An 18-year-old, previously healthy male presents to the emergency department after sustaining an injury to his right shoulder after colliding with another player during a football game. On examination, there is a loss of the normal rounded appearance of the shoulder. You suspect the patient may have a shoulder dislocation. He has no history of shoulder dislocations in the past. Will you order an x-ray or perform a point-of-care ultrasound to confirm the diagnosis?

Background: Despite shoulder dislocations being a very common injury presenting to the ED, it has only been covered once on SGEM#121. This episode tried to answer whether it was better for the shoulder to be immobilized in an external or internal rotation post-reduction. We still don't know if one position is superior to another.

Emergency physicians frequently perform pre- and post-reduction x-rays for patients with shoulder dislocations. However, some prior studies suggest that the routine performance of these x-rays may not be necessary, especially in patients with recurrent dislocations who have not sustained any direct trauma [1-2].

Point-of-care ultrasound (POCUS) has previously been studied for the use of the diagnosis of shoulder dislocations with most prior data suggesting that POCUS is highly sensitive and specific for the diagnosis of shoulder dislocations [3-4].

As with other applications of POCUS, the use of ultrasound for shoulder dislocations has the potential to reduce the time to diagnosis, reduce radiation exposure, and lower cost. However, prior studies about the use of POCUS for shoulder dislocations have used a variety of scanning techniques and some have utilized as few as 2 sonographers [4]. One study found only a 54% sensitivity for identifying persistent dislocation after a reduction attempt [5].

Reference: Secko et al. Musculoskeletal Ultrasonography to Diagnose Dislocated Shoulders: A Prospective Cohort. Ann Emerg Med Feb 2020

Population: Adult patients with suspected shoulder dislocations who presented to one of two EDs when a study investigator was present.

Exclusions: Patients with multiple traumatic injuries, decreased level of consciousness, or hemodynamic instability.

Comparison: Pre- and post-reduction x-rays.

Intervention: Pre- and post-reduction POCUS utilizing a posterior approach in which they traced the scapular spine towards the glenohumeral joint. The POCUS technique they used is basically as follows — the sonographer palpates the spine of the scapula, and then places the ultrasound probe directly over the scapular spine. The study protocol allowed the sonographer to choose either a linear or curvilinear probe. The sonographer then follows the scapular spine laterally until the glenoid and humerus are identified. Using this technique, the glenoid and humeral head both look like hyperechoic semicircles. They should be very close to each other, and if not, that indicates a shoulder dislocation. After assessing for dislocation, the sonographer can assess for fracture by fanning the probe from a cephalic to caudal direction. A fracture appears as a disruption in the normal contour of the hyperechoic humerus. (shown below in Figure 1 from the manuscript).

Outcomes:

- Primary Outcome: The diagnostic accuracy of POCUS for shoulder dislocations.
- Secondary Outcomes: Presence or absence of fracture, time from triage to POCUS exam as compared to x-ray, time from POCUS exam initiation to diagnosis, determination of glenohumeral distance of non-dislocated and dislocated shoulders, and sonographer confidence in diagnosis (from 0-10).

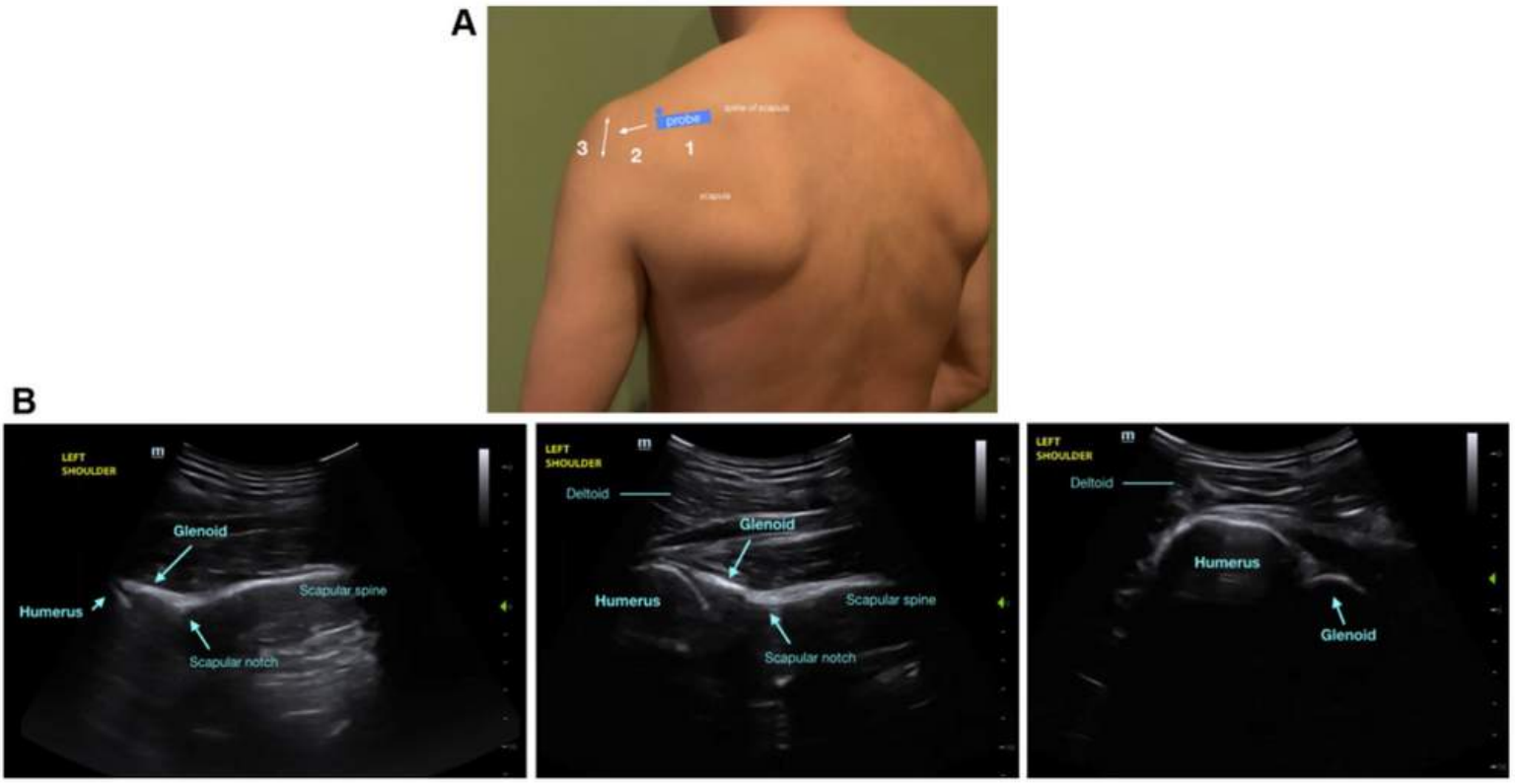


Figure 1. A, Proper probe placement on the patient and the 3-step sequence to examine the shoulder from the posterior approach. The blue dot above the probe corresponds to the probe indicator. B, The corresponding ultrasonographic images to the probe placement in A at the level of the scapular spine (1), the glenohumeral joint (2), and the humerus (3).

Authors' Conclusions

"A posterior approach point-of-care ultrasonographic study is a quick and accurate tool to diagnose dislocated shoulders. Ultrasonography was also able to accurately identify humeral fractures and significantly reduce the time to diagnosis from triage compared with standard radiography."

Quality Checklist for Observational Study

- ☑ 1. Did the study address a clearly focused issue?
- ☑ 2. Did the authors use an appropriate method to answer their question?
- ☒ 3. Was the cohort recruited in an acceptable way?
- ? 4. Was the exposure accurately measured to minimize bias?
- ☑/☒ 5. Was the outcome accurately measured to minimize bias?
- ? 6. Have the authors identified all-important confounding factors?
- ☑ 7. Was the follow up of subjects complete enough?
- ? 8. How precise are the results? Fairly precise given the small sample size
- ☑ 9. Do you believe the results?
- ? 10. Can the results be applied to the local population?
- ☑ 11. Do the results of this study fit with other available evidence?

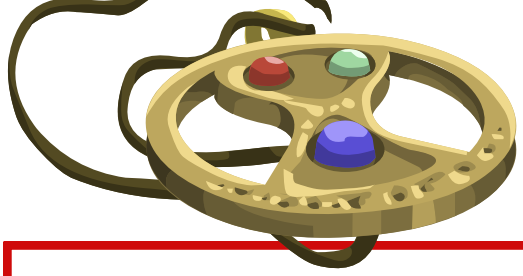
Case Outcomes

Key Results:
They enrolled 65 patients in the study. The median age was 40 years, 58% being male, 49% had a dislocation (29 anterior, 2 posterior and 1 inferior) and 32% had a history of dislocation.

POCUS had a100% sensitivity, specificity, PPV, and NPV for diagnosing shoulder dislocation.

- **Primary Outcome:**
  - Sensitivity 100% (95% CI; 87-100)
  - Specificity 100% (95% CI; 87-100)
  - PPV 100% (95% CI; 87-100)
  - NPV 100% (95% CI; 87-100)

- **Secondary Outcomes:**
  - 25/65 (38%) had fractures with 13 being Hill-Sachs/Bankart's
  - Non-Hill-Sachs/Bankart's Fracture:Sensitivity 92% (95% CI; 60-99.6), specificity 100% (95% CI; 92-100), PPV 100% (95% CI; 68-100) and NPV of 98% (95% CI; 89- 99.9).
  - POCUS was 43 minutes faster from exam to diagnosis compared to x-ray.
  - The median glenohumeral distance was –1.83 cm (IQR –1.98 to –1.41 cm) in anterior dislocations, 0.22 cm (IQR 0.10 to 0.35 cm) on non-dislocated shoulders, and 3.30 cm (IQR 2.59 to 4.00 cm) in posterior dislocations
  - Sonographers' confidence in their POCUS diagnosis was 9.1 of 10 in non-dislocated cases and 9.4 of 10 in dislocated cases.



Time to Talk Nerdy

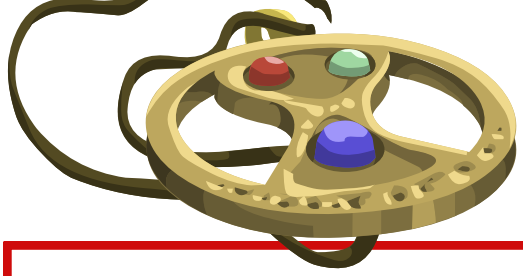
1) Accuracy of POCUS to Confirm Shoulder Dislocation: The data suggests that POCUS is highly sensitive and specific for the diagnosis of shoulder dislocation. However, this study utilized a convenience sample of patients that were all ultra sounded by one of six sonographers who were either ultrasound fellows or ultrasound fellowship-trained attendings.

That being said, there is some evidence that less-skilled sonographers can use this technique with high accuracy. In fact, the authors cited a study by my friend Shadi Lahham from UC Irvine, in which novice sonographers had a 100% sensitivity and specificity using a posterior approach POCUS examination [6]. Overall, given the study at hand and the previous studies assessing POCUS for shoulder dislocations, we can say pretty confidently that POCUS, especially the posterior approach, has very high sensitivity and specificity for the diagnosis of shoulder dislocations.

The sonographers were very confident in their diagnoses (9.1/10). This was not surprising given the small group of skilled sonographers performed all the ultrasounds. It is unclear if POCUS would have the same diagnostic accuracy in the hands of a community emergency physician.

Additionally, while the study was technically “multicenter” in that two facilities were involved, one of the two sites enrolled only 5 patients. Therefore, this was mostly a single center study. For these reasons, we question the external validity of the study, and I’m not sure that if the ultrasounds were performed by typical community emergency physicians that you would achieve such impressive results.

2) Accuracy of POCUS to Confirm Shoulder Reduction: In the study at hand, 27 of 32 subjects with dislocations had post-reduction POCUS exams performed to confirm adequate reduction. Per the study protocol, all 32 were supposed to have had a post-reduction POCUS performed, but there were five cases where this did not happen. The manuscript says it was because the



Time to Talk Nerdy

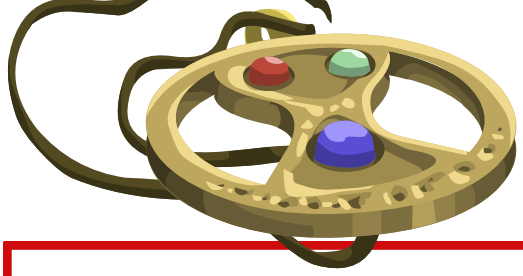
study sonographer was unavailable after the reduction for various reasons without further explanation. This could have introduced some bias and increases our skepticism of the results.

3) Accuracy of POCUS for Shoulder Fracture Diagnosis: Of the 65 patients, there were 25 (38%) with fractures. POCUS identified only 52% of those fractures. However, all but one of the missed fractures was a Hill-Sach's deformity or a Bankart lesion. There were 12 non-Hill Sach's/Bankart's fractures in this study, and POCUS identified 11 of those 12. The one missed fracture was a surgical neck fracture. Overall, POCUS was 92% sensitive (95% CI; 60% to 99.6%) and 100% specific (95% CI; 92% to 100%) for non–Hill-Sachs/Bankart's fractures.

Hill-Sach's and Bankart's fractures are generally not relevant to the emergency management of patients with shoulder dislocations, so it's probably okay to miss those fractures.

However, an 8% miss rate of non-Hill Sach's/Bankart's fractures is too high for American medicine. Moreover, given the fact that the confidence interval on the sensitivity goes all the way down to 60% and that the sonographers were all likely to be more skilled than average, an 8% miss rate may be lower than what would be expected if your standard community emergency docs started using POCUS for shoulder injuries.

4) Measuring the Glenohumeral Distance: The sonographers in this study calculated the "glenohumeral distance". This isthe distance between the glenoid and the tip of the humeral head. The median glenohumeral distance was –1.83 cm in anterior dislocations, 0.22 cm on nondislocated shoulders, and 3.30 cm in posterior dislocations. Negative numbers indicate the humeral head moved away from the ultrasound probe while positive numbers indicate the humeral head moved closer to the probe.



Time to Talk Nerdy

This is a bit difficult to understand without a picture, so we'll put a figure in the blog to demonstrate what the authors were actually measuring. The authors found the optimal cutoff to distinguish an anterior dislocation from a nondislocated shoulder was -0.5 cm.

The point of measuring the glenohumeral distance is that when the shoulder is dislocated, the separation between the glenoid and humeral head should be pretty easy to see as the distance between the two is substantial: usually about 2 cm for anterior dislocations and about 3 cm for posterior dislocations.

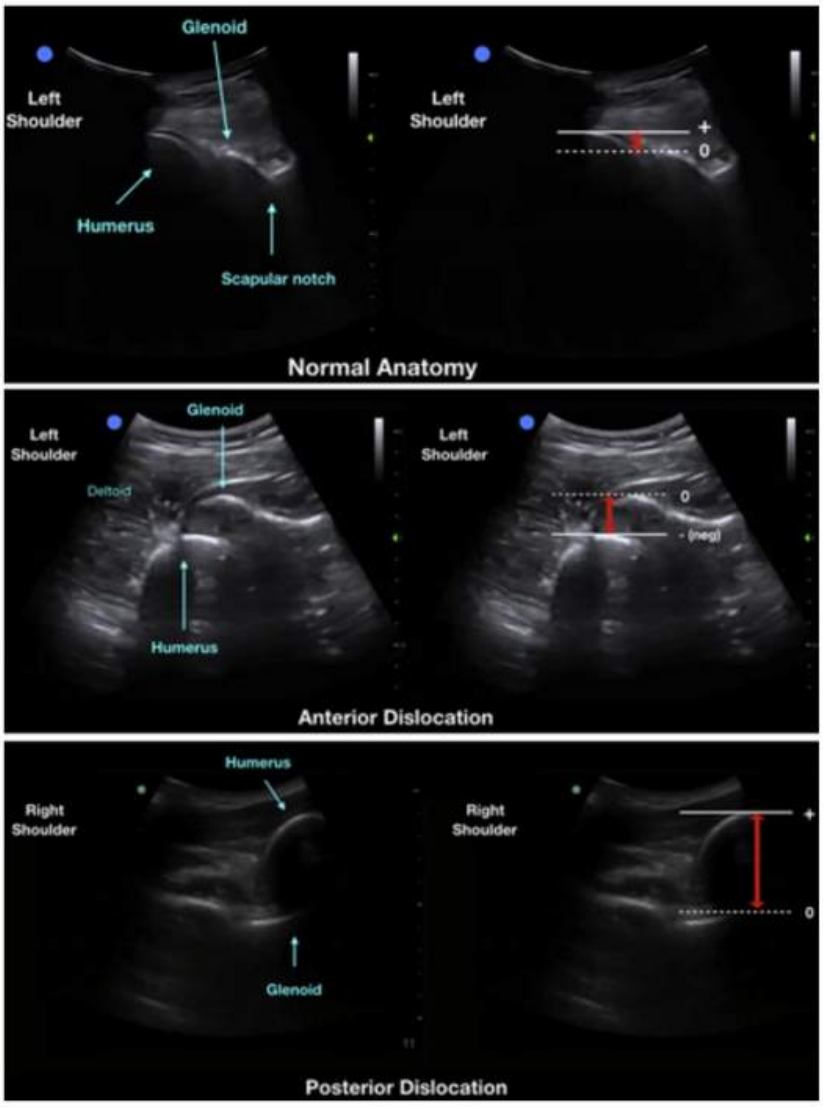
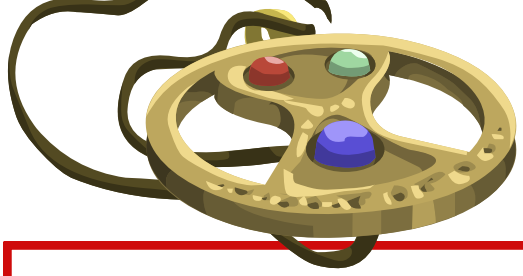


Figure 2: The red arrows show the glenohumeral distance.



Time to Talk Nerdy

5) Time Saved with POCUS: The median time to POCUS from triage was 51 minutes (IQR: 36-77) as compared to 101 minutes (IQR: 73-134) for x-ray. The amount of time saved in the real world (if any) is entirely dependent on the system in which the physician is working.

POCUS could save time in facilities that have long waits for x-rays. However, in a facility with single-physician coverage, the x-ray tech may complete the x-ray before the physician has a chance to perform an ultrasound. Therefore, I don't think we can say that POCUS would consistently result in a more rapid diagnosis in all facilities.

Comment on Authors' Conclusion Compared to SGEM Conclusion: We generally agree with the authors' conclusions.

Clinical Application: I don't think ultrasound should take the place of x-ray at this time with regards to the evaluation of patients who have sustained a shoulder injury. Primarily, this is because the accuracy of POCUS for the diagnosis of shoulder fractures has not been demonstrated yet. There were only 12 non-Hill Sach's/Bankart's fractures in this study, so it's hard to draw precise conclusions about POCUS for shoulder fractures. However, if there is really an 8% or more miss rate, POCUS should not be used for patients in whom shoulder fracture is on the differential diagnosis. In their discussion, the authors argued that POCUS was accurate for the diagnosis of shoulder fractures, and as support for this statement they cited a prior meta-analysis that had reported that the sensitivity of POCUS for detecting fractures associated with shoulder dislocations was 97.9% [3]. However, when they mentioned that study, they neglected to report that that calculation was based on tiny numbers such that the 95% CI was 10.5 to 100%.

Remember, there is already evidence that you don't need to get an x-ray to confirm the diagnosis of shoulder dislocation on every patient [1], especially those with prior dislocations and no direct shoulder trauma. The main reason to get an x-ray for many cases is, in fact, to make sure there is not a fracture as opposed to or along with the shoulder dislocation. Therefore, in some cases of shoulder injury, no imaging (not even POCUS) is needed to accurately diagnose the shoulder dislocation. In other cases, the x-ray is needed, not so much because you need to confirm the shoulder dislocation, but to exclude fractures. Pending further data to support the use of POCUS to accurately diagnose shoulder fractures, POCUS should not replace x-ray for shoulder injuries.

On the other hand, I like the idea the authors suggested of using POCUS to confirm the successful reduction of a shoulder dislocation. Prior data has already found that, in some cases, it may not be necessary to perform any imaging after a shoulder reduction [2]. However, if you aren't completely sure if you have reduced a dislocated shoulder and you don't have any reason to believe that you caused a shoulder fracture with your reduction attempt (which is very rare), POCUS is likely sufficient to confirm the reduction as opposed to x-ray. Additionally, if a patient was sedated for a shoulder reduction attempt, POCUS could be used to confirm the reduction while the patient is still sedated to avoid the messy situation of having to re-sedate the patient.

What Do I Tell My Patient? You have a shoulder injury. Ultrasound is very accurate for the diagnosis of shoulder dislocations, but x-ray remains the first line imaging test to assess for both dislocation and fracture. I am concerned that you could have a fracture or a dislocation, so we are going to perform an x-ray.

Case Resolution: Given the direct trauma sustained by the patient in his football game and thus concern for possible fracture in addition to the concern for shoulder dislocation, an x-ray of the shoulder is performed. The x-ray reveals a shoulder dislocation without an associated fracture. The shoulder is reduced, and reduction is confirmed with POCUS. The patient is discharged home with appropriate discharge instructions and follow-up advice.

Episode End Notes

Do you use POCUS for diagnosing shoulder dislocations?
thesgem.com/2020/03/sgem28... #FOAMus
@westernsono @5MinSono @pocusfoamed
@POCUS_Society @PracticalPOCUS @the_TOTAL_EM

No	**79.7%**
Yes	20.3%

59 votes · Final results

11:00 AM · Mar 31, 2020 · Twitter Web App

POCUS for shoulder dislocation

Prospective convenience cohort: 65 adults with suspected shoulder dislocation

Excl: multiple injuries, decreased consciousness, haemodynamically unstable

#paperinapic
@kirstychallen

Pre-reduction

32 dislocation on USS
32 dislocation on XR

33 no dislocation on USS
33 no dislocation on XR

Sens 100% (CI 87-100), spec 100% (CI 87-100), PPV 100% (CI 87-100), NPV 100% (CI 87-100)

Post-reduction

0 dislocation on USS
0 dislocation on XR

27 reduced on USS
27 reduced on XR

Spec 100% (CI 87-100)

Fracture

13 fractures on USS
13 fractures on XR

52 no fracture on USS
12 fracture on XR

Sens 52% (CI 31-72), spec 100% (CI 91-100), PPV 100%, NPV 77% (CI 69-83)

Secko Ann EM 10.1016/j.annemergmed.2020.01.008 SGEM #288

289

I WANT A DOG TO RELIEVE MY STRESS IN THE EMERGENCY DEPARTMENT

Clinical Question:

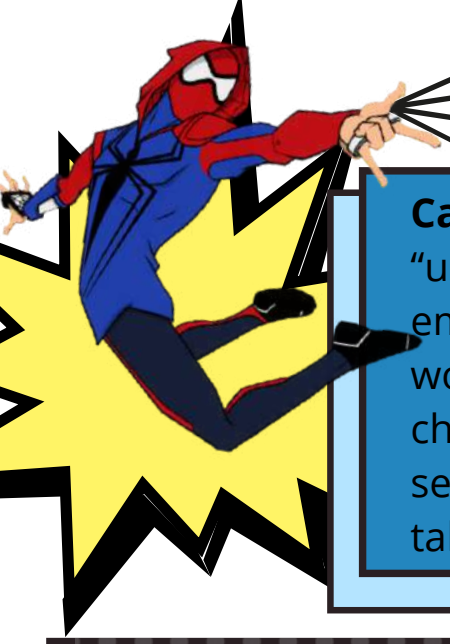
Does dog therapy result in lower perceived stress than deliberate coloring or control when applied as a break during an Emergency Medicine shift?

Bottom Line:

Novel approaches to managing stress and burnout are welcomed in Emergency Medicine. If you like dogs, we encourage you to maximize the joy in your life and play with a dog whenever possible. Dog therapy during emergency shifts is promising, but at this point probably needs to be considered unproven.

Guests:

Dr. Justin Morgenstern is an emergency physician and the creator of the excellent #FOAMed project called First10EM.com



Case Overview

Case: It has been a hard shift. You wish you could say "uncharacteristically", but recently all your shifts in the emergency department have felt a little hard. The increased workload due to COVID-19 hasn't been helping. You sit down to chart after a difficult resuscitation, and the charge nurse, seeing that you look a little stressed, asks if you would like to take a break to play with a dog.

Background: Medicine is an incredibly rewarding profession. However, it is undeniably marked by significant levels of stress. Reports of burnout are high across medicine, and even higher in emergency medicine (1,2). A study of USA physicians showed that they had more than 50% with at least one symptom of burnout. Emergency physicians reported the highest prevalence of burnout at around 70% (3).

Burnout is associated with a loss of empathy and compassion towards patients, decreased job satisfaction, and shorter careers in medicine (4,5). It has also been associated with negative impacts on patient care including self-perceived medical error (6), risk of medical errors (7), and quality of care (8,9).

We have covered burnout a few times on the SGEM including my own personal experience of being on the edge of burnout:

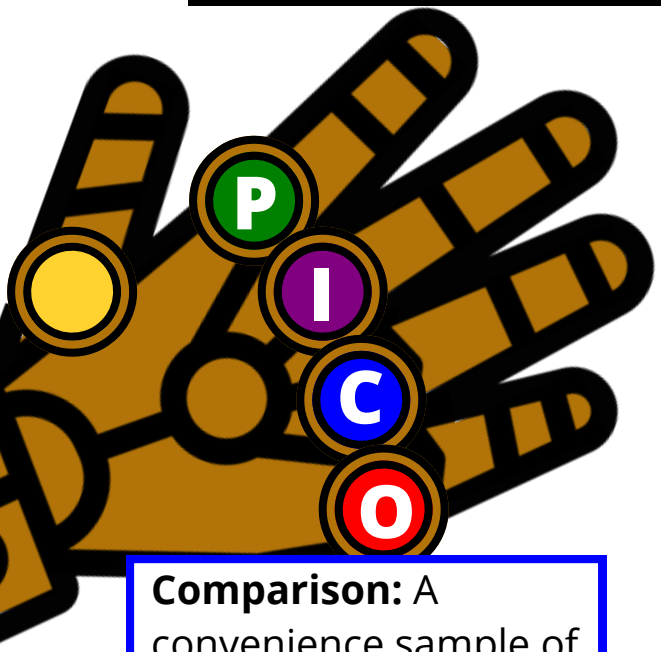
- Five Tips: To Avoid Emergency Medicine Burnout
- SGEM#178:Mindfulness – It's not Better to Burnout than it is to Rust
- SGEM Xtra: On the Edge of Burnout ACEM18
- SGEM Xtra: CAEP Wellness Week 2019
- YouTube: Being on the Edge of Burnout One Year Later

There is some prior literature that exposure to animals decreases stress (10,11). Theoretically, time spent deliberately coloring as a mindfulness practice could also decrease stress (12). Therefore, these authors designed a prospective, randomized trial comparing the effects of dog therapy, deliberate coloring, and control on stress levels for emergency department providers (13).

Reference: Kline et al. Randomized trial of therapy dogs versus deliberative coloring (art therapy) to reduce stress in emergency medicine providers. AEM April 2020

Population: Emergency care providers, including nurses, residents, and physicians, from a single center emergency department.

Exclusions: Dislike, allergy, fear, or other reason not to interact with a therapy dog.



Comparison: A convenience sample of providers that were not offered any break.

Intervention: There were two interventions, which occurred approximately midway through the provider's shift. Dog therapy consisted of an interaction with a therapy dog, which providers could pet or touch if they wished. The coloring group was provided with three mandalas to choose to color and a complete set of coloring pencils. Both of these activities occurred in a quiet room, physically separated from the clinical care area, with no electronic devices, telephone, window, or overhead speaker.

Outcomes:

- **Primary Outcomes:** There were two primary outcomes. The first was a self-assessment of stress using a visual analogue scale. The second was a 10-item validated perceived stress scores, altered to focus providers on the past several hours rather than months, as it was originally designed. These were both measured at the beginning of the shift, about 30 minutes after the intervention, and near the end of the shift.

- **Secondary Outcomes:** They looked also looked at a FACES scales as a measure of stress, and provider cortisol levels.

This is an SGEMHOP episode which means we have the lead author on the show. Dr. Jeff Kline (@klinelab) is the Vice Chair of Research in Emergency Medicine and a professor of physiology, Indiana University School of Medicine. He is the editor in chief of AEM, creator of Pulmonary Embolism Rule-out Criteria (PERC) Rule and has published extensively in the area of pulmonary emboli.

Authors' Conclusions

"This randomized, controlled clinical trial demonstrates preliminary evidence that a five minute therapy dog interaction while on shift can reduce provider stress in Emergency Department physicians and nurses."

Quality Checklist for Randomized Clinical Trials

- ☑ 1. The study population included or focused on those in the emergency department.
- ☒ 2. The teams were adequately randomized.
- ? 3. The randomization process was concealed.
- ☑ 4. The teams were analyzed in the groups to which they were randomized.
- ☒ 5. The study teams were recruited consecutively (i.e. no selection bias).
- ? 6. The teams in both groups were similar with respect to prognostic factors.
- ☒ 7. All participants (patients, clinicians, outcome assessors) were unaware of group allocation.
- ☑ 8. All groups were treated equally except for the intervention.
- ☑ 9. Follow-up was complete (i.e. at least 80% for both groups).
- ☑ 10. All patient-important outcomes were considered.
- ? 11. The treatment effect was large enough and precise enough to be clinically significant.

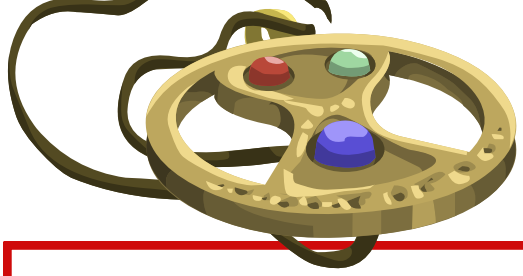
Case Outcomes

Key Results:
They enrolled 127 providers, but five withdrew because they thought their shift was too busy to participate. 47% were resident physicians, 23% were attending physicians, and 30% were nurses. They were most frequently (60%) enrolled during an evening shift.

The coloring intervention took a median of five minutes and 26 seconds. In the dog group, providers spent a median of five minutes and 49 seconds with the dogs and had significant interaction with both the dog and the dog's handler.

- **Primary Outcome:**
  - Stress based on the VAS was the same in all three groups at the beginning of the shift (18mm) but rose in the coloring group and fell in the dog group.
  - Stress based on the validated stress score rose in the control group, but otherwise was not statistically significant.

- **Secondary Outcomes:** In all three groups, cortisol levels were highest at the beginning of the shift and decrease over time. The cortisol level fell more in both intervention groups.



Time to Talk Nerdy

We asked Jeff ten questions to get a greater understand of his publication. Listen to the SGEMHOP podcast to hear all of his answers.

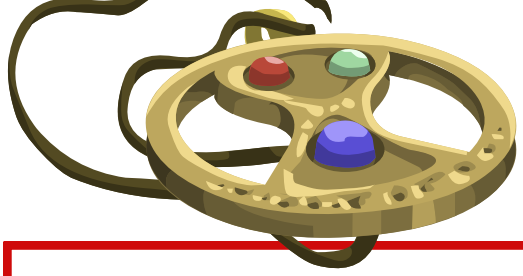
1) Allocation Concealment: Allocation concealment is one of those EBM terms that gets thrown around a lot but isn't often discussed. It's really important, because if you can guess what group you are going to be in, it might affect your decision to join the study. For example, in this study, if I thought I was going to be in the dog group, I would definitely say yes, but I have no interest in coloring, so probably would have said no. Can you comment on your allocation concealment procedures and whether you think they are adequate?

2) Nocebo / Convenience Sample: First, the idea of nocebo is fascinating, and it would be great if you could explain your logic for not randomizing the control group to the listeners. Second, I worry about the convenience sample as a source of bias. The study's objective was not blinded, so it is possible that the convenience sample could have been selected on particularly stressful days or particularly not stressful days, which would impact the results.

3) Two Primary Outcomes: This paper had two co-primary outcomes, but as we frequently say on the SGEM, *"there can only be one."*

Perhaps as the editor in chief of Academic Emergency Medicine, you can settle this one for us. Are you really allowed to have more than one primary outcome?

4) Statistical vs Clinical Significance: Overall, the results suggest a statistical decrease in stress in the group exposed to dogs. However, it is unclear whether the magnitude of change was large enough to be noticeable. Do you think the results are clinically significant?



Time to Talk Nerdy

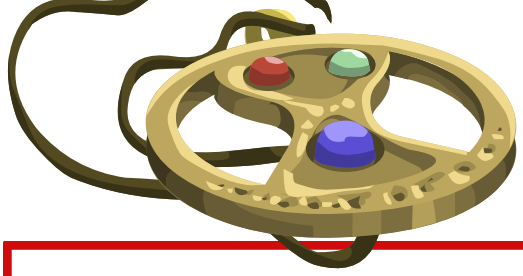
5) Blinding: Obviously, it is essentially impossible to blind a study like this, but the lack of blinding does make it harder to interpret the subjective feelings of stress. It is possible that people just like dogs (who doesn't), and the lower scores don't really reflect stress.

6) Short vs Long Term Outcomes: You focused on same-day stress, but presumably for burnout, long term outcomes might be more important. Do you think these results will extrapolate to longer term benefits?

7) Language: I noticed that one of the coloring options had crude language. I found the message funny, and it would have lifted my spirits on shift, but I can imagine problems if the completed picture accidentally found its way into a patient's hands. They might not understand the emergency provider's darker humour.

8) Harms from Dogs: Did you consider potential harms from the interventions? For example, you let participants opt out if they had dislike, fear, or had allergies to dogs. Personally, I love dogs, but I am also incredibly allergic. I can imagine ignoring my allergies to play with the dog mid shift, but then regretting that choice and having increased stress as I trying to manage my remaining patients with incredibly itchy eyes and an endlessly runny nose.

9) Scheduling the Intervention vs Stress Relief on Demand: In this study, the intervention was scheduled for a specific time during the shift. Emergency shifts aren't very amenable to strict schedules. In fact, when someone tries to schedule something at a specific time during one of my shifts, it tends to increase stress. I wonder whether interventions like this would be more effective if they were available when the provider felt they needed them – such as after a stressful resuscitation. You mention this in the discussion section – can you describe what you think is the ideal set up for a program like this?



Time to Talk Nerdy

10) Treatment Effect: As mentioned you had two primary outcomes. They showed different results. Which one should the SGEMers believe?

Comment on Authors' Conclusion Compared to SGEM Conclusion: We agree that this study represents preliminary evidence that a brief interaction with a dog can reduce stress on shift, but more research is required to confirm the effect, look at the long term benefits of such a program, and determine whether the magnitude of the effect is worth the cost and potential harms.

Clinical Application: I don't think hospitals should be rushing to start dog therapy programs yet. However, if they are already in place for patients, making them available to staff as well makes sense.

What Do I Tell the Staff? Stress is a huge problem in emergency medicine. You don't need to play with a dog, but you absolutely need to take breaks and look after yourself. This is so you are able to provide the best care to patients, based on the best evidence.

Case Resolution: You are thrilled at the opportunity to take a few minutes away from the department. You have been trying to teach your residents for years that short breaks are important – both for your own health, but also to let you concentrate on your next patients. The availability of a dog to play with is just and added bonus and keeps you off twitter for those five minutes.

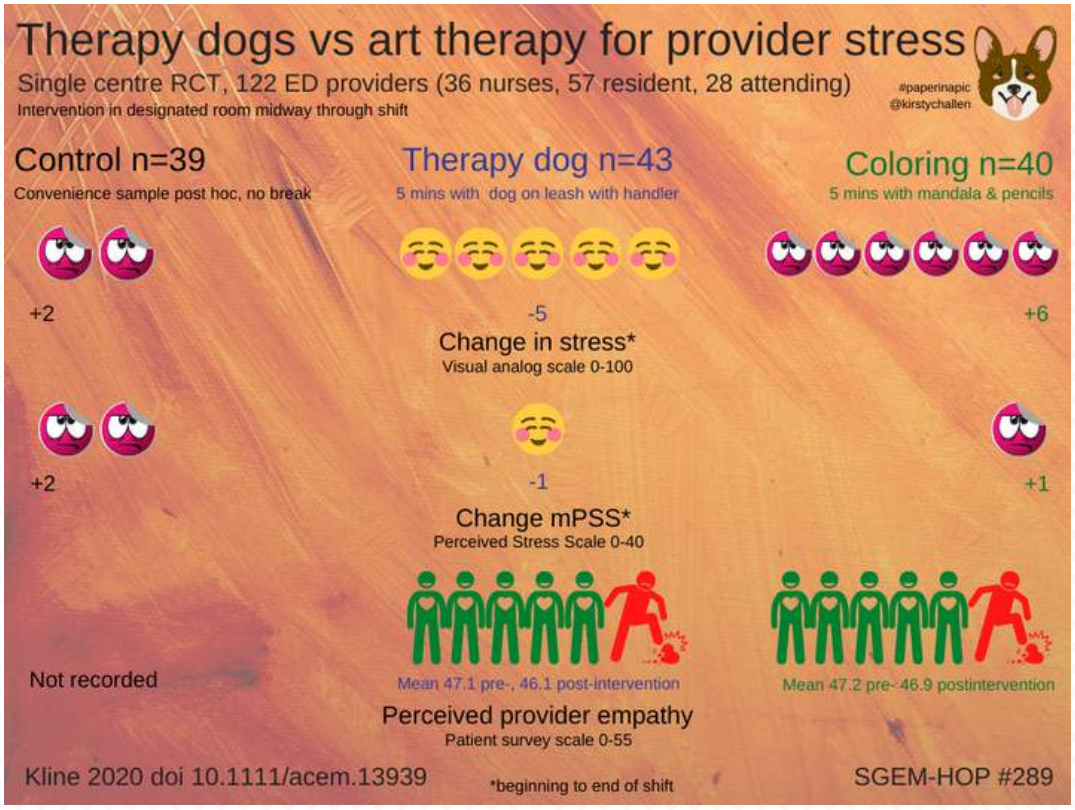
Episode End Notes

Dr. Ken Milne - EBM and Rural
@TheSGEM

What would you prefer on shift for a 5 min stress relief break? thesgem.com/2020/04/sgem28... @First10EM @klinelab @SAEMonline @AcademicEmerMed #sgemhop

Colouring book	5%
Playing with a dog	**72%**
Meditation	13%
Other (tweet idea)	10%

264 votes · Final results



290

NEUROLOGIST LED STROKE TEAMS - WORKING 9 TO 5

Clinical Question:

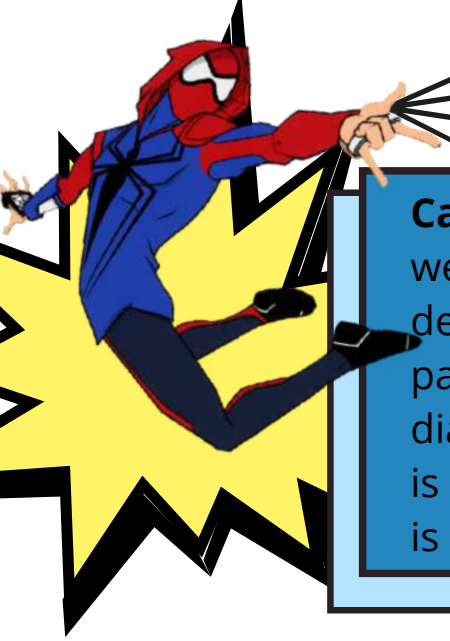
Does the presence of a neurologist led stroke team affect the likelihood of receiving TPA and does that improve a patient-oriented outcome?

Bottom Line:

Neurologists led stroke teams give TPA more often but it did not result in statistically better patient-oriented outcomes in this study.

Guests:

Dr. Chuck Sheppard is an attending Emergency Department Physician at Mercy Hospital in Springfield, Missouri and the medical director for Mercy Life Line air medical service. He has been practicing in Emergency Medicine for over 40 years and involved in EMS services for over 30 years.



Case Overview

Case: 56-year-old female with sudden onset of left arm and leg weakness with slurred speech presents to the emergency department (ED). She was last seen well two hours prior. Her past medical history includes hypertension and type II diabetes. She is not on any anticoagulation except ASA. There is no previous history of stroke. The neurology led stroke team is not available and you wonder if that will affect her outcome.

Background: Treatment for acute ischemic stroke has been debated between neurologists and emergency physicians for years now. A recent PRO/CON debate on the subject was published in CJEM April 2020 with Dr. Eddy Lang and myself.

It was the legend of emergency medicine, Dr. Jerome Hoffman that really raised the concern about the lack of evidence for using thrombolytics in acute ischemic stroke. He was interviewed on an SGEM Xtra segment called No Retreat, No Surrender.

We have covered acute ischemic stroke many times on the SGEM.

- SGEM#29: Stroke Me, Stroke Me
- SGEM#70: The Secret of NINDS
- SGEM Xtra:Thrombolysis for Acute Stroke
- SGEM Xtra: Walk of Life
- SGEM#269: Pre-Hospital Nitroglycerin for Acute Stroke Patients?

Reference: Juergens et al. Effectiveness of emergency physician determinations of the need for thrombolytic therapy in acute stroke. Proc Baylor Univ Med Center Oct 2019

Population: All patients presenting to the ED meeting stroke activation criteria

Intervention: Neurologist led stroke team

Comparison: No neurologist led stroke team

Outcomes:

- **Primary Outcomes:** Rate of tPA administration
- **Secondary Outcomes:** Door-to-needle times, modified Rankin Scale (mRS) at discharge, change in National Institutes of Health Stroke Scale (NIHSS), and discharge disposition

Authors' Conclusions

"Emergency physicians administered significantly less thrombolytics than did neurologists. No significant difference was observed in outcomes, including mRS and admission-to-discharge change in NIHSS."

Quality Checklist for Observational Study

- ☑ 1. Did the study address a clearly focused issue?
- ☑ 2. Did the authors use an appropriate method to answer their question?
- ☑ 3. Was the cohort recruited in an acceptable way?
- ☑ 4. Was the exposure accurately measured to minimize bias?
- ☑ 5. Was the outcome accurately measured to minimize bias?
- ☐ 6. Have the authors identified all-important confounding factors?
- ☑ 7. Was the follow up of subjects complete enough?
- ☑ 8. How precise are the results? Fairly precise given the small sample size
- ☑ 9. Do you believe the results?
- ☐ 10. Can the results be applied to the local population?
- ☑ 11. Do the results of this study fit with other available evidence?

Case Outcomes

Key Results:
There were 415 stroke activations during the study period (Jan 1, 2015 to June 30, 2016). Of those activations, 153 (37%) were managed by the neurologist led team and 262 (63%) were treated by emergency physicians. The median age was early 60's with slightly more female patients in the cohort.

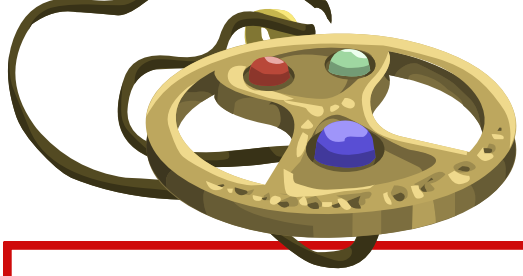
Three-quarters arrived by EMS and the median NIHSS score was 7 for the EM physicians and 6 for the neurologists. The diagnosis was hemorrhagic stroke (~10%), ischemic stroke (~70%), neurological/psychiatric (~15%) and other (~5%).

Neurologists gave TPA 13% more often than EM physicians.

- **Primary Outcome:** Rate of tPA administration
  - 26.3% EM physicians and 39.2% neurologists (p=0.006)

- **Secondary Outcomes:**
  - No statistical difference in mRS score at discharge

	EM Physicians	Neurologists	P Value
Door-to-needle	52min	43.5min	0.036
NIHSS Change	2	2	0.439
Death	7 (6%)	6 (7%)	0.740



Time to Talk Nerdy

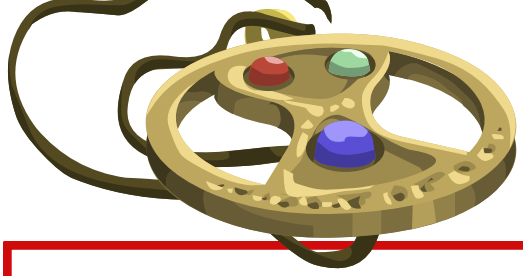
1. Single Center: This was a single center study that may have a unique practice pattern limiting its external validity to other practice environments. As someone who practices in a rural environment, we transport our stroke patients “code stroke” to a higher level of care or use telemedicine with a neurologist who decides on tPA administration.

2. Retrospective Study: This was a retrospective single-center study and results demonstrate association not causation. There could be unmeasured confounders responsible for the observed differences in the results.

3. When Thrombolysed: The neurologists led the team Monday to Friday during business hours. There could be differences that were not measured on nights, weekends and holidays. The baseline NIHSS score was one-point different at baseline between the two cohorts. We know that the severity of the stroke at presentation has a strong influence on the final outcome. We also don’t know if the radiology coverage after hours and on weekends was different.

4. Time to Thrombolysis and Mimics: tPA was administered statistically earlier in the neurologist led stroke team. Previous studies have shown time is not brain and it is possible they were thromoblysing more TIAs or stroke mimics as mentioned by Dr. Hoffman on his SGEM Xtra episode. This could bias the study toward benefit of tPA. Despite this potential bias there was not statistical difference in mRS score at discharge.

5. Harms: Limited data was captured with regards to harm. There were more deaths (mRS 6) and mortality at discharge with neurologist led teams but this was not statistically significant. They provided no information on intracranial hemorrhage, symptomatic intracranial hemorrhages or other bleeds. It is hard to evaluate the net patient efficacy without this information on adverse events.



Time to Talk Nerdy

Even if there was a small signal of benefit with neurologists led teams it could be offset by an increase in harms/adverse events. Given the data provided we do not know what the net impact was in this retrospective, single-center study.

Comment on Authors' Conclusion Compared to SGEM Conclusion: We generally agree with the authors' conclusions.

Clinical Application: It appears that while a “neurologist led stroke team” may be important for other reasons, it appears that in the absence of one only decreases the chance of getting tPA but doesn’t affect the outcome. It is unsure how a neurologist led stroke team would impact outcomes in the new era of endovascular treatment (EVT).

What Do I Tell My Patient? You appear to be having a stroke and we have a system in place to treat your stroke even though the neurologist is not here at this moment. We will take good care of you and the evidence is that your outcomes will be just as good as if the stroke team was led by a neurologist in our hospital.

Case Resolution: Based on this study you can reassure the patient that the lack of a neurologist led stroke team may decrease her chances of getting thrombolysis (clot busting drug) but that will probably not affect her outcome.

Episode End Notes

Dr. Ken Milne - EBM and Rural
@TheSGEM

Who do you think should lead acute stroke teams in the ED to achieve the best patient outcomes?
thesgem.com/2020/04/sgem29... @ACEPNow @SAEMonline @CAEP_Docs @srrezaie @Rick_Pescatore

Neurologists	33.2%
EM Doctors	**36.5%**
Does not matter	25.1%
Other?	5.1%

334 votes · Final results

10:29 AM · Apr 28, 2020 · Twitter for iPhone

Neurologist vs EM led stroke team

Single center retrospective cohort, 2015-6
415 patients meeting stroke activation criteria

#paperinapic
@kirstychallen

Neurologist-led team n=153 Business hours Monday - Friday		Emergency Medicine-led team n=262 Evenings, nights, weekends
60 (39%)	Rate of tPA administration	69 (26%)
43 min (IQR 36-53)	Median door-to-needle time	52 min (IQR 37-70)
2 (IQR 0-7)	Discharge NIHSS	3 (IQR 0-8)
6/83 (7%)	Death	7/122 (6%)

Juergens Proc Bayl Uni Med Cent 2019;32:485

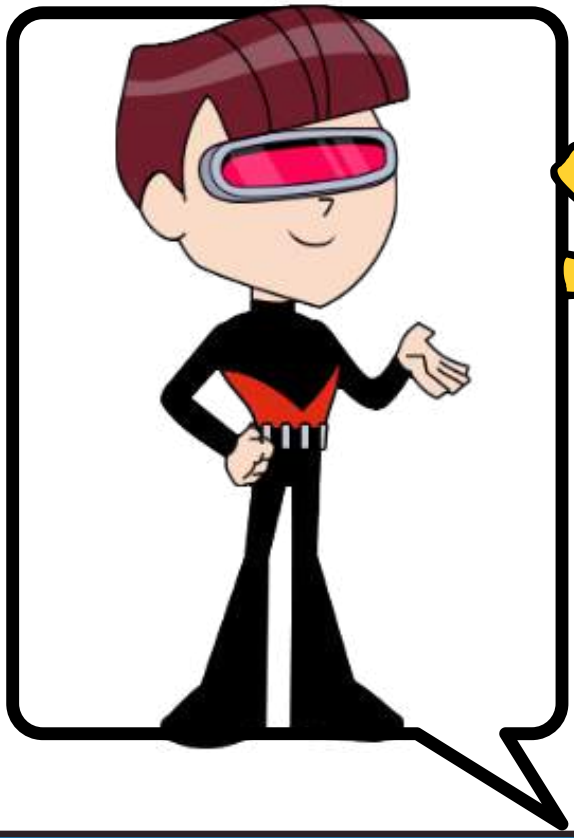
SGEM #290

291

WHO'S GONNA DRIVE YOU TO... THE ED - WITH LIGHTS & SIRENS?

Clinical Question:

What is the association between warning lights and sirens use by EMS and crash-related delays?

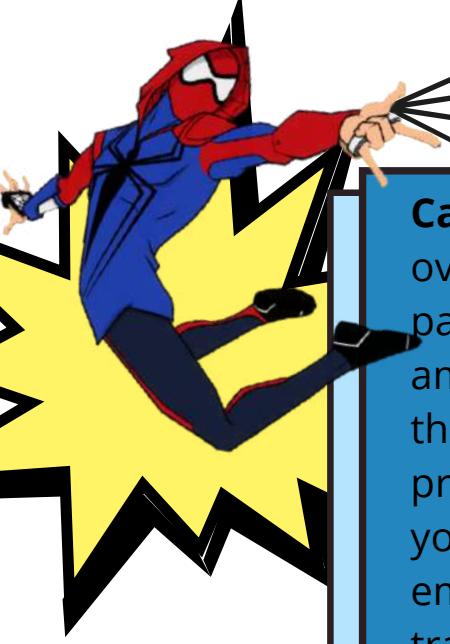


Bottom Line:

The use of warning lights and sirens was associated with a significant increase in the risk of crashing in the transport phase.

Guests:

Dr. Robert Edmonds is an emergency physician in the US Air Force in Virginia. This is Bob's eleventh visit to the SGEM.



Case Overview

Case: You are visiting with your father, a 64-year-old overweight man with hypertension. He describes significant pain in his chest upon awakening and tells you to call an ambulance. The EMS crew arrives and performs a 3 lead EKG that does not show an ST elevated myocardial infarction. They prepare to load your father into the ambulance, and since you're his only child and he's a talker, he mentions you're an emergency physician. The crew then asks if you want them to transport your father Code 3 with full lights and sirens.

Background: The use of warning lights and sirens in ambulances is fairly widespread. Their use is associated with marginally faster response and transport times (7).

Several studies have found ambulance crashes occurring while lights and sirens are used to have a higher injury rate, and a majority of fatal ambulance crashes involve their use (12-15).

EMS agencies have varying guidelines on when to use lights and sirens, and the amount of time saved with lights and sirens is approximately 1-3 minutes (REF). This means the intervention is likely unhelpful for the patient in many transports.

Reference: Watanabe et al. Is Use of Warning Lights and Sirens Associated With Increased Risk of Ambulance Crashes? A Contemporary Analysis Using National EMS Information System (NEMSIS) Data. Annals of Emergency Medicine. July 2019

Population: All dispatches of a transport-capable ground EMS vehicle to a 911 emergency scene from the 2016 National EMS Information System, both the response to the scene and the transport from the scene.

Excluded: Interfacility transfers, intercepts, medical transports, and standbys; responses by nontransport or rescue vehicles, mutual aid activations, and supervisor responses; and events documented as responses or transports by rotor-wing or fixed-wing air-medical services.

Intervention: Use of lights and sirens

Comparison: No lights and sirens

Outcomes: Crash-related delay (proxy for EMS vehicle crash)

Authors' Conclusions

"Ambulance use of lights and sirens is associated with increased risk of ambulance crashes. The association is greatest during the transport phase. EMS providers should weigh these risks against any potential time savings associated with lights and sirens use."

Quality Checklist for Observational Study

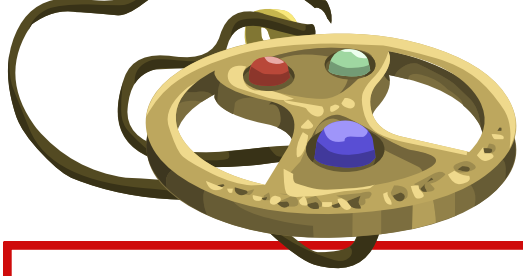
- [x] 1. Did the study address a clearly focused issue?
- [x] 2. Did the authors use an appropriate method to answer their question?
- [x] 3. Was the cohort recruited in an acceptable way?
- [x] 4. Was the exposure accurately measured to minimize bias?
- [x] 5. Was the outcome accurately measured to minimize bias?
- [x] 6. Have the authors identified all-important confounding factors?
- [x] 7. Was the follow up of subjects complete enough?
- [x] 8. How precise are the results? Fairly precise given the small sample size
- [x] 9. Do you believe the results?
- [x] 10. Can the results be applied to the local population?
- [x] 11. Do the results of this study fit with other available evidence?

Case Outcomes

Key Results:
The 2016 NEMSIS database contained 20.4 million 911 dispatches of ground EMS. There was a total of 2,539 crash-related delays.

There was a greater odds ratio of crashing with the use of lights and sirens.

Phase	Without Lights & Sirens per 100,000	With Lights & Sirens per100,000	Adjusted Odds Ratio (95% CI)
Response	4.8	5.4	1.5 (1.2 to 1.9)
Transport	7.0	17.1	2.90 (2.2 to 3.9)



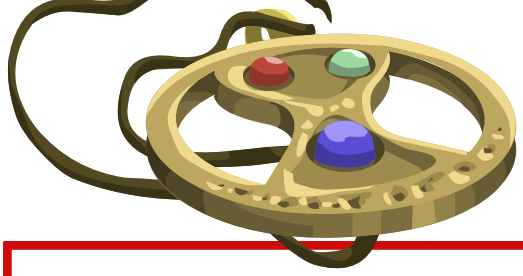
Time to Talk Nerdy

1) Reporting Bias: The authors mention how the study is entirely dependent on crash related delays. It is unknown how widespread reporting of crash-related delays is and since this is dependent on individual agencies self-reporting, there may be bias from the agencies to report this more commonly when lights and sirens are used, as this was already believed at the time of the study to induce additional risk. Alternatively, as the authors point out, some upgrades to lights and sirens may occur after an ambulance crash has occurred, which would bias the results.

2) Association not Causation: It would not be correct to conclude that lights and sirens cause crashes from this publication. This was a retrospective database study not a randomized controlled trial. There could have been unmeasured confounders responsible for the observed results.

3) Partial Lights and Sirens: The authors teased apart three scenarios- complete absence of lights and sirens, full use of lights and sirens, and partial use of lights and sirens. These partial use cases include both cases where there was initially no lights and sirens and then they upgraded to lights and sirens, as well as cases where the crew started with lights and sirens, and they downgraded, turning off the lights and sirens. Due to the retrospective nature of this study, it's not possible to discern at a systematic level how these upgrade and downgrade situations are determined and if there is a theme to these which would impact the results.

4) Peltzman Effect: This is a theory that proposes people will be more likely to engage in risky behavior when safety measures have been introduced. This change in behaviour will compensate for any benefit achieved by intervention. It is named after Sam Peltzman who in the 1970's hypothesized that mandating seatbelts in cars would increase risky behaviour and results in more crashes/injuries. His proposal was controversial and the data from seatbelts ultimately demonstrated a net benefit. However, there are a number of examples of the Peltzman effect in medicine, there can also be



Time to Talk Nerdy

unintended consequences of health care interventions (smoking cessation, electronic health records, rapid response teams, etc). When an intervention is introduced it can nudge behaviour of the physician and the patient resulting in compensatory responses that may have a net negative impact (Prasad and Jena 2014).
Lights and siren use by EMS may give the paramedics a false sense of security. They may drive more aggressively that results in a greater number of crashes.

5) Lack of Patient Oriented Outcomes: Although the direct comparison of lights and sirens and crashes is important, it would have been interesting if data could be collected on patient important outcomes, such as mortality, injuries to the patients or EMS crews, or duration of delays.

Comment on Authors' Conclusion Compared to SGEM Conclusion: We agree with the authors that there is an associated increase in crashes with the use of lights and sirens, but this appears to be much less statistically compelling in the response phase.

Clinical Application: For clinicians involved in the decisions regarding EMS utilization, this study further focuses on the need for judicious use of lights and sirens. As noted in the accompanying editorial by Tanaka in the same issue of Annals, “the Fire Department of the City of New York estimated a 32% reduction in crashes during their test period with updated lights and sirens protocols.” When this is coupled with the fairly minor reduction in transport time of only 1-3 minutes with the use of lights and sirens, it makes a strong case to limit the use of lights and sirens for only the patients with the direst need for timely emergency medical care.

What Do I Tell My Patient? The ambulance crew will make a choice about whether it’s appropriate to use lights and sirens to transport you to the hospital. Even if they don’t go with lights and sirens, they’re still going to get you to the hospital quickly, and there’s less risk of crashing.

Case Resolution: You tell the EMS crew to use their best judgement, and they drive to the nearest emergency room without the use of lights and sirens. Your father is diagnosed with a pulmonary embolism and convalesces in the hospital for a few days until he is uneventfully discharged home on apixaban.
Dr. Robert Edmonds

Episode End Notes

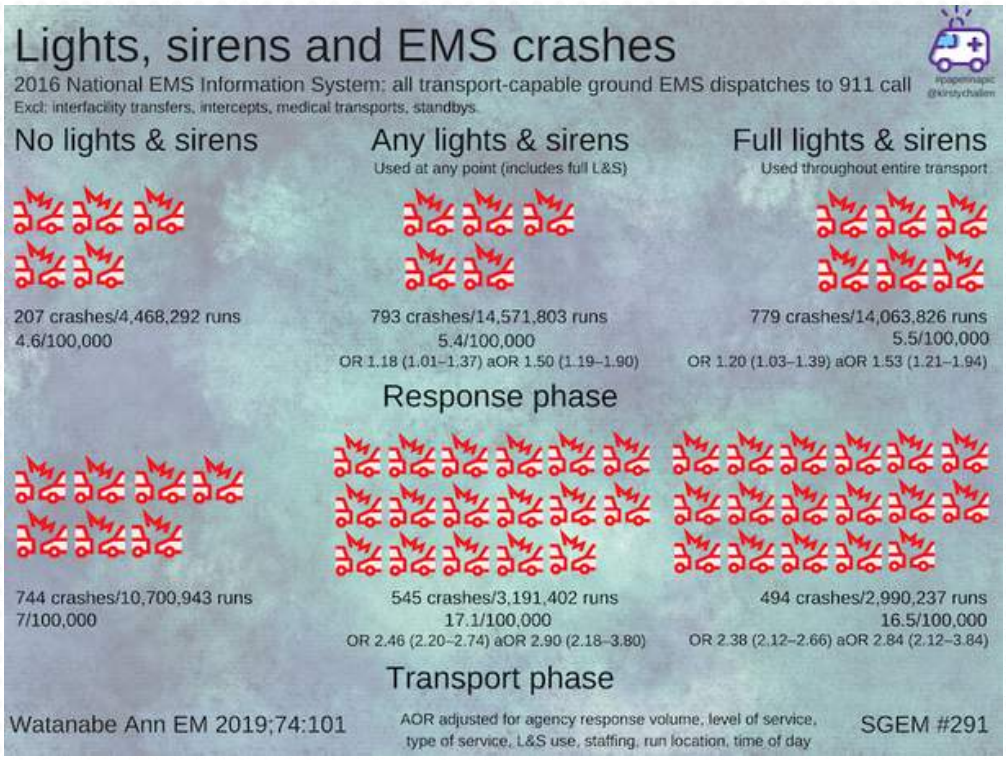
Dr. Ken Milne - EBM and Rural
@TheSGEM

What phase is associated with the greatest odds of accidents?

thesgem.com/2020/05/sgem29...

@hp_ems @EMSWorldFans @EMSTODAY @EMSBlogs @AnnalsofEM @DrHowieMell @hotSahs @the_TOTAL_EM

Response	43.6%
Transport	**56.4%**



292

WITH OR WITHOUT YOU - ENDOVASCULAR TREATMENT WITH OR WITHOUT TPA FOR LARGE VESSEL OCCLUSIONS

Clinical Question:

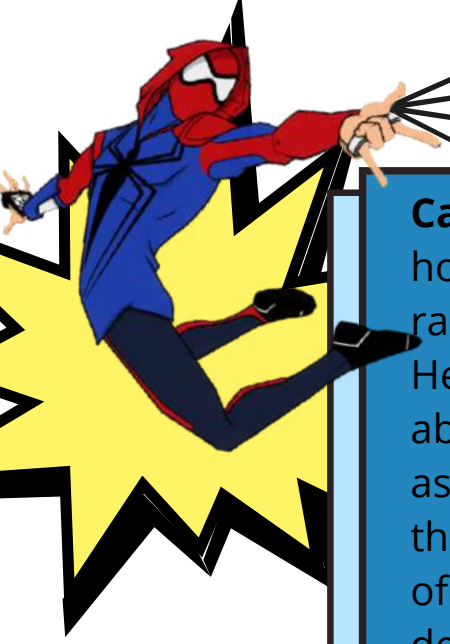
Is endovascular therapy alone non-inferior to endovascular therapy plus systemic thrombolytics in the treatment of patients with large vessel occlusion strokes presenting within 4.5h of onset?

Bottom Line:

There does not appear to be a role for systemic thrombolysis in acute ischemic stroke for appropriate patients when EVT is readily available.

Guest:

Dr. Anand Swaminathan is an Assistant Professor of Emergency Medicine at St. Joseph's Regional Medical Center in Paterson, NJ. Managing editor of EM:RAP and Associate Editor at REBEL EM.



Case Overview

Case: A 53-year-old previously healthy man presents with 1.5 hours of right sided weakness as well as slurred speech. A rapid bedside assessment gives you a National Institute of Health Stroke Score/Scale (NIHSS) of 9 and you are concerned about a large vessel occlusion (LVO) based on the high NIHSS as well as the presence of both an upper extremity drift and the speech abnormality. A non-contrast CT shows no evidence of intracranial hemorrhage. A CT angiogram plus CT perfusion demonstrate a clot in the left proximal middle cerebral artery (MCA) with a small infarcted area and a large penumbra. Based on your institution's current guidelines, the patient is a candidate for endovascular therapy, but they are also within the current window for the administration of alteplase. You wonder if you should give the alteplase while waiting for your neurointerventional team?

Background: The issue of thrombolytics for stroke has been debated since at least 1995. This is the year that the famous NINDS trial was published. We cover this as an SGEM classic that all EM physicians should know about on SGEM#70. Our bottom line was that we were skeptical thrombolysis has a net patient-oriented benefit for acute ischemic strokes.

We have covered this issue of thrombolysis for acute ischemic stroke a number of times on the SGEM

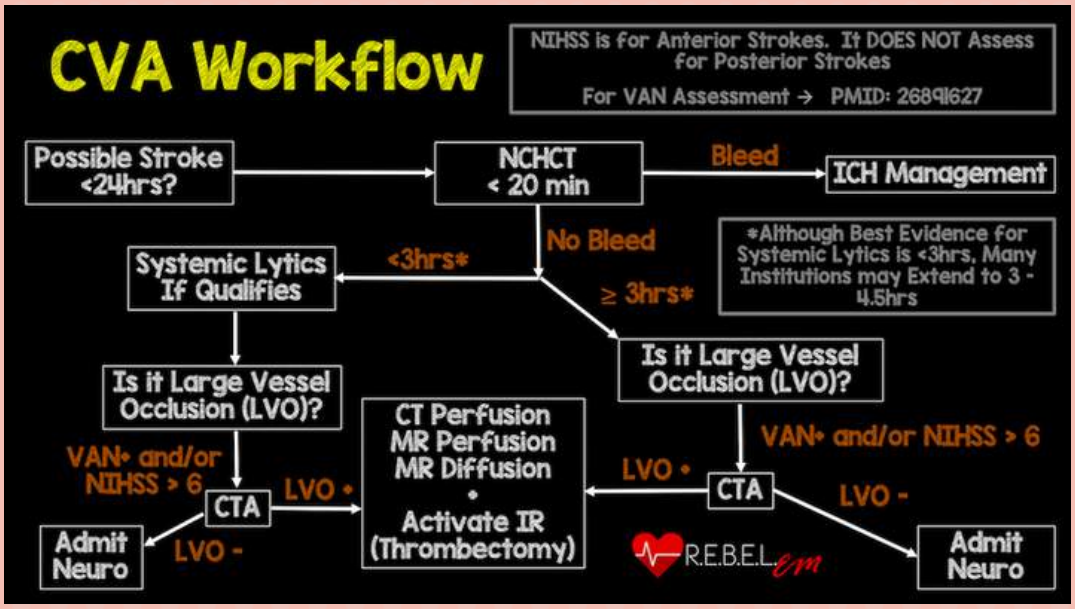
- SGEM#29: Stroke Me, Stroke Me
- SGEM Xtra:Thrombolysis for Acute Stroke
- SGEM#290: Neurologist Led Stroke Teams – Working 9 to 5

You also had the Legend of Emergency Medicine, Dr. Jerome Hoffman on to reflect upon the last 25 years and the thrombolysis for acute ischemic stroke debate (No Retreat, No Surrender)

I also invited my EBM friend, Dr. Eddy Lang onto the SGEM to discuss his perspective on the issue (SGEM Xtra).

Background: This led to a pro/con publication in the Canadian Journal of Emergency Medicine (CJEM) tPA should be the initial treatment in eligible patients presenting with an acute ischemic stroke (Milne et al CJEM April 2020).

The publication of the MR CLEAN trial in January 2015 changed the face of ischemic stroke care. This was the first study demonstrating a benefit to endovascular treatment of a specific subset of ischemic stroke patients: those with LVOpresenting within sixhours of symptom onset. MR CLEAN was followed by a flurry of publications seeking to replicate and refine treatment as well as expand the window for treatment. The REBEL EM team reviewed this literature back in 2018 and, with the help of Dr. Evie Marcolini, created the below workflow:



One major component of LVO management is the use of systemic thrombolytics in patients presenting within the current thrombolytic treatment window prior to endovascular intervention. However, it's unclear if systemic thrombolytic administration results in better outcomes or if it simply exposes the patient to increased risks at a higher cost.

Limited evidence questions the utility of the current approach with thrombolytics plus endovascular therapy (Phan 2017, Rai 2018). There is a clear need for further research into systemic thrombolytics dosing and use.

Reference: Yang P et al. Endovascular thrombectomy with or without intravenous alteplase in acute stroke. NJEM 2020.

Population: Adult patients (18 years of age or older) presenting within 4.5 hours of ischemic stroke symptom onset and with cerebral vascular occlusion on CT angiography of the intracranial internal carotid artery or middle cerebral artery (first and/or second segments) and an NIHSS > 1 and if endovascular thrombectomy was intended to be performed.

Excluded: Disability from a previous stroke or contraindication to IV alteplase and any contra-indication for thrombolysis according to American Heart Association (AHA) guidelines

Intervention: Endovascular thrombectomy alone

Comparison: Endovascular thrombectomy + systemic alteplase 0.9 mg/kg

Outcomes:

- **Primary Outcome:** Modified Rankin Scale (mRS) score assessed at 90 days after randomization looking for non-inferiority (defined as a lower end of the odds ratio > 0.80)
- **Secondary Outcomes:** Death from any cause at 90 days, successful reperfusion before thrombectomy, recanalization at 24-72 hours (assessed by CTA), NIHSS score at 24 hours, and 5-7 days, final lesion volume on CT and mRS comparisons
- **Safety Outcomes:** All hemorrhages and symptomatic intracranial hemorrhages according to the Heidelberg criteria, occurrence of pseudoaneurysm and groin hematoma at the site of arterial puncture used for thrombectomy, cerebral infarction in a new vascular territory at five to seven days, and mortality within 90 days.

Authors' Conclusions

"In Chinese patients with acute ischemic stroke from large-vessel occlusion, endovascular thrombectomy alone was noninferior with regard to functional outcome, within a 20% margin of confidence, to endovascular thrombectomy preceded by intravenous alteplase administered within 4.5 hours after symptom onset."

Quality Checklist for Randomized Clinical Trials

- [?] 1. The study population included or focused on those in the emergency department.
- [✓] 2. The teams were adequately randomized.
- [✓] 3. The randomization process was concealed.
- [✓] 4. The teams were analyzed in the groups to which they were randomized.
- [?] 5. The study teams were recruited consecutively (i.e. no selection bias).
- [✓] 6. The teams in both groups were similar with respect to prognostic factors.
- [✗] 7. All participants (patients, clinicians, outcome assessors) were unaware of group allocation.
- [?] 8. All groups were treated equally except for the intervention.
- [✓] 9. Follow-up was complete (i.e. at least 80% for both groups).
- [✓] 10. All patient-important outcomes were considered.
- [✗] 11. The treatment effect was large enough and precise enough to be clinically significant.

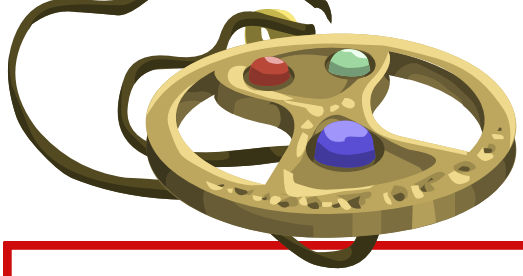
Case Outcomes

Key Results:
They screened 1,586 patients for eligibility and 654 were included in the final analysis. The median age was 69 years and slightly more were male. The median NIHSS score was 17.

- **Primary Outcome:** Adjusted odds ratio for the mRS
  - aOR = 1.07 (95% CI 0.81 TO 1.40)
  - Demonstrates non-inferiority as lower limit of non-inferiority was set at 0.80

- **Secondary Outcomes:**

	Thrombectomy Alone	Combination Therapy	Relative Risk (95% CI)
Mortality at 90 Days	17.7%	18.8%	0.94 (0.68 - 1.30)
Symptomatic ICH	4.3%	6.1%	0.70 (0.36 - 1.37)
Successful Reperfusion Prior to EVT	2.4%	7.0%	0.33 (0.14 - 0.74)
Overall Successful Reperfusion	79.4%	84.5%	0.70 (0.47 - 1.06)
Recanalization at 24-72 Hours	85.1%	89.1%	0.71 (0.42 - 1.20)



Time to Talk Nerdy

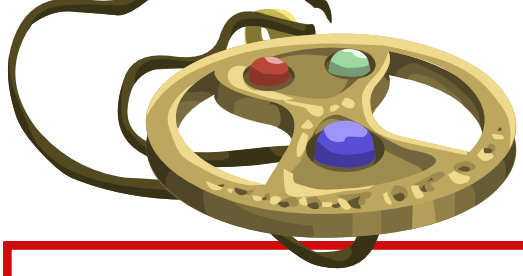
1) Consecutive Patients and External Validity – The manuscript did not explicitly say patients were recruited consecutively. Without this information it is hard to comment on whether or not there was selection bias. We are also concerned about the external validity of a stroke trial conducted in China compared to the care provided in the USA.

2) Declined to Participate – Of eligible patients, 15% (240/1,586) declined to participate. There was no information provided on this group in the published paper or supplementary material. Patients deciding to participate could have been different from those who decided not to participate. This too could have introduced some selection bias.

3) Lack of Blinding: The treating physicians and study participants were not blinded to group allocation. This could have biased the study towards the EVT alone if that hypothesis was known to these two groups.

4) Intention-To-Treat (ITT): You will often hear us comment about whether or not the trial has used an ITT analysis. This is a quality indicator for superiority designs. However, for non-interiority trials a per-protocol analysis is the more conservative approach to minimize bias.Using an ITT can bias the results toward the null hypothesis. The per-protocol analysis could only be found in the supplemental appendix.

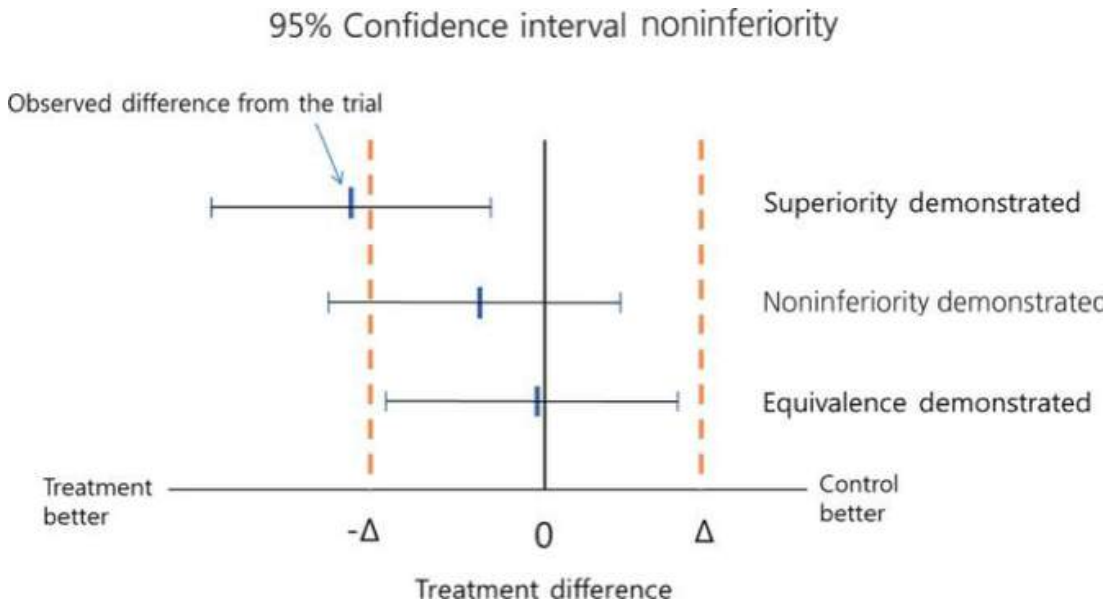
A non-inferiority design seeks to establish a novel treatment is not worse than a standard treatment by more than a predetermined acceptable amount. The null hypothesis for a non-inferiority study states for a given outcome, treatment A (a novel treatment) is worse than treatment B (an accepted, validated treatment) by more than a non-inferiority margin called the delta (Δ). In contrast, the alternate hypothesis states for a given outcome, treatment A is not worse than treatment B by more than Δ.



Time to Talk Nerdy

This type of study design is often used when two circumstances are met: a placebo trial would be unethical, due to the existence of a treatment proven superior to placebo, and the novel treatment offers other advantages (e.g., cost, ease of use, less invasiveness, fewer adverse effects, etc.).

Setting the non-inferiority margin should be specified a priori. It can be set at a statistically significant difference or a clinically significant difference. Subjectivity can be introduced when determining what is considered clinically significant. A number of guidelines exist like the CONSORT extension statement to help researcher properly design non-inferiority trials.



5) Outcomes: Outcome data was obtained via interviews performed in person or by phone. Phone interviews are suboptimal for assessing functionality. This could add more statistical noise into the data and bias the results to finding non-inferiority. We could not find how many assessments were done in person and how many were done by phone. It would be interesting to see if there were any differences in outcome that could be attributed to the method of assessing the outcome.

Comment on Authors' Conclusion Compared to SGEM Conclusion: We generally agree with the authors' conclusions.

Clinical Application: Additional studies are needed but, given the potential harms of systemic thrombolytics, there should be careful consideration about their use in patients with LVO strokes who are proceeding to endovascular therapy.

What Do I Tell My Patient? The scan of your head shows you are having a stroke. It is being caused by a clot in a large blood vessel in your brain. We have a team that can get the clot out. This will give you a good chance of having a good recovery. The team will be here soon to tell you more details about the potential benefits and potential risks of the surgery.

Case Resolution: Based on the best available evidence and the potential for harm, you decide to hold off on administration of systemic thrombolytics. Your neurointerventional team calls for the patient 20 minutes after you get the report from radiology and you bring him up to the interventional suite. The patient has a clot retriever deployed which returns circulation to the affected area. Although they have a long road to recovery, the patient is discharged to a rehab setting with only a mild weakness in the arm and fully recovered speech.

Episode End Notes

Dr. Ken Milne - EBM and Rural
@TheSGEM

A patient with a acute ischemic stroke and is a candidate for EVT. They are also within the current window for the administration of tPA. What do you do? thesgem.com/2020/05/sgem29.. #FOAMed #EBM @EMSwami @srrezaie @KirstyChallen @AliRaja_MD @EddyLang1 @SAEMEBM @meganranney

EVT with tPA	**56%**
EVT without tPA	44%

273 votes · Final results

11:11 AM · May 26, 2020 · Twitter Web App

Endovascular therapy +/- TPA in acute stroke

Multicentre non-inferiority RCT, China

Adults within 4.5h symptom onset, NIHSS>1, occlusion intracranial internal carotid artery/first or proximal second segment middle cerebral artery/both
Excl: disability from previous stroke, contraindication to alteplase

#paperinapic
@kirstychallen

Endovascular thrombectomy n=327		Thrombectomy + IV TPA n=329 Alteplase 0.9mg/kg
Median 3 IQR 2-5	mRS at 90 days	Median 3 IQR 2-5
58 (18%)	Death at 90 days	62 (19%)
14 (4%)	Symptomatic ICH	20 (6%)
Median 12 IQR 5-20	NIHSS at 24 hours	Median 12 IQR 5-22

Zhang NEJM 2020 10.1056/NEJMoa2001123

mRS: modified Rankin Scale
ICH: intracranial hemorrhage

SGEM #292

293

CRASH IN THE US, CRASH IN THE US, CRASH-2 IN THE USA

Clinical Question:

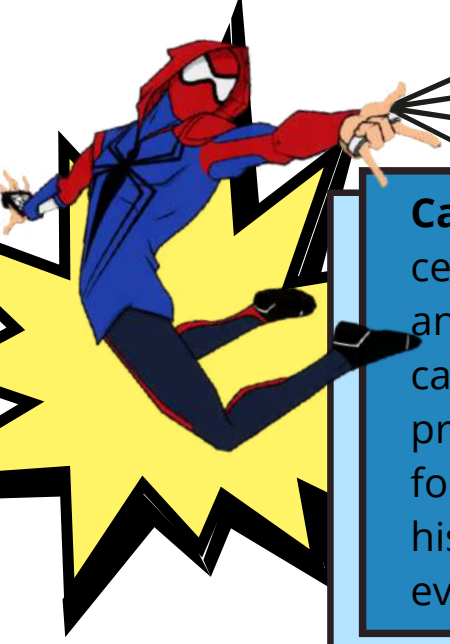
What is the mortality and thromboembolic events in adult trauma patients receiving TXA in an American level 1 trauma center?

Bottom Line:

The evidence supports the use of TXA in the treatment of adult patients with blunt trauma, but the increased risk of thromboembolism is concerning.

Guest:

Dr. Corey Heitz is an emergency physician in Roanoke, Virginia. He is also the CME editor for Academic Emergency Medicine.



Case Overview

Case: A 44-year-old male presents to your level 1 trauma center by EMS after a motor vehicle collision. He is hypotensive and tachycardic. You suspect abdomen and pelvic trauma and calculate his injury severity score (ISS) to be 22. Your hospital protocol is to give tranexamic acid (TXA) 1g IV over 10 minutes followed by a 1g infusion over eight hours. You wonder what his over-all chance of dying or developing a thromboembolic event when treated with TXA.

Background: TXA is synthetic derivative of lysine that controls bleeding by inhibiting fibrinolysis and thus stabilizing clots that are formed. We have covered TXA as a treatment modality a number of times on the SGEM. The evidence for TXA providing a patient-oriented outcome (POO) has been mixed. It seems to work for epistaxis (SGEM#53 and SGEM#210), failed to demonstrate a decrease in all-cause mortality in post-partum hemorrhage (SGEM#214), and did not result in an improved neurologic outcome in hemorrhagic strokes (SGEM#236).

REBEL EM has looked at using TXA for those conditions plus a few others (we will include a table in the show notes). It is unclear if it provides a benefit for gastrointestinal bleeds (GIB). Nebulized TXA shows promise for both post-tonsillectomy bleeding and hemoptysis. However, better studies are needed to confirm these observations.

Tranexamic Acid (TXA) for Everything That Bleeds?

TXA Use	Yes or No	Dosing
Trauma ≤3hrs • Thinking MTP	YES	1g IV over 10min • 1g IV over 8hr
ICH	NO	---
PPH	+/-	1g IV over 10min
GIB	+/-	???
Epistaxis	YES	500mg Soaked Pledget
Post-Tonsillectomy	YES	250mg Nebulized (<25kg) OR 500 - 1000mg Nebulized (≥25kg)
Hemoptysis	YES	250mg Nebulized (<25kg) OR 500 - 1000mg Nebulized (≥25kg)

Dr. Anand Swaminathan and I covered the classic CRASH-2 Trial (SGEM#80). This study published in 2010 showed an absolute mortality reduction of 1.5% in adult trauma patients giving a number needed to treat to prevent one death of 67 (Shakur et al. Lancet 2010)

CRASH-3 was a well-designed, large, multi-centred randomized placebo controlled trial published in October 2019 (The Lancet). It asked if TXA had a mortality benefit in patients with isolated head trauma (SGEM#270)? While there was a suggestion of benefit in a secondary subgroup analysis, the primary outcome demonstrated no statistical difference in head-injury related mortality with TXA compared to placebo (18.5% TXA vs. 19.8% placebo, RR 0.94 [95% CI 0.86 to 1.02]).

One of the limitations to both CRASH-2 and CRASH-3 was the external validity. The majority of sites involved were in middle to low income countries. CRASH-3 had one Canadian site and the USA had no participating centres. Transfusion practices and identification of adverse events may differ in developing countries compared to the USA.

Reference: Erramouspe et al. Mortality and Complication Rates in Adult Trauma Patients Receiving Tranexamic Acid: A Single-center Experience in the Post–CRASH-2 Era. AEM May 2020

Population: Adults (18 years or older) who received TXA after an acute traumatic injury

Intervention: TXA 1g IV over 10 minutes and maintenance infusion of 1g IV over 8 hours

Excluded: Patients who received oral TXA, received it for elective surgery or nontrauma indications, received TXA 8 hours or longer afte the injury, and patients with cardiac arrest at time of ED arrival.

Comparison: None

Outcomes:

- **Primary Outcome:** In-hospital mortality
- **Safety Outcome:** Thromboembolic event within 28 day

This is an SGEMHOP episode and we are pleased to have both the lead author and senior author on the episode.

Dr. Joaquin Erramouspe is a medical doctor, who finished medical school in Uruguay, moved to the USA for further training and research, and now, is working as a researcher at Queensland University of Technology while obtaining his masters in science.

Dr. Daniel Nishijima is an emergency medicine physician at University of California Davis. His research focus is on trauma and neurological emergencies, particularly those with coagulation disorders.

Authors' Conclusions

"Adult trauma patients receiving TXA had similar incidences of death but higher incidences of thromboembolic events compared to the CRASH-2 trial. Variation in patient characteristics, injury severity, TXA dosing, and surgery and transfusion rates could explain these observed differences. Further research is necessary to provide additional insight into the incidence and risk factors of thromboembolic events in TXA use."

Quality Checklist for Observational Study

- [x] 1. Did the study address a clearly focused issue?
- [x] 2. Did the authors use an appropriate method to answer their question?
- [x] 3. Was the cohort recruited in an acceptable way?
- [x] 4. Was the exposure accurately measured to minimize bias?
- [x] 5. Was the outcome accurately measured to minimize bias?
- [x] 6. Have the authors identified all-important confounding factors?
- [x] 7. Was the follow up of subjects complete enough?
- [x] 8. How precise are the results? Fairly precise given the small sample size
- [x] 9. Do you believe the results?
- [ ] 10. Can the results be applied to the local population?
- [x] 11. Do the results of this study fit with other available evidence?

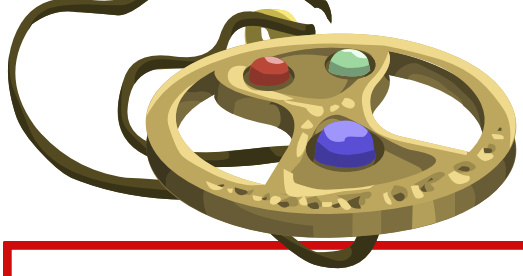
Case Outcomes

Key Results:
This retrospective study included 273 patients with a mean age of 43.8 years and 74% male.

All-cause mortality was 12.8% and thromboembolic events were 6.6%

Difference between the current study and the previously published CRASH-2 study.

	Current Study	CRASH-2
Mean Age (years)	43.8	34.6
Male Sex	74%	83.6%
All-Cause Mortality	12.8%	14.5%
Bleeding Mortality	2.2%	4.9%
Thromboembolic Event	6.6%	2.0%
Any Surgery	64.8%	47.9%
Blood Products Transfused	74%	50.4%



Time to Talk Nerdy

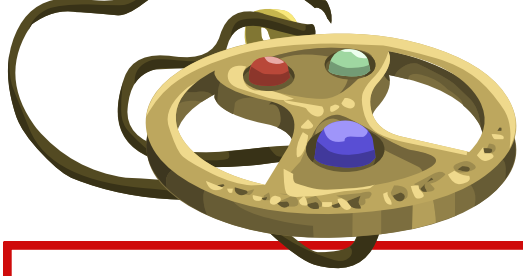
We have five nerdy question to ask Joaquin and Daniel to better understand their teams study. Listen to the podcast on iTunes to hear his responses.

1) Chart Review: You referenced Kaji et al. Looking through the retro-spectoscope: reducing bias in emergency medicine chart review studies (Annals of EM 2014). What additional benefit does this publication add to the quality check list for observational studies published by my EBM mentor Dr. Andrew Worster? (Annals of EM 2005).

2) External Validity: This study was conducted at a single Level 1 trauma center. How do you think it would compare to other Level 1 Trauma Centers in the USA?

- None of our trauma centres in Canada see the volumes that you do in the large US trauma centres. This is because of the lack of penetrating trauma. I have worked full time for 25 years in an ED and never seen a gunshot injury. Most of the trauma we see is from blunt force injury. Do you think the results would be similar in a Canadian trauma centre?
- What about non-level 1 trauma centers in the USA?
- I thought that CRASH-2 and CRASH-3 had a lot of external validity to where I work in a rural/critical access hospital. We don't have a CT scanner or a surgeon and our massive transfusion protocol is both units of O-negative blood. We usually give TXA to our trauma patients but transfer them quickly to our local trauma centre. Did your study include or exclude patients transferred to your hospital who had TXA provided prior to arrival?

3) Lack of Control: There was no control group in this study, but you did compare your results to the CRASH-2 study. Let's go through some of the differences and comment on how that may have impacted your results or explain your findings:



Time to Talk Nerdy

- Demographic Differences – The patients were older and there were less men in your cohort.
- Mortality Differences – There was less all-cause mortality and less bleeding mortality in your study compared to CRASH-2.
- Differences in Any Surgeries and Blood Products Transfused – You had more patients taken to the operating room for surgery and more transfusions of blood products.
- Thromboembolism – Previous studies have reassured that the risk of thromboembolism is low. However, in your study you had more than three times the events as CRASH-2 (6.6% vs 2.0%). Is this because you had better methods to detect these adverse events using your EMR or is it some other reason?

4) Comparison Group: There were 31/321 (10%) of patients who did not receive TXA. Do you have any more information on why they did not receive TXA and who they did clinically?

5) Next Steps: What are the unanswered questions you have about TXA use in adult trauma patients?

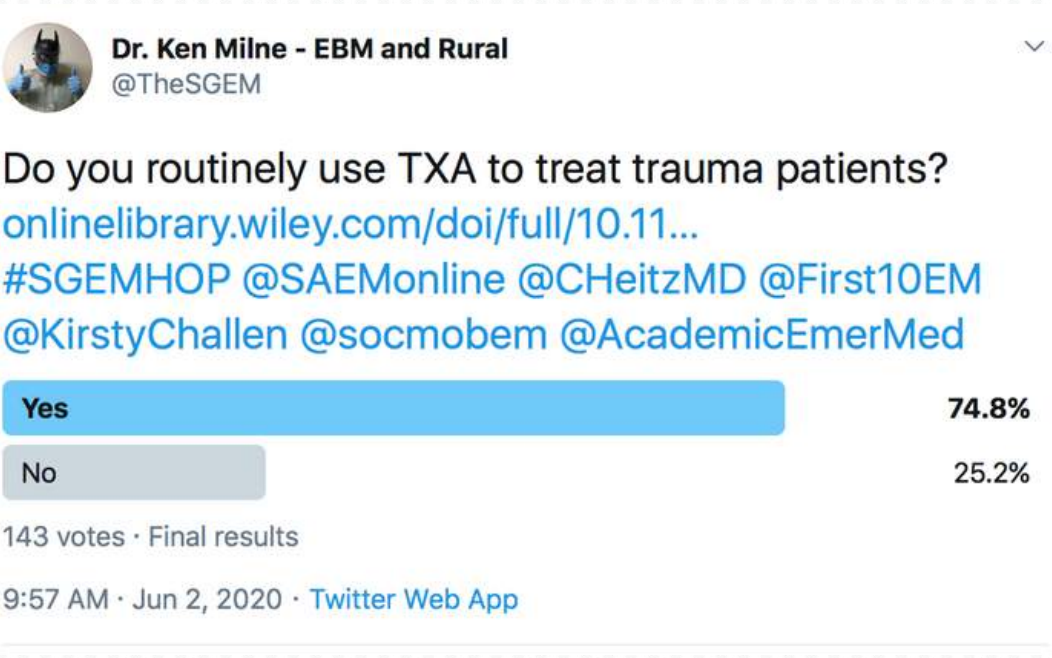
Comment on Authors' Conclusion Compared to SGEM Conclusion: We generally agree with the authors' conclusions.

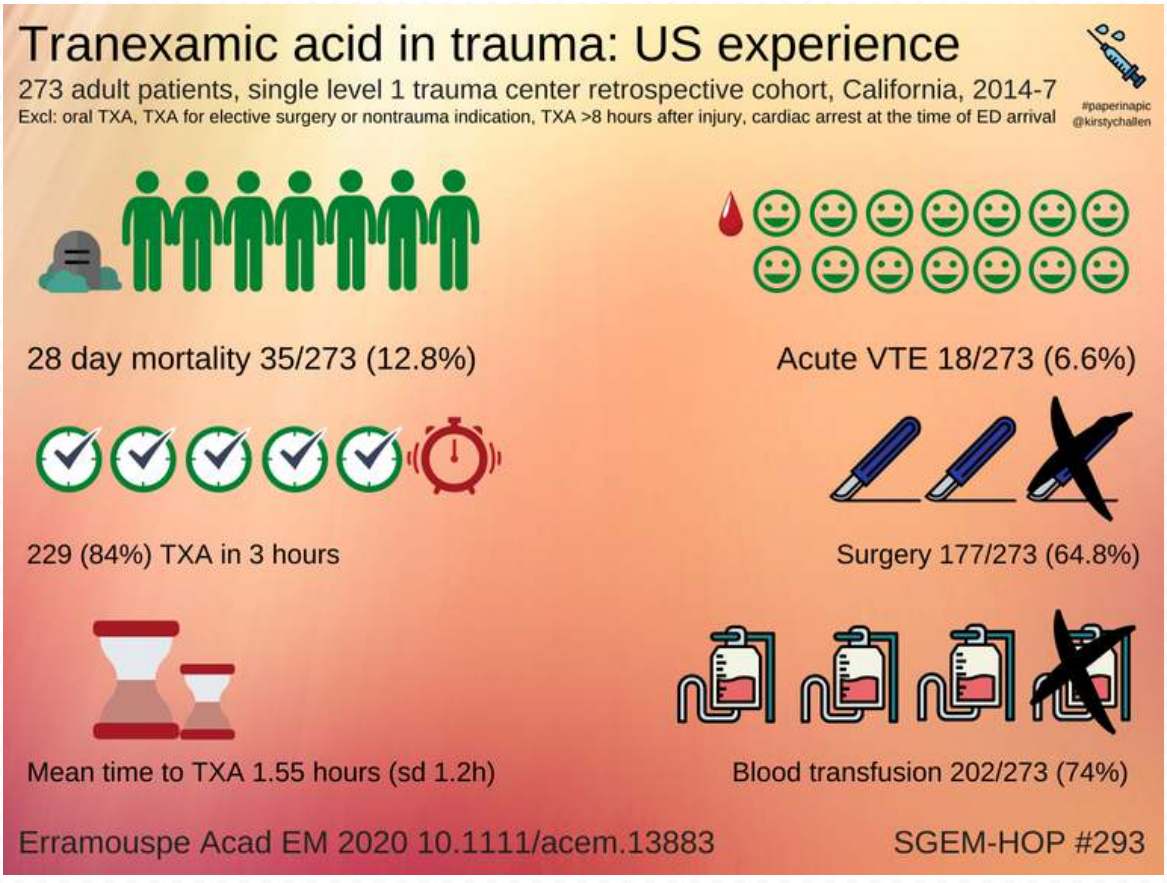
Clinical Application: TXA has an absolute mortality benefit of 1.5% in CRASH-2. This new retrospective study will not change my practice but does increase our concern about thromboembolic events.

What Do I Tell My Patient? It looks like you have internal bleeding. We are going to give you blood products as well as a medicine called TXA. This can help stop the bleeding and improve your chance of survival. There is a low risk of increasing blood clotting. The surgeons will take to more about taking you to the operating room.

Case Resolution: The patient is intubated; his pelvis is placed in a binder and you start your hospital's massive transfusion protocol. A FAST exam is positive, and the surgeons start debating whether to get more advanced imaging or take the patient directly to operating room for an exploratory laparotomy. You step out of the room and make a mental note to look up the patient tomorrow on your next shift.

Episode End Notes





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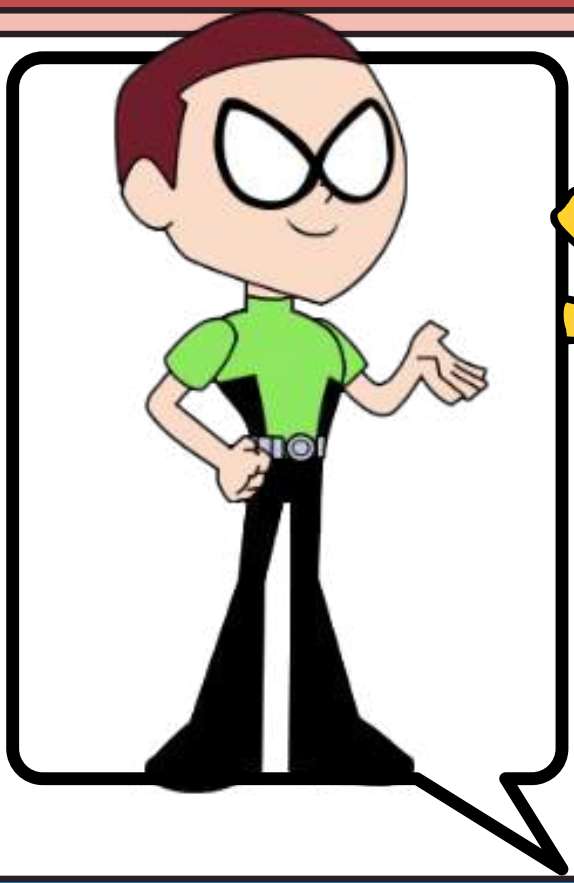
BLOOD PRESSURE - DO BETTER, KEEP RISING WITH NOREPI

Clinical Question:

Does starting norepinephrine earlier in septic shock lead to earlier shock control?



Bottom Line:

Early norepinephrine can change some MOOS (map, lactate, urinary output) but does not seem to change any POOS (in-hospital or 28-day mortality) in adult patients with septic shock

Guest:

Dr. Max Hockstein trained as an Emergency Medicine physician at University of Texas Southwestern and is finishing his Intensive Care fellowship at Emory. Max is then going to Georgetown to be an attending in both EM and ICU.

Case Overview

Case: It's another day in your emergency department (ED). Six hours into your shift, you finish dispo'ing the "really quick sign-out" from the night before. The triage nurse places a 61 year-old-man with fever, hypotension, cough into the smallest room in the ED. You scan through the EMR and see the blood pressure is 60/40. Being an astute emergency physician, you surmise that this value is one number column short of normal. It's uncomfortably low – is it time to start a norepinephrine infusion?

Background: I think we have covered sepsis more often than any other topic on the SGEM. It was the landmark paper published 19 years ago by Dr. Emanuel Rivers on early goal directed therapy in the treatment of severe sepsis and septic shock that sensitized the medical community (Rivers et al NEJM 2001).

- SGEM#44: Pause (Etomidate and Rapid Sequence Intubation in Sepsis)
- SGEM#69: Cry Me A River (Early Goal Directed Therapy) ProCESS Trial
- SGEM#90: Hunting High and Low (Best MAP for Sepsis Patients)
- SGEM#92: ARISE Up, ARISE Up (EGDT vs. Usual Care for Sepsis)
- SGEM#113: EGDT – ProMISe(s) ProMISe(s)
- SGEM#174: Don't Believe the Hype – Vitamin C Cocktail for Sepsis
- SGEM#207: Ahh (Don't) Push It – Pre-Hospital IV Antibiotics for Sepsis.

One of the goals of the early treatment of septic shock is to restore end-organ perfusion. Significant effort has been placed on the administration of IV crystalloids to address concerns for hypovolemia in septic shock. However, it has become evident that patients are often over-resuscitated with IV fluids which adversely impacts outcome. As such, the idea of the early norepinephrine administration to restore end-organ perfusion in septic shock has been suggested.

Trials that examine outcomes in shock, historically, have examined two types of outcomes: patient-oriented outcomes (POOs) and monitor-oriented outcomes (MOOs). POOs focus on occurrences that matter to patients while MOOs do not.

Many trials examining vasoactive infusions use MOOs as an endpoint(s) targeted to the medication's intended use (i.e. increase in MAP). Much like titrating a therapy to an outcome, MOOs are frequently easier to monitor (ex: blood pressure, heart rate, mean arterial pressure, oxygen saturation, etc).

An old adage in resuscitating the hypotensive patient "first, fill the tank" has gone largely unchallenged over the past several years. Oddly enough, however, shortening the duration of shock time-to-shock-resolution hasn't translated to any measurably better outcomes.

Reference: Permpikul et al.Early Use of Norepinephrine in Septic Shock Resuscitation (CENSER): A Randomized Trial. Respir Crit Care Med 2019.

Population: Adult patients (18 year of age and older) presenting to the ED with a mean arterial pressure (MAP) < 65 mmHg. Infection needed to be the suspected cause of the hypotension. Patients also had to meet 2012 surviving sepsis diagnostic criteria.

Intervention: Early norepinephrine adjusted to 0.05ug/kg/min for 24hrs plus usual care

Excluded: Acute cardiac and cerebral conditions, pulmonary edema, status asthmaticus, gastrointestinal bleeding, pregnancy, burn, drug overdose, trauma, need immediate surgery and cancer.

Comparison: Placebo plus usual care (intravenous fluids, appropriate antibiotics, source control and organ support as directed by the attending physician)

Outcomes:

- **Primary Outcome:** Shock control (sustained MAP > 65mmHg) by six hours after diagnosis of sepsis with hypotension together with adequate tissue perfusion (urine flow >0.5ml/kg/h for two consecutive hours or a decrease in serum lactate by > 10% from the initial lactate level).
- **Secondary Outcomes:** 28-day mortality and hospital mortality, time from initial treatment to achieving target MAP and tissue perfusion goal (and within six hours), urine output within six hours, rate of respiratory failure requiring mechanical ventilator support, rate of renal failure requiring renal replacement therapy, lactate clearance, and number of organ support-free days to day 28 were also recorded.

Authors' Conclusions

"Early norepinephrine was significantly associated with increased shock control by 6 hours. Further studies are needed before this approach is introduced in clinical resuscitation practice."

Quality Checklist for Randomized Clinical Trials

- ☑ 1. The study population included or focused on those in the emergency department.
- ☑ 2. The teams were adequately randomized.
- ☑ 3. The randomization process was concealed.
- ☑ 4. The teams were analyzed in the groups to which they were randomized.
- ☑ 5. The study teams were recruited consecutively (i.e. no selection bias).
- ☑ 6. The teams in both groups were similar with respect to prognostic factors.
- ? 7. All participants (patients, clinicians, outcome assessors) were unaware of group allocation.
- ☑ 8. All groups were treated equally except for the intervention.
- ☑ 9. Follow-up was complete (i.e. at least 80% for both groups).
- ☑ 10. All patient-important outcomes were considered.
- ? 11. The treatment effect was large enough and precise enough to be clinically significant.

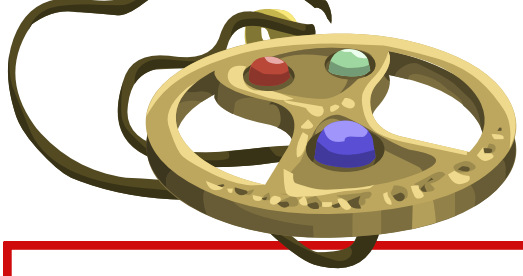
Case Outcomes

Key Results:
There were 310 patients included in the trial. The median age was in the late 60's with slightly more females. The main sources of infections were urinary tract 30%, pneumonia 25%, intra-abdominal 20%, skin and soft tissue 10%.

Shock was significantly higher in early norepinephrine group.

- **Primary Outcome:** Shock control by six hours was 76.1% in early norepinephrine group vs. 48.4% in the control group.

	Early Norepinephrine	Control Group	P-Value
Time to Shock Control	93 minutes	192 minutes	<0.001
28 Day Mortality	15.5%	21.9%	0.15
Hospital Mortality	22.6%	24.5%	0.69
Pulmonary Edema	14.4%	27,7%	0.004
Target Urine Output <6hrs	69%	48.4%	<0.001
Lactate Level <2 by 6hrs	47.1%	40.3%	0.29
Lactate Clearance >10%	41.3%	27,7%	0.09
Renal Replacement Tx	12.3%	14.8%	0.51
IV Fluids 0-6hrs	2,450ml	2,600ml	0.33
Mechanical Ventilation	37.4%	38.1%	0.91
New Arrhythmia	11.0%	20.0%	0.03
Limb/Intestinal Ischemia	3.2%	1.9%	0.47



Time to Talk Nerdy

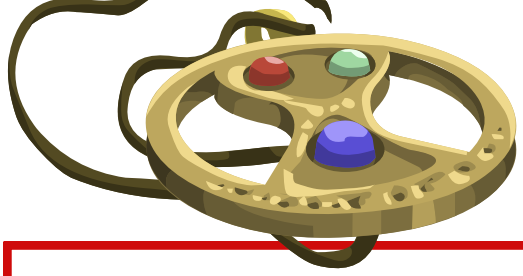
1) Time-to-Shock-Control: Intuitively, you would think that the less time that people spend in hemodynamic “shambles“, the better they would do. Think of all the trials that tried to improve time-to-shock-control like the CORTICUS trial.ed This probably has something to do with our evolution and the human ability to withstand wide ranges of hemodynamic derangements. Regardless, no study has been able to show that the less time patients spend in shock, the better they will do.

The metric they used for shock-control (urine output and lactate clearance) were suboptimal. Neither of these clearly demonstrates shock control. Lactate clearance is unreliable and can be misleading- especially in patients that are receiving therapies that increase the concentration of glycolytic intermediates or increase their clearance.

2) Blinding: There is a possibility that the study was unblinded. This is because the norepinephrine gives a rapid rise blood pressure which could be noticed by the treating clinician. The unblinding could have introduced some bias into the trial. The researchers could have checked on this by asking the clinicians to guess patient group allocation.

3) MOOs and POOs: Do you really think patients care how long it took them to get shock-control, what their lactate level or urine output is per hour or what was their MAP? These are monitor-oriented outcomes (MOOs). What patients care about more is being dead or alive (80’s tune Dead or Alive) which would be a patient- oriented outcome (POO). An even better POO would be alive and physically well.

4) Intravenous Fluids: Early norepinephrine use didn’t decrease the amount of volume people received. So, maybe, despite having earlier shock control, the tendency was to complete 30 mL/kg mandate. It is a weird predicament



Time to Talk Nerdy

we've placed ourselves into where we have to think about a catecholamine as a "fluid-sparing agent." Our goal should be to stop people from going from raisin to grape, so we don't have to take them from grape to raisin later (if we get the chance).

5) Adverse Events: The observed adverse events in this trial also told us what we already know: skin necrosis rates were equal between the two groups. Also note that half of the patients got norepinephrine through a peripheral line. There was less cardiogenic pulmonary edema in the early norepinephrine group, however, this was puzzling since the groups received approximately the same amount of IV fluid. This may be because of the (trivial) beta-1 effects of the norepinephrine. There were also less new-onset arrhythmias in the early norepinephrine group.

Comment on Authors' Conclusion Compared to SGEM Conclusion: We agree with the authors that norepinephrine raises blood pressure, MAP, urinary output and lactate clearance. However, we did not need a study to tell us that information. This makes the paper's conclusion no better than the ATHOS-3 trial. This paper showed that giving NE early is feasible and not unreasonable.

Clinical Application: This trial does not change anything for me. Hypotension is an emergency and as emergency physicians, we are good at treating it. This was a well-designed trial that should generate tempered enthusiasm for early norepinephrine while further trials are being performed. The ongoing CLOVERS trial will hopefully shed some light on many of the hypothesis-generating questions that the secondary outcomes of this trial left us with.

What Do I Tell My Patient? You have a pneumonia. This is an infection in your lungs. It is making your blood pressure dangerously low. We can increase your blood pressure by giving you some IV fluids. We can also raise your blood pressure with a medicine called norepinephrine. This medicine can be turned up to keep you blood pressure closer to normal while we give the antibiotics time to work.

Case Resolution: While a bag of isotonic crystalloid of choice is being infused through one peripheral IV, fixed-dose norepinephrine at 0.05 ug/kg/min is started through the other. The patient is then taken to the intensive care unit where he makes a full recovery after three days of treatment for his community acquired pneumonia.

Episode End Notes

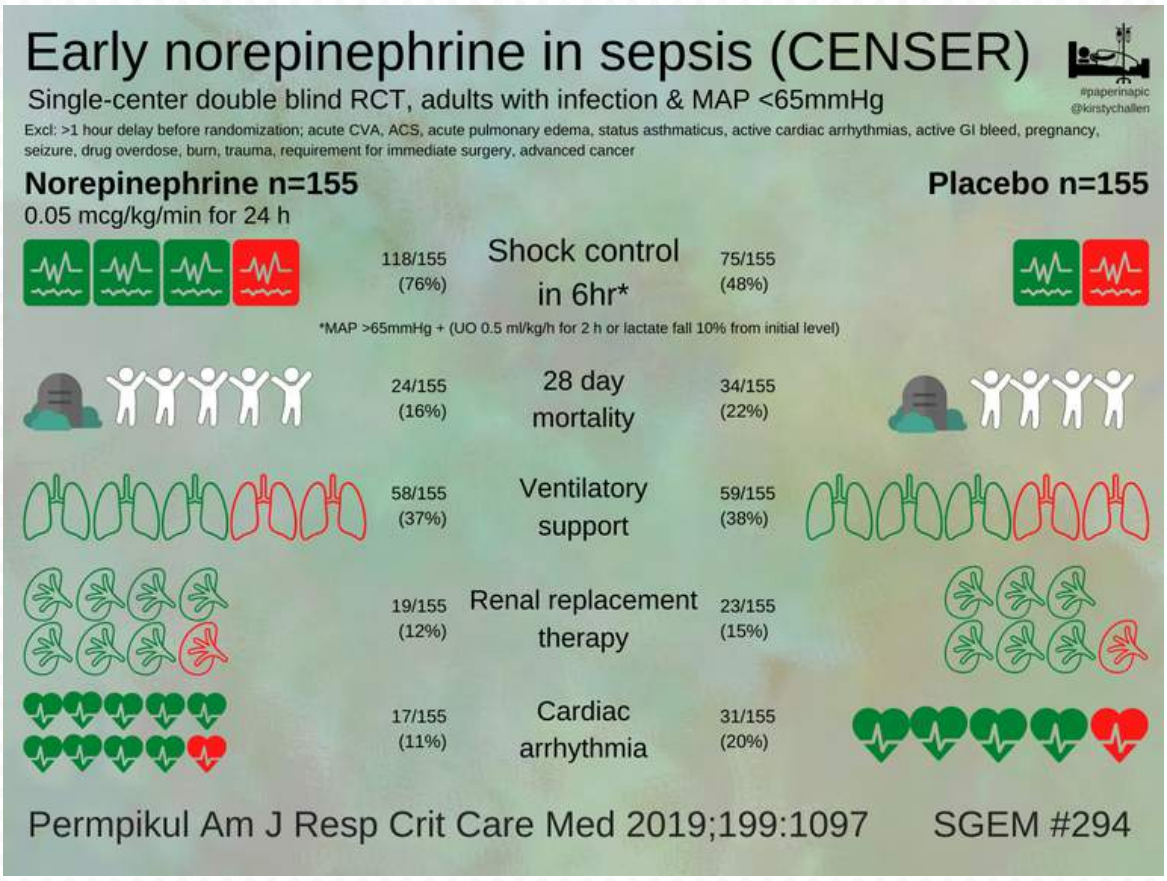
Dr. Ken Milne - EBM and Rural
@TheSGEM

What type of outcome is time to achieving a MAP of >65mmHg in a patient with septic shock using norepinephrine? thesgem.com/2020/06/sgem29... #FOAMed #EBM @MaxHockstein @srrezaie

POO	7.4%
MOO	39.9%
What are POOs and MOOs?	**52.7%**

148 votes · Final results

9:50 AM · Jun 9, 2020 · Twitter Web App



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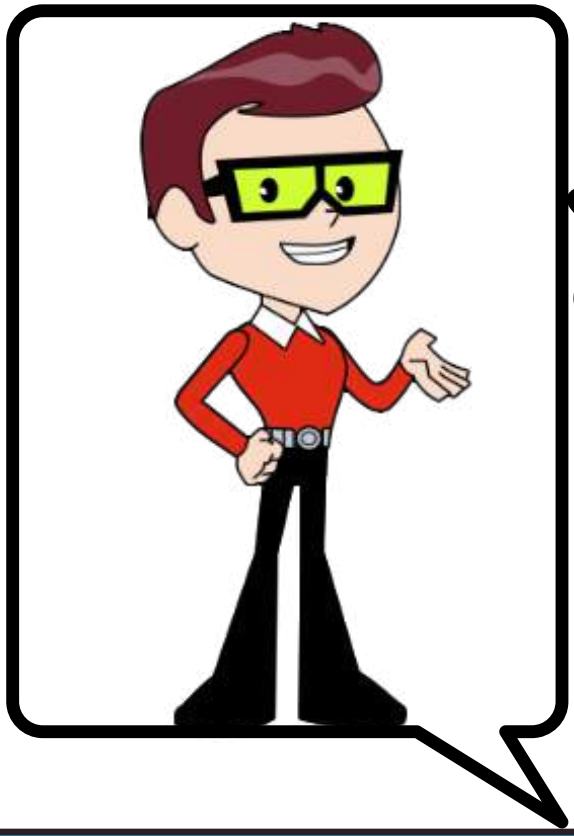
TEACHER TEACHER - TELL ME HOW TO DO IT (DIAGNOSE A PE)

Clinical Question:

What are the barriers and facilitators to tthe uptake of evidence-based practice in the ED evaluation for pulmonary embolism?



Bottom Line:

Use an evidence-based decision tool to help in the work-up of patients suspected of having a pulmonary embolism.

Guest:

Dr. Chris Bond is an Emergency Medicine Physician and Assistant Professor at the University of Calgary. He is also an avid FOAM supporter/producer through various online outlets including TheSGEM.

Case Overview

Case: A 63-year-old female presents to the emergency department (ED) with chest pain for the past eight hours. It is pleuritic, worse with certain movements and associated with some shortness of breath. Her vital signs are within normal limits and oxygen saturation is 95% on room air. An ECG, chest x-ray and troponin are all within normal limits and she has no calf swelling or tenderness. She does have a previous history of DVT/PE 12 years ago after returning from a transatlantic flight. She has also been doing more work around the house and lifting the past few weeks because of COVID and has some mild chest wall tenderness on palpation. The remainder of her Wells' criteria are unremarkable. How do you proceed in evaluating this patient for pulmonary embolism (PE)?

Background: Pulmonary embolism is a common ED diagnosis with an estimated 1-2% of all patients presenting to United States EDs undergoing CT for suspected PE (1). However, less than 10% of these scans show PE (2-4). We have covered the topic of PE frequently on the SGEM.

- SGEM#51: Home (Discharging Patients with Acute Pulmonary Emboli Home from the Emergency Department)
- SGEM#118: I Hope you Had a Negative D-dimer (ADJUST PE Study)
- SGEM#126: Take me to the Rivaroxaban – Outpatient treatment of VTE
- SGEM#163: Shuffle off to Buffalo to Talk Thrombolysis for Acute Pulmonary Embolism
- SGEM#219: Shout, Shout, PERC Rule Them Out
- SGEM#277: In the Pregnant YEARS – Diagnosing Pulmonary Embolism
- SGEM#282: It's All 'bout that Bayes, 'Bout that Bayes- No Trouble – In Diagnosing Pulmonary Embolism

There are multiple validated risk stratification tools to evaluate for PE and reduce inappropriate testing, including the Pulmonary Embolism Rule Out Criteria (PERC), Wells'score, YEARS algorithm and D-Dimer testing (5-7). There have also been more recent adjustments to D-Dimer threshold based on clinical probability as calculated by a trichotomized Wells score (8).

Unfortunately, clinician uptake of these validated tools has been incomplete, with some ED studies finding 25% of patients who warranted no laboratory or imaging studies still received testing (4, 9-12.) Low-value testing increases costs, ED length of stay and subjects patients to unnecessary ionizing radiation and risk of anaphylaxis from intravenous contrast dye (13-14). Moreover, false positives CT scans are common and estimated to be between 10-26%, resulting in unnecessary anti-coagulation and risk to patients (15-17).

This can ultimately lead to over-testing, over-diagnosing and over-treating. The American Board of Internal Medicine (ABIM) started the project called Choosing Wisely to try and mitigate this problem. The SGEM looked at this imitative on an SGEM Xtra. The American College of Emergency Physicians (ACEP) is part of the Choosing Wisely program and has a number of recommendations. One of the recommendations is on CT scans for ruling out PE. They have encouraged physicians *to*"

- *"Avoid CT pulmonary angiography in emergency department patients with a low-pretest probability of pulmonary embolism and either a negative Pulmonary Embolism Rule-Out Criteria (PERC) or a negative D-dimer." ACEP 2014*

The Right Care Alliance (RCA) was established in 2015. Certainly, patients at times need less care but they also at times need more care. This group's goal is to advocate for the goldilocks zone of care, not too much but also not too little (SGEM Xtra).

Reference: Westafer et al. Provider Perspectives on the Use of Evidence-based Risk Stratification Tools in the Evaluation of Pulmonary Embolism: A Qualitative Study. AEM June 2020.

Population: Emergency physicians

Intervention: The use of evidence-based risk stratification tools

As this is a qualitative study, we will use a modified PICO question

Comparison: The evaluation of acute pulmonary embolism

This is an SGEMHOP episode and we have the lead author of this quantitative study, Dr. Lauren Westafer. Lauren is an emergency medicine physician practicing in Massachusetts, and avid FOAM producer.

Authors' Conclusions

"Our findings suggest that common barriers exist to the use of risk stratification tools in the evaluation of pulmonary embolism in the ED and provide insight into where to focus efforts for future implementation endeavors. Overall, provider-level factors such as risk avoidance and lack of knowledge of the tools dominated as barriers, while inner-setting factors were identified as facilitators. Future efforts to improve evidence based diagnosis of pulmonary embolism should focus on implementation strategies targeting these domains."

CASP Checklist for Qualitative Research

- ☑ 1. Was there a clear statement of the aims of the research?
- ☑ 2. Is a qualitative methodology appropriate?
- ☑ 3. Was the research design appropriate to address the aims of the research?
- ☒ 4. Was the recruitment strategy appropriate to the aims of the research?*
- ☑ 5. Was the data collected in a way that addressed the research issue?
- ? 6. Has the relationship between researcher and participants been adequately considered?
- ☑ 7. Have ethical issues been taken into consideration?
- ☑ 8. Was the data analysis sufficiently rigorous?
- ☑ 9. Is there a clear statement of findings?
- ? 10. How valuable is the research?**

* Emails were sent to a purposive sample of physicians, many of whom were colleagues of the principal investigators and thus there would be bias as to those physicians potentially known practice patterns and potential responses. We do know that two physicians declined, and an effort was made to have a cross-section experience (years in practice), gender and practice setting (academic vs. community based).

**The external validity of this study is seriously questionable given the small number of participants and practice setting of four Northeastern US emergency settings. There may be generalizability to the American practice setting, but I question its applicability in Canada, Europe, the ANZACS and other areas of the world. That said, there is value in recognizing what barriers and facilitators practicing physicians find for the use of any clinical decision making or decision instrument. The same themes often emerge regardless of where you are in the world. For example, fear, anxiety, uncertainty, knowledge gaps and medicolegal risk are all barriers that need to be addressed when working up patients for any disease process. The study also identifies that physicians are more comfortable making decisions that are clearly aligned with institutional goals/policies as well as in line with their colleagues practice patterns. Audit and feedback were also identified as a helpful tool by some physicians. Audit and feedback can be an extremely powerful tool if delivered well, I will encourage those who are interested to read the following paper. *"Audit and Feedback for individual practitioners in the Emergency Department: An Evidence-based and Practical Approach"* was recently published in CJEM and covers critical elements of implementing an ED based audit and feedback program (Dowling et al CJEM 2020).

Case Outcomes

Key Results:
They had 23 physicians from a total of 12 academic and community hospitals in New England were interviewed. Two potential participants declined.

Participants had a median of 14 years in practice, 48% practiced solely in an academic setting, 20% practiced exclusively in a community ED and the remaining 32% practiced in a combination of academic and community EDs.

All clinicians reported some familiarity and some use of risk-stratification tools, particularly PERC in the workup of PE.

Barriers: Clinician-level barriers to use risk-stratification tools centered on knowledge, belief about consequences and emotions.

There was a lack of knowledge regarding validated cutoffs for the Wells score, lack of knowledge of a trichotomized Wells threshold, and most providers would only use a D-dimer for patients with a Wells score less than or equal to 3. Providers reported more confidence in their gestalt than risk stratification tools. They commonly reported that if a patient satisfied *"PE is the most likely diagnosis"* or there was a prior history of venous thromboembolism (VTE) or had active malignancy, the patient would automatically be too high risk to order a D-Dimer.

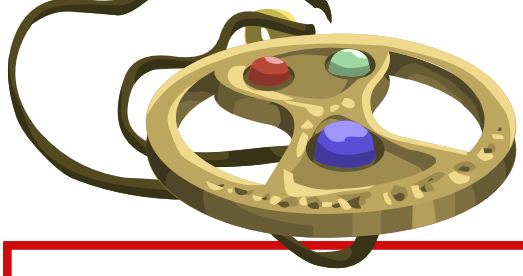
Beliefs about consequences of using the tools, particularly risk avoidance and fear of missing PE were also common provider-level barriers. Nearly all participants were unaware of existing professional guidelines on PE.

Facilitators: Study participants reported facilitators primarily at the level of the institutional setting. All clinicians felt that institutional support and a clear easy-to-follow algorithm endorsed by their hospital or group would facilitate their use of evidence-based approaches. This would also need to be easily accessible on shift.

Case Outcomes

They also felt this would provide perceived medicolegal protection and establish a cultural norm of practice, and cited peer pressure as a root cause to motivate them to change practice.

Clinicians felt that simplicity of PERC facilitated its use, while the element of gestalt incorporated into Wells made it more challenging to use.
Audit and feedback also emerged as an implementation strategy, noting that they would not want to be an outlier among their colleagues.



Time to Talk Nerdy

1.**Feedback:** Do these physicians receive data on their CT PE ordering rate for patients presenting with chest pain, shortness of breath (SOB) or other presenting complaints?

2. **Peers:** Was there a peer comparator data available?

3. **US Population:** Were all of the citations listed in the article regarding CT PE ordering rate in United States populations or were there international ones as well?

4. **External Validity:** How do you think having data from New England could affects the external validity of your study?

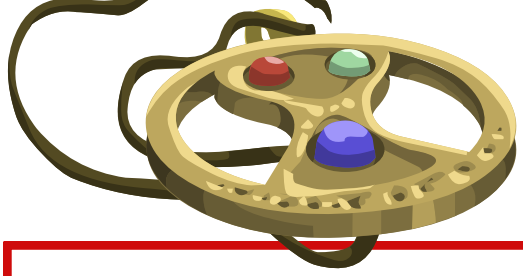
5. **Familiar:** You knew six of 23 participants as colleagues in this study. How do you think your selection of participants affected your results?

6. **Knowledge Translation:** The Wells study is 20 years old. We know that it can take 17 years for 14% of high-quality, clinically relevant information to reach the patient (Morris, Wooding and Grant RSMJ 2011). If knowledge translation (KT) has not reached these physicians after 20 years what leaks in the leaky pipe model would you suggest going forward to achieve this KT (Diner et al AEM 2007)?

7. **Pregnancy:** Was diagnosis of PE in pregnancy considered?

8. **Patient Satisfaction:** Was patient satisfaction influencing decision making discussed?

9. **Over-Diagnosis and Treatment:** Did you discuss over diagnosis and anticoagulation for subsegmental PEs resulting in potential patient harm



Time to Talk Nerdy

being a risk of PE evaluation?

10. **Personal Practice:** What is your personal practice for working up patients suspected of having a PE?

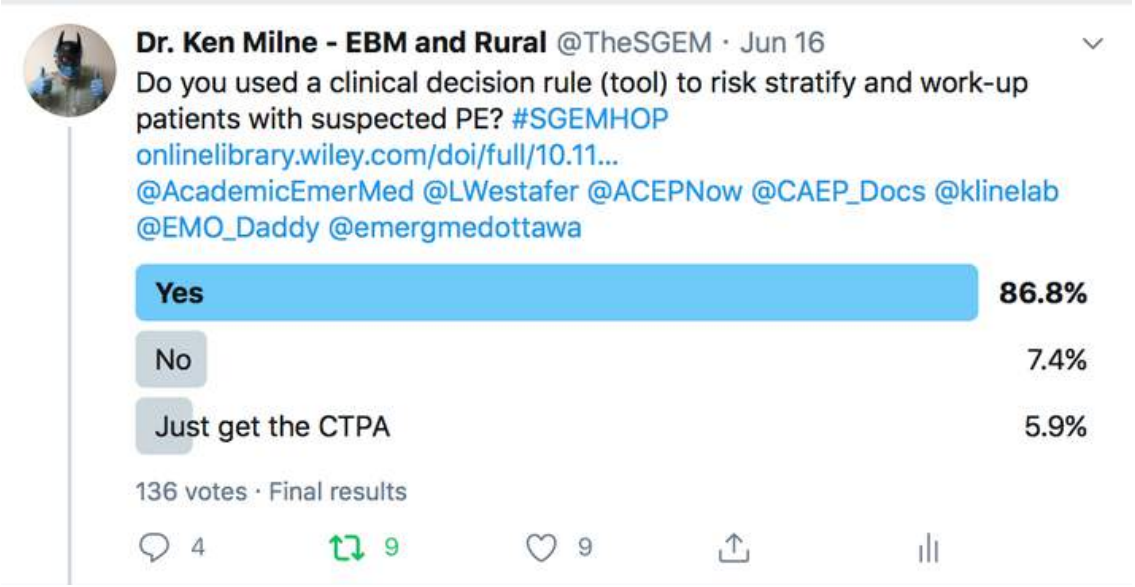
Comment on Authors' Conclusion Compared to SGEM Conclusion: We agree with the authors' conclusions.

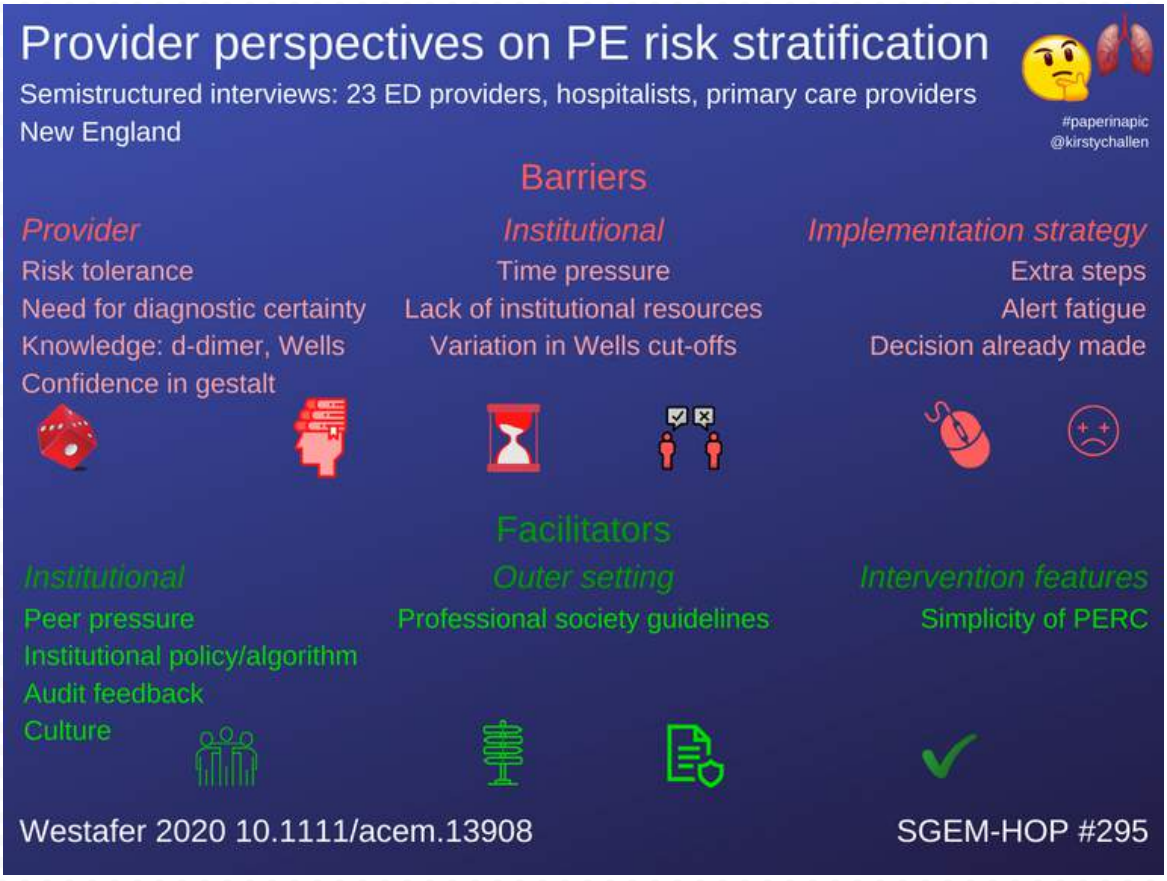
Clinical Application: We will use the Wells' score and PERC rule in the work-up of suspected PE. You can also consider using YEARS and the PEG-ED studies to adjust your D-dimer thresholds.

What Do I Tell My Patient? After reviewing your story, physical exam findings and testing, I think the most likely cause of your chest pain is muscular and it is very unlikely to be a dangerous or life-threatening cause. I suggest you try some heat and acetaminophen or ibuprofen for the pain and follow up with your primary care provider. Come back if you are having significantly more pain, shortness of breath or are feeling lightheaded or faint.

Case Resolution: You use an evidence-based tool to calculate the patient's Wells' score as 1.5mg/L, given she has had a previous DVT/PE, but you do not feel that PE is the most likely diagnosis. She is PERC positive because of her age so you perform a D-Dimer that returns negative at 0.47mg/L. At this point you reassure the patient and tell her she most likely has musculoskeletal chest pain and to try some heat, acetaminophen or ibuprofen for her pain. If she notices that she is becoming shorter of breath, has uncontrolled pain or is feeling syncopal, she should return to the ED. Otherwise you suggest she follow up with her primary care provider.

Episode End Notes





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SHE'S GOT THE FEVER BUT DOES SHE NEED AN LP, ANTIBIOTICS OR AN ADMISSION?

Clinical Question:

Can a clinical prediction rule (tool) using laboratory data identify febrile infants under 60 days of age who are at low risk for serious bacterial infection (UTI, bacteremia, and bacterial meningitis) and reduce unnecessary lumbar punctures, antibiotic exposure, and hospitalization?

Bottom Line:

Use an evidence-based decision tool to help in the work-up of patients suspected of having a pulmonary embolism.

Guest:

Dr. Dennis Ren is a Pediatric Emergency Medicine fellow at Children's National Hospital in Washington, DC.

Case Overview

Case: A 5-week-old full term female presents to the Emergency Department (ED) for fever with rectal temp of 100.6F (38.1C). Her mother states that she has been fussier today. She also seems “congested” and is not feeding as well. She continues to have the usual number of wet diapers. The mother is worried about her sick baby. She wants to know if they will need a spinal tap, be placed on antibiotics or will need to be admitted to the hospital?

Background: Fever without source in infants less than three months old represents a significant diagnostic dilemma for clinicians. Several criteria have been developed previously, including the Rochester (Jaskiewicz et al 1994), Boston (Baskin et al 1992) and Philadelphia (Baker et al 1993) criteria to help clinicians stratify the risk of serious bacterial infections (SBI).

Febrile infants commonly present to the emergency department. It is estimated 8-13% may have SBI that may include urinary tract infections, bacteremia, and bacterial meningitis. It is difficult to identify which infants have SBI by clinical examination alone. There are serious consequences from missed SBI. Workup for SBI may include lumbar puncture, antibiotics, and hospitalization.

These criteria (Rochester, Boston and Philadelphia) could be considered out of date in our current era of vaccinations. We covered a new protocol called the Step-by-Step approach on SGEM#171. The “Step-by-Step”rule combined both clinical factors and laboratory factors in febrile infants aged 22 to 90 days. It had a sensitivity of 98.9% to detect all SBIs.

The SGEM Bottom Line #171: “If you have availability of serum procalcitonin measurement in a clinically-relevant time frame, the Step-by-Step approach to fever without source in infants 90 days old or younger is better than using the Rochester criteria or Lab-score methods. With the caveat that you should be careful with infants between 22-28 days old or those who present within two hours of fever onset.”

It is important to balance the consequences of missing an SBI with performing unnecessary procedures (lumbar punctures), exposing infants to antibiotics, and prolonging hospital stay. The new study proposes a novel way of identifying low risk febrile infants 29-60 days based on three objective lab criteria.

Reference: Kuppermann et al. A Clinical Prediction Rule to Identify Febrile Infants 60 Days and Younger at Low Risk for Serious Bacterial Infections. JAMA Pediatr. 2019.

Population: Febrile infants <60 days of age who look good and whose blood cultures were obtained to rule out SBI (fever was a rectal temperature of at least 38C)

Infants who looked critically ill, had antibiotics in the previous 48 hours, history of prematurity (≤36 weeks' gestation), pre-existing medical conditions, indwelling devices or soft tissue infections.

Intervention: Derivation and validation of accurate clinical prediction rule (tool) for infants at low risk of SBI using a negative urinalysis, ANC <4,090/uL, and procalcitonin 1.71 ng/ml or less

Comparison: Pre-existing algorithms combining subjective clinical findings and lab markers

Outcomes: Accuracy of the prediction rule to identify infants at low risk for SBI (sensitivity, specificity, negative prediction value and negative likelihood ratio).

- SBI was defined as bacterial meningitis, bacteremia or UTI.
  - UTI was defined as growth of a single urine pathogen with at least 1,000 cfu/ml on culture obtained by suprapubic aspiration, at least 50,000 cfu/ml from catheterized specimens or 10,000-50,000 cfu/ml from catheterized specimens in association with an abnormal urinalysis (presences of leukocytes esterase, nitrite or pyuria).

	Philadelphia	Rochester	Boston
Age	29-60d	≤60days	28-89d
Temp	≥38.2C	≥38C	≥38C
History	Not specified	Term infant No perinatal Abx No underlying disease Not hospitalized longer than the mother	No immunizations < 48h No antimicrobial < 48h Not dehydrated
Physical Exam	Well-appearing Unremarkable exam	Well-appearing No ear, soft tissue or bone infection	Well-appearing No ear, soft tissue, or bone infection
Labs (define Lower risk)	WBC<15,000 Band-neutrophil ratio<0.2 UA <10wbc/hpf Urine gm stain: negative CSF<8wbc CSF gm stain: negative CXR: no infiltrate Stool: no RBC, no WBC	WBC 5,000-15,000 Absolute band <1500/mm3 UA≤10wbc/hpf Stool smeal <5WBC/hpf	WBC <20,000 CSF<10/mm3 UA<10wbc/hpf CXR: no infiltrate

Authors' Conclusions

"We derived and validated an accurate prediction rule to identify febrile infants 60 days and younger at low risk for SBIs using the urinalysis, ANC, and procalcitonin levels. Once further validated on an independent cohort, clinical application of the rule has the potential to decrease unnecessary lumbar punctures, antibiotic administration, and hospitalizations."

Quality Checklist for Clinical Decision Tools

- ☑ 1. The study population included or focused on those in the ED.
- ☑ 2. The patients were representative of those with the problem.
- ☑ 3. All important predictor variables and outcomes were explicitly specified.
- ☑ 4. This is a prospective, multicenter study including a broad spectrum of patients and clinicians (level II).
- ☑ 5. Clinicians interpret individual predictor variables and score the clinical decision rule reliably and accurately.
- ☒ 6. This is an impact analysis of a previously validated CDR (level I).
- ? 7. For Level I studies, impact on clinician behavior and patient-centric outcomes is reported.
- ? 8. The follow-up was sufficiently long and complete.
- ? 9. The effect was large enough and precise enough to be clinically significant.

Case Outcomes

Key Results:
The study included 1,821 febrile infants <60 days of age who had blood cultures collected. The mean age was 36 days old, 42% female, 2/3 had a fever of <12 hours prior to the ED visit, median YOS was 6.0 and SBI positive in 9.3% (7.7% from UTI alone).

Low risk prediction rule was derived based on three variables:

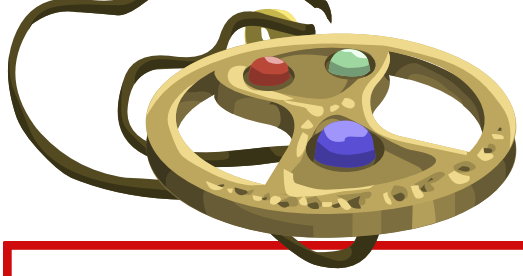
1. Normal urinalysis
2. Absolute Neutrophil Count (ANC) ≤4,090/μL
3. Serum procalcitonin ≤1.71 ng/ml

Sensitivity of 97.7%, specificity of 60%, NPV of 99.6% and LR- of 0.04

	Point Estimate	95% Confidence Interval
Sensitivity	97.7%	91.3% to 99.6%
Specificity	60.0%	56.6% to 63.3%
Negative Predictive Value	99.6%	98.4% to 99.9%
Negative Likelihood Ratio	0.04	0.01 to 0.15

No infants with bacterial meningitis were missed.

There were 1,266 infants >28 days of age. The clinical prediction rule stratified 776/1,266 (61.3%) as low risk for SBI. Of that low risk subgroup, 523/776 (67.4%) had lumbar punctures performed. This is the number of lumbar punctures that could possibly be avoided in this age group for low-risk patients.

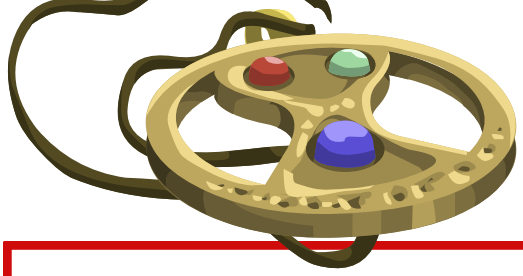


Time to Talk Nerdy

Overall, this is a very well-executed study with practice changing potential. The PECARN group does some great research. We covered the very important paper by Kupperman et al (NEJM 2018) looking at fluid infusion rates for children with diabetic ketoacidosis on SGEM#255.

1) Procalcitonin: This study lost a portion of eligible participants due to procalcitonin sample issues (41%). It is difficult to say whether or not this would have changed the results or analysis. The authors state that this group was similar to those with the procalcitonin measurements. There is a slight difference in SBI positive percentage in those who have procalcitonin test results available compared to those who did not (9.3% vs. 12%).
Laboratory tests besides procalcitonin like CRP, band counts and viral studies were not included. Past studies demonstrate concurrent viral infections may decrease risk of SBI but does not exclude SBI.
The procalcitonin samples were centrifuged and frozen at -80C, batched, and all sent to a central laboratory. This can increase the precision of the results by decreasing variability. Having 26 different laboratories running the procalcitonin levels could introduce more variability into the results. This would potentially decrease the precision by increasing the 95% confidence interval around the point estimate for the diagnostic accuracy of the clinical prediction rule.
To avoid over-fitting the data, they rounded off the ANC to 4,000/uL but more significantly decreased the procalcitonin level from 1.71 ng/ml to 0.5 ng/ml to see what would happen to the diagnostic accuracy.
The sensitivity remained identical and the specificity decreased a little with rounding off the ANC and decreasing the procalcitonin level.

2) Urinary Tract Infection: The definition used in this study followed the AAP guidelines that we detailed in the PICO. However, they did use a lower threshold for colony forming units.The reason for including this lower threshold was to account for lower colonies of bacteria sometimes found in urine of younger infants. This definition makes the prediction rule a bit more conservative.



Time to Talk Nerdy

3) Younger vs Older Infants: There was a difference between the two subgroup of infants identified a priori. Overall, 9.3% had SBIs but it was 13% in younger infants (≤28 days of age) vs. 7.7% in the older population (infants >28 days of age). Most of the SBI were UTI. Five infants had bacteremia and meningitis. Ten infants had UTI and bacteremia. One poor infant in the ≤28-day age group had UTI, bacteremia, and meningitis.

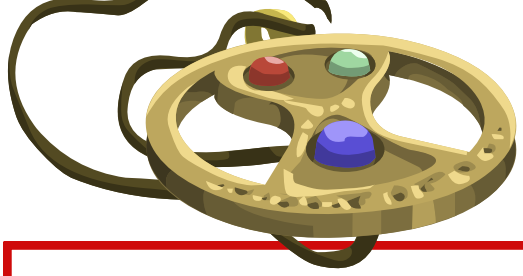
4) Number of Cases: We need to be careful about just considering negative predictive value (NPV). NPV is dependent on prevalence of disease while likelihood ratios are not dependant on prevalence of disease. They identified 170 infants with SBI (9.3%) which gives a fairly tight 95% CI for NPV. However, there were only four cases of bacterial meningitis alone (0.2%) which can make the NPV look pretty good (100%) but with very wide 95% CI.

We cannot just consider the number of cases identified but also the number of missed cases. In this study there were three missed cases of SBI using the clinical prediction rule. Two of the missed patients had culture positive urine without pyuria (E. coli and Pseudomonas) were in validation set. One patient with positive blood culture for Enterobacter cloacae was in derivation set but repeat blood cultures prior to antibiotics were never positive. No cases of bacterial meningitis were missed.

Four patients had herpes simplex virus (HSV) infections. Three with HSV in central nervous system (CNS) and one in nasopharynx. This is important because HSV most often presents in the first month of life.

5) Bias: This is something that systematically moves us away from the “truth” (best point estimate of effect) and is not random noise in the data. There could have been a number of sources of bias in this study.

One potential bias would be selection bias. To be included in the cohort they had to have blood cultures drawn. What were the differences in characteristics in those with blood cultures obtained and those infants



Time to Talk Nerdy

without? Both groups presented to the ED with fever. They also only enrolled patients when a research coordinator was available. These two things could have introduced some selection bias.

Another potential bias would be differential verification bias (double gold standard). This occurs when the test results influence the choice of the reference standard. So, a positive index test gets an immediate/gold standard test whereas the patients with a negative index test get clinical follow-up for disease. In this study, only 77% of febrile infants got a lumbar puncture to rule out meningitis. Those who did not get an LP had their families contacted by telephone 8 to 14 days after the ED visit and/or reviewed their medical records. This type of bias can raise or lower sensitivity/specificity

Comment on Authors' Conclusion Compared to SGEM Conclusion: We agree with the authors' conclusions.

Clinical Application: This is a well-designed and executed study that offers a novel way of identifying low risk febrile infants age 29-60 days based on objective lab criteria. The clinical prediction rule with three objective lab findings can help identify infants at low risk for SBI and may spare patients the need for lumbar puncture, empiric antibiotics, and hospitalization. I would NOT apply this rule to infants ≤28 days as they have higher risk of infection including HSV which the rule does not account for and the procalcitonin of ≤1.71 ng/mL is cut off when urinalysis and ANC are normal. As a reminder, clinical prediction rules do NOT replace clinical judgement. Prediction rules should help guide clinical judgement not dictate clinical care. Clinical predication tools often have lower diagnostic accuracy and wider confidence intervals when external validation is performed. This tool should be externally validated before recommending its general use

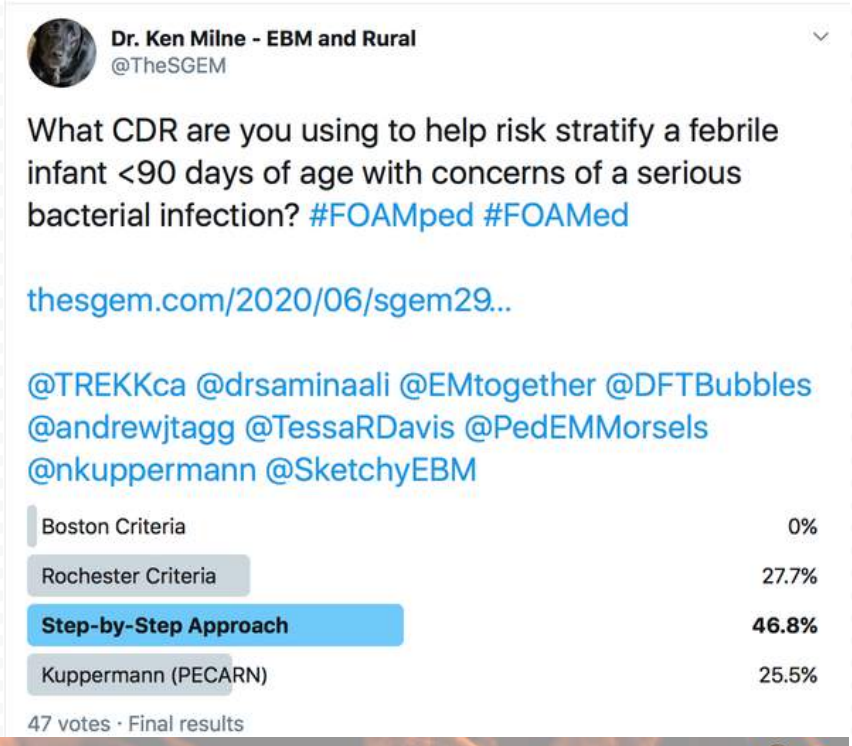
What Do I Tell My Patient (parents/caregivers)? In babies under the age of 60 days with fever, we always think about the possibility of infection. This could be an infection in the urine, blood, or spinal fluid which coats the brain. I would like to start by testing your infant's urine and blood for signs of infection. Depending on those results, we may need to perform a lumbar puncture to obtain spinal fluid, give antibiotics, or have your child stay in the hospital. We can talk more after the initial results come back.

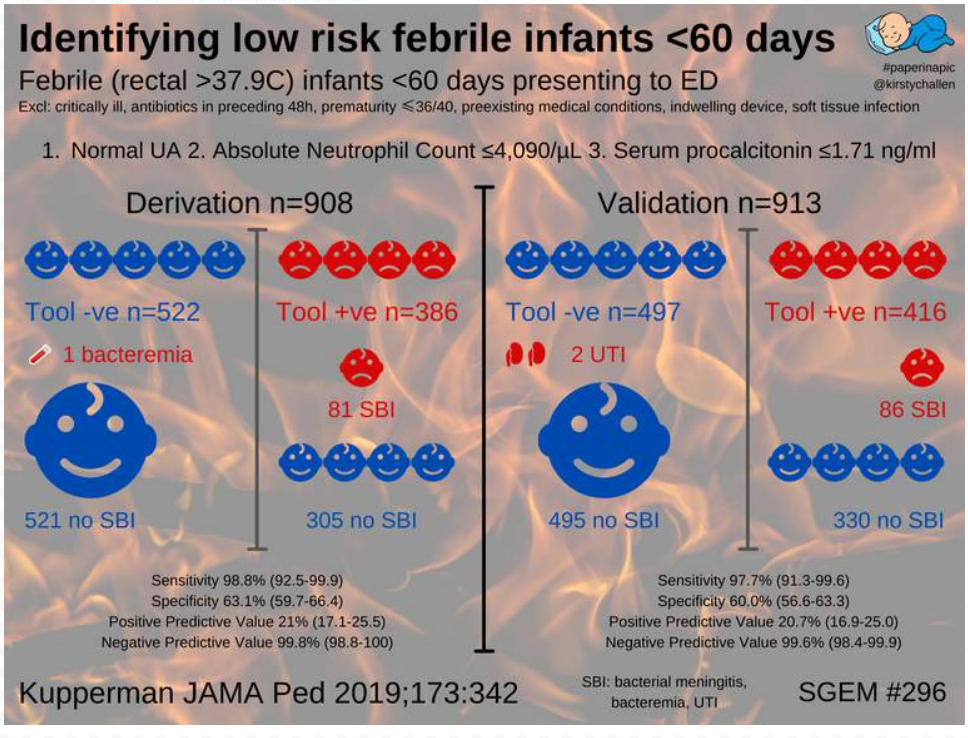
Case Resolution: You explain to the mother that given her baby's age (35 days), she is at risk of SBI. You need to check the blood and urine for signs of infection. Pending the results, you may also need to do an LP. Urine and blood samples are obtained and sent for culture. The urinalysis is unremarkable. The blood tests demonstrate an ANC and procalcitonin below their respective cut offs. The patient has taken a bottle in the ED and is now afebrile with stable vital signs. You do not administer antibiotics or admit the infant to the hospital. You reassure the mother it is OK to go home. She is told to follow up in the next 1-2 days with her pediatrician or return to the ED if she has any concerns.

Episode End Notes

Other FOAMed Resources:

- Academic Life in Emergency Medicine: PECARN Infant Fever Rule Age 29-60 days
- REBEL EM: A Clinical Prediction Rule for Febrile Infants ≤60 days at Low Risk for Serious Bacterial Infections.
- Don't Forget the Bubbles: Fever Under 60 Days of Age
- Core EM: PECARN Febrile Neonate Decision Rule Derivation and Internal Validation





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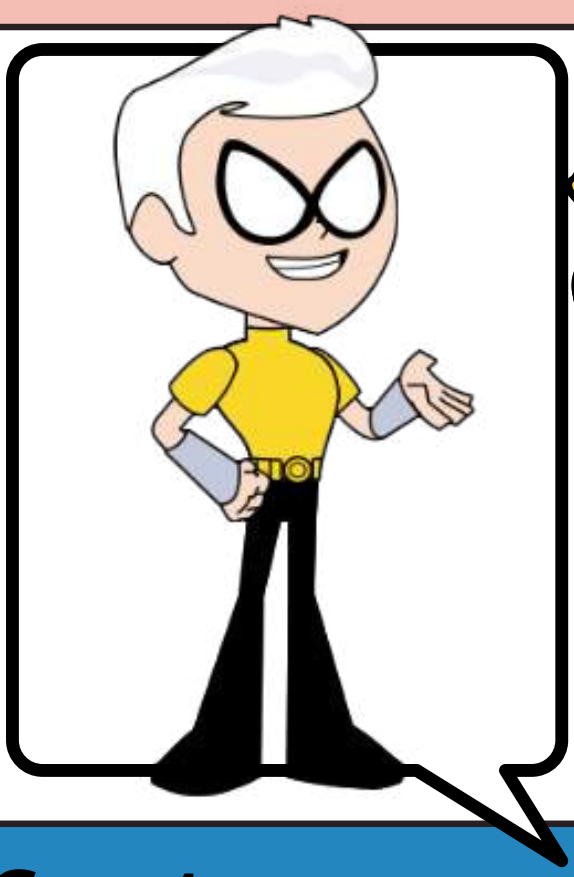
TPA ADVOCATES BE LIKE - NEVER GONNA GIVE YOU UP

Clinical Question:

Is thrombolysis for acute ischaemic stroke in the 3-4.5h time frame post symptom onset, safe and effective?

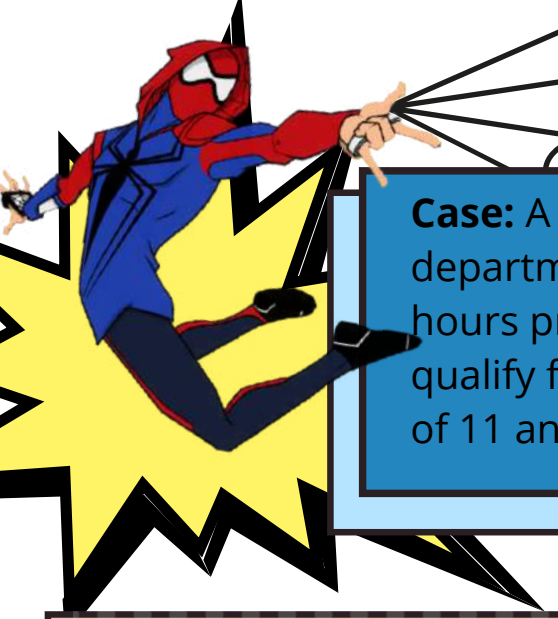


Bottom Line:

Reanalysis of the original ECASS III data does not support the potential benefit of TPA given between 3-4.5h after onset of stroke symptoms and confirms the known potential harm.

Guest:

Professor Daniel Fatovich is an emergency physician and clinical researcher based at Royal Perth Hospital, Western Australia. He is Head of the Centre for Clinical Research in Emergency Medicine, Harry Perkins Institute of Medical Research; Professor of Emergency Medicine, University of Western Australia; and Director of Research for Royal Perth Hospital.



Case Overview

Case: A 65-year-old man arrives from home to the emergency department by EMS with right-sided weakness beginning three hours prior. Advance neuroimaging demonstrates he does not qualify for endovascular clot retrieval. He has an NIHSS score of 11 and no contra-indications for systemic thrombolysis.

Background: Thrombolysis for acute ischemic stroke has to be one of, if not the most, controversial subjects of my career. The debate dates back to the classic NINDS paper published in the NEJM in 1995. We reviewed that publication with Dr. Anand Swaminathan on SGEM#70.

Some people might argue that it's less relevant now because of endovascular clot retrieval, but it's a living example of issues with research methodology, critical appraisal, bias, conflicts of interest, etc. These elements are continuously present in medicine – look at all the COVID-19 literature – made worse by the preprint archives of non-peer reviewed papers.

- Thrombolysis in acute ischaemic stroke. The Lancet 2012
- Truth, thinking and thrombolysis. EMA 2016
- Response from Prof. Fatovich to Stroke thrombolysis: Leaving the past, understanding the present and moving forward. EMA 2013
- The "Fragility" of Stroke Thrombolysis. TMJ 2020
- Believing is seeing: Stroke thrombolysis remains unproven after the third international stroke trial (IST-3). EMA 2012
- Don't Just Do Something, Stand There! The Value and Art of Deliberate Clinical Inertia. EMA 2018

It was Dr. Jerome Hoffman that introduced me to this issue and was a basis of my skepticism. I used to think if the study was published in a high-impact journal it must be true. His mentorship and teaching are why I consider Dr. Hoffman a legend of emergency medicine.

Background: Thrombolysis for acute ischemic stroke has to be one of, if not the most, controversial subjects of my career. The debate dates back to the classic NINDS paper published in the NEJM in 1995. We reviewed that publication with Dr. Anand Swaminathan on SGEM#70.

We have covered the issue of thrombolysis for acute ischemic stroke a number of times on the SGEM. I have also published a review on the topic of thrombolytics for stroke beyond three hours (Carpenter et al JEM 2011). More recently, I published a pro/con debate on the subject with Dr. Eddy Lange looking at the evidence (Milne et al CJEM 2020).

- SGEM#29: Stroke Me, Stroke Me
- SGEM Xtra: Walk of Life
- SGEM Xtra: No Retreat, No Surrender
- SGEM#269: Pre-Hospital Nitroglycerin for Acute Stroke Patients?
- SGEM#290: Neurologist Led Stroke Teams – Working 9 to 5

There has been a lot of skepticism around thrombolysis in acute ischemic stroke since the beginning. A reanalysis of the NINDS data by Dr. Hoffman and Dr. Schriger was published in Annals of Emergency Medicine in 2009. At least one other reanalysis has questioned the 2009 reanalysis (Saver et al Ann Emerg Med 2010). Thus, there is a degree of uncertainty in the NINDS-II results.

The major takeaway from this reanalysis was that the baseline imbalance in stroke severity led to the difference in outcomes. If tPA really works, we should see a bigger change in the NIHSS score in the tPA group vs. the placebo group. Yet the difference was 0.0. People can forget that a clinical trial has internal validity if and only if the imbalance between groups, bias in the assessment of outcome, and chance, have been excluded as possible explanations for the difference in outcomes. Baseline imbalance is a recurring theme. So, replication studies are hugely important.

It was the NINDS trial that changed guidelines and practices to provide thrombolysis in patients with stroke symptoms less than three hours after onset. This despite the multiple other trials that did not show efficacy and reported an increase in harm (bleeding). The increase in adverse events prompting some to be stopped early (SGEM Xtra:Thrombolysis for Acute Stroke).

Trial	Journal	Time	Primary Benefit	Harm
MAST -Italy (n=622)	Lancet 1995	<6hr	**None**	Increased early death
ECASS-I (n=620)	JAMA 1995	<6hr	**None**	Beneift not outweigh the risk
NINDS-I (n=291)	NEJM 1995	<3hr	**None**	No difference
NINDS -II (n=333)	NEJM 1995	<3hr	~13% absolute benefit mRS at 90d	Increase ICH
MAST - Eu (n=310)	NEJM 1996	<6hr	**None**	**Stopped early due to harm**
ASK (n=340)	JAMA 1996	<4hr	**None**	**Stopped early due to harm**
ECASS-II (n=800)	Lancet 1998	<6hr	**None**	No difference
ATLANTIS-B (n=613)	JAMA 1999	3-4hr	**None**	**Stopped early *"unlikely to prove beneficial"***
ATLANTIS-A (n=142)	Stroke 2000	<6hr	**None**	**Stopped early due to harm**
ECASS-III (n=821)	NEJM 2008	3-4.5hr	7% absolute benefit	Increase ICH
DIAS-2 (n=193)	Lancet 2009	3-9hr	**None**	No difference
IST-3 (n=3035)	Lancet 2012	<6hr	**None**	No difference

The only other randomized control trial claiming benefit for the primary outcome was ECASS III (Hacke et al NEJM 2008). ECASS I and II did not show a benefit with thrombolysis. ECASS III reported a 7% absolute benefit of improved mRS at 90 days compared to placebo, 9% increase in intracranial hemorrhage, 2% increase in symptomatic intracranial hemorrhage and no significant difference in mortality.

The American College of Emergency Physicians (ACEP) is the largest organization of EM physicians in the world. ACEP has a clinical policy statement on the issue (Brown et al AEM 2015). They looked at the <3 hour time frame and the 3-4.5 hour time frame.

ACEP made no level *"A"* recommendations but did make level B and C recommendations.

- Is IV tPA safe and effective for patients with acute ischemic stroke if given within 3 hours of symptom onset?
  - **Level B Recommendations:** With a goal to improve functional outcomes, IV tPA should be offered and may be given to selected patients with acute ischemic stroke within 3 hours after symptom onset at institutions where systems are in place to safely administer the medication. The increased risk of symptomatic intracerebral hemorrhage (sICH) should be considered when deciding whether to administer IV tPA to patients with acute ischemic stroke.
  - **Level C Recommendations:** When feasible, shared decision-making between the patient (and/or his or her surrogate) and a member of the health care team should include a discussion of potential benefits and harms prior to the decision whether to administer IV tPA for acute ischemic stroke. (Consensus recommendation)

- Is IV tPA safe and effective for patients with acute ischemic stroke treated between 3 to 4.5 hours after symptom onset?
  - **Level B Recommendations**: Despite the known risk of sICH and the variability in the degree of benefit in functional outcomes, IV tPA may be offered and may be given to carefully selected patients with acute ischemic stroke within 3 to 4.5 hours after symptom onset at institutions where systems are in place to safely administer the medication.
  - **Level C Recommendations:** When feasible, shared decision-making between the patient (and/or his or her surrogate) and a member of the health care team should include a discussion of potential benefits and harms prior to the decision whether to administer IV tPA for acute ischemic stroke. (Consensus recommendation)

ECASS III was published in 2008. Now, 12 years later there is a reanalysis of the trial similar to the reanalysis of the NINDS 14 years after it was published.

Reference: Alper et al. Thrombolysis with alteplase 3–4.5 hours after acute ischaemic stroke: trial reanalysis adjusted for baseline imbalances. BMJ Evidence Based Medicine 2020

Population: Adult patients age 18-80 years of age with at least 30 minutes of acute ischemic stroke symptoms presenting between 3-4.5 hours after onset of symptoms with no significant improvement.

Intervention: tPA 0.9 mg/kg; initial 10% bolus, remainder over 60 minutes

Comparison: Placebo

Main Exclusion: Intracranial hemorrhage, time of symptom onset unknown, symptoms rapidly improving or only minor before start of infusion, severe stroke as assessed clinically (e.g., NIHSS score >25) or by appropriate imaging techniques, seizure at the onset of stroke, stroke or serious head trauma within the previous 3 months, combination of previous stroke and diabetes mellitus, administration of heparin within the 48 hours preceding the onset of stroke, with an activated partial-thromboplastin time at presentation exceeding the upper limit of the normal range, platelet count of <100,000/mm2, systolic >185 mmHg or diastolic pressure >110 mmHg, or aggressive treatment (IV medication) necessary to reduce BP to these limits. blood glucose < 50 mg/dL or > 400 mg/dL, symptoms suggestive of subarachnoid hemorrhage, even if CT scan was normal, oral anticoagulant treatment, major surgery or severe trauma within the previous 3 months or other major disorders associated with an increased risk of bleeding.

Outcomes:

- **Primary Outcome:** Modified Rankin Scale (mRS) score 0-1 (favourable) vs. 2-6 (unfavourable) at 90 days
- **Secondary Outcomes:** Global outcome measure that combined 90 day outcomes of mRS 0-1, >=95 Barthel index, NIHSS score 0-1, score of 1 GOS; mortality at 90 days; any ICH, symptomatic ICH, symptomatic edema (defined as brain edema with mass effect as the predominant cause of clinical deterioration), and other serious adverse events.

Authors' Conclusions

"Reanalysis of the ECASS III trial data with multiple approaches adjusting for baseline imbalances does not support any significant benefits and continues to support harms for the use of alteplase 3–4.5 hours after stroke onset. Clinicians, patients and policy makers should reconsider interpretations and decisions regarding management of acute ischaemic stroke that were based on ECASS III results."

Quality Checklist for Randomized Clinical Trials

- ☑ 1. The study population included or focused on those in the emergency department.
- ☑ 2. The teams were adequately randomized.
- ☑ 3. The randomization process was concealed.
- ☑ 4. The teams were analyzed in the groups to which they were randomized.
- ? 5. The study teams were recruited consecutively (i.e. no selection bias).
- ☒ 6. The teams in both groups were similar with respect to prognostic factors.
- ☑ 7. All participants (patients, clinicians, outcome assessors) were unaware of group allocation.
- ☑ 8. All groups were treated equally except for the intervention.
- ☑ 9. Follow-up was complete (i.e. at least 80% for both groups).
- ☑ 10. All patient-important outcomes were considered.
- ☒ 11. The treatment effect was large enough and precise enough to be clinically significant.

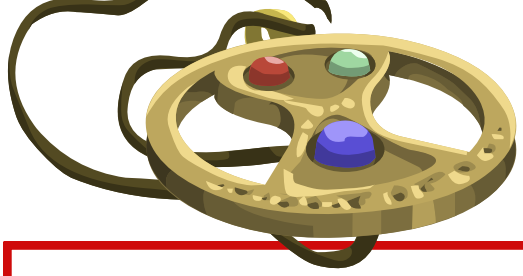
Case Outcomes

Key Results:
They included 821 patients in the trial with a mean age of 65 years and 60% male.

After adjusting for baseline imbalances, multiple methods failed to find statistically significant benefits with thrombolysis given 3-4.5h after stroke onset and confirmed significant increase in harm.

Table 3 Adjusted analyses of primary efficacy outcome with previously used and modified approaches

Model*	n†	OR (95% CI)	P value
mRS score of 0 or 1 at 90 days, analysis adjusted for baseline NIHSS score, time from onset to treatment (OTT), smoking and prior hypertension as reported in Hacke *et al*[1] and Bluhmki *et al*[16]			
Previously reported adjusted analysis[1 16]	785	**1.42 (1.02 to 1.98)**	**0.037**
Missing—impute, NIHSS score—continuous, OTT—continuous	794	1.25 (0.91 to 1.73)	0.173
Missing—impute, NIHSS score—continuous, OTT—categorical	794	1.33 (0.96 to 1.85)	0.086
Missing—impute, NIHSS score—categorical, OTT—continuous	794	1.29 (0.94 to 1.78)	0.121
Missing—impute, NIHSS score—categorical, OTT—categorical	794	1.38 (0.99 to 1.92)	0.054
Missing—exclude, NIHSS score—continuous, OTT—continuous	785	1.30 (0.94 to 1.80)	0.119
Missing—exclude, NIHSS score—continuous, OTT—categorical	785	1.38 (0.99 to 1.93)	0.056
Missing—exclude, NIHSS score—categorical, OTT—continuous	785	1.33 (0.96 to 1.84)	0.087
Missing—exclude, NIHSS score—categorical, OTT—categorical	785	**1.42 (1.02 to 1.98)**	**0.037**
mRS score of 0 or 1 at 90 days, analysis adjusted for history of stroke, baseline NIHSS score, OTT, smoking, prior hypertension and nine other variables as reported in Bluhmki *et al*[16] ('full model')			
Previously reported 'full model'[16]	784	**1.43 (1.02 to 2.00)**	**0.040**
Missing—impute, NIHSS score—continuous, OTT—continuous	791	1.27 (0.91 to 1.76)	0.156
Missing—impute, NIHSS score—continuous, OTT—categorical	791	1.34 (0.96 to 1.87)	0.086
Missing—impute, NIHSS score—categorical, OTT—continuous	791	1.31 (0.94 to 1.81)	0.112
Missing—impute, NIHSS score—categorical, OTT—categorical	791	1.38 (0.99 to 1.93)	0.059
Missing—exclude, NIHSS score—continuous, OTT—continuous	782	1.32 (0.95 to 1.84)	0.102
Missing-exclude, NIHSS score-continuous, OTT-categorical	782	1.39 (0.99 to 1.95)	0.055
Missing-exclude, NIHSS score-categorical, OTT-continuous	782	1.35 (0.97 to 1.88)	0.076
Missing-exclude, NIHSS score-categorical, OTT-categorical	782	**1.43 (1.02 to 2.00)**	**0.039**



Time to Talk Nerdy

1. Inter-Rater Reliability (IRR): The IRR of outcome assessments using the mRS are moderate at best [1,2]. A clinical trial has internal validity if and only if the imbalance between groups and bias in the assessment of outcome and chance, have been excluded as possible explanations for the observed difference in outcomes.

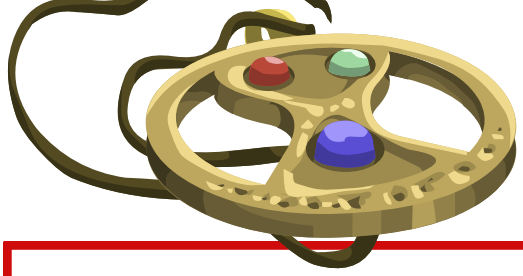
2. Fragility Index (FI): The FI is a method to understand how statistically reproducible a study is [3]. It is the minimum number of patients who would need to have a different outcome to change the p value from < 0.05 to > 0.05, ie from statistically significant to insignificant (the 0.05 threshold as a measure of statistical significance is problematic).

A low FI means that only a small number of patients would have to have their outcome change for the trial to lose statistical significance. It is simply calculated by repeatedly applying Fisher's exact test, while successively reallocating patients, one at a time, from the favourable outcome group to the other (control) group. The FI of the original ECASS-III data is 1. So, only one patient would have to have a different outcome to change the result of the study. This fragility is consistent with the new re-analysis study by Alper, which found no significant benefit for tPA [4].

IST-3 was the largest RCT looking at tPA for acute ischemic stroke in treated patients up to 6 hours. It failed to show a benefit for its primary outcome. In the 3-4.5 hour subgroup (n = 1,177), no difference in functional outcomes in those randomized to tPA vs. placebo (32% tPA vs 38% placebo (OR 0.73) was reported.

				Adjusted odds ratio (99% CI)	Adjusted p value
Time to randomisation (h)					0·613
0–3	132/431 (30·6%)	95/418 (22·7%)		1·64 (1·03–2·62)	
3–4·5	182/577 (31·5%)	226/600 (37·7%)		0·73 (0·50–1·07)	
>4·5	240/507 (47·3%)	213/500 (42·6%)		1·31 (0·89–1·93)	

However, this was obtained by using a 99% confidence interval (0.50-1.07). Readers will be aware that the conventional reporting approach is the 95%



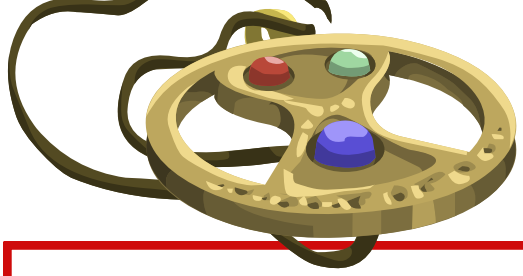
Time to Talk Nerdy

CI. Using the traditional 95% CI results in a statistically significant association with placebo for good functional outcome compared to tPA

3. Baseline Imbalances: A strong predictor of how someone will do after a stroke is how bad their symptoms were at presentation. There was an important baseline imbalance in stroke between the two groups in the ECASS III trial. This is a feature seen before in stroke studies (eg with studies on Factor VII for intracranial hemorrhage). This was first highlighted by Shy in 2014, who noted that the online version of the ECASS III paper was changed in 2013 to reflect the actual p value of 0.003, vs. the originally published p 0.03 [5]. The authors had originally defined significant p values for these comparisons as < 0.004, so the correction marked stroke history as a significant difference between the two groups. Clinically, it is known that recurrent strokes have a worse outcome than first strokes. So, the difference in outcome could be fully explained by the baseline imbalance.

4. NINDS Reanalysis: The re-analysis of ECASS III by Alper in BMJ EBM is similar to the re-analysis of NINDS by Hoffman & Schriger who found that baseline imbalance in stroke severity was likely responsible for the difference in outcome [6].

5. Time is Not Brain: In 2018, the author of the original phrase “time is brain” wrote: “It is no longer reasonable to believe that the effect of time on the ischaemic process represents an absolute paradigm. It is increasingly evident that the volume of injured tissue within a given interval after the estimated time of onset shows considerable variability in large part due to the beneficial effect of a robust collateral circulation.” [7]
The effect of any intervention in stroke is due to factors such as the precise automated measurement of a small ischaemic core, a large reversible penumbra, and the use of thrombectomy in highly selected patients with detailed consent,coupled with absence of treatment harm [8]. The endovascular trials have demonstrated that it is possible to identify a cohort of patients who will benefit from revascularization, independent of time of



Time to Talk Nerdy

onset, when perfusion imaging is paired with an effective treatment modality. This has not been achieved for stroke thrombolysis using tPA.

Comment on Authors' Conclusion Compared to SGEM Conclusion: We agree with the conclusions made by the Alper et al who reanalyzes ECASS III affirming the lack of benefit for tPA. We also agree that replication studies are needed [9,10].

We do not agree with the conclusion of the original ECASS III authors.

Clinical Application: This furthers our skepticism about the thrombolytic literature for acute ischemic stroke especially in this later time frame. It will modify how we present the information to patients. On a broader scale, you decide locally to discuss this with your EM group and advocate for policy makers to re-consider their recommendations.

What Do I Tell My Patient? You are having a stroke. It is being caused by a clot in the brain. There is a drug that has been used to try and dissolve clots. Older data showed that 7% of people may do better by 3 months. The drug does cause a potential 10% increase in bleeding in the brain. Two percent more of people getting this drug will have symptoms of the brain bleeding. It is not a life-saving drug and the same number of people die from this type of stroke (~8%). The existing guidelines say this medication may be offered to patients like you. However, a new look at the original data has raised some concerns. When re-analyzing the evidence, it showed the increase in harm was the same (bleeding in the brain). However, the potential benefits were unfortunately not confirmed. That means we are not confident this drug will have any benefit. We are confident that puts you at greater risk for bleeding.

Case Resolution: You provide the man with the latest information on thrombolysis for stroke. He decides not to move forward with systemic tPA administration.

Episode End Notes

Should stroke guidelines be revisited & consider this new information?

Re-analysts of ECASS-III fails to confirm efficacy but does confirm increase harm in tPA.

thesgem.com/2020/07/sgem29...

@ACEPNow @jeremyfaust @CAEP_Docs @EddyLang1 @AliRaja_MD @EMSwami @srrezaie @thenntgroup

Yes	**95.9%**
No	4.1%

121 votes · Final results

7:58 AM · Jul 7, 2020 · Twitter for iPhone

TPA at 3-4.5 hours: ECASS III reanalysis

#paperinapic @kirstychallen

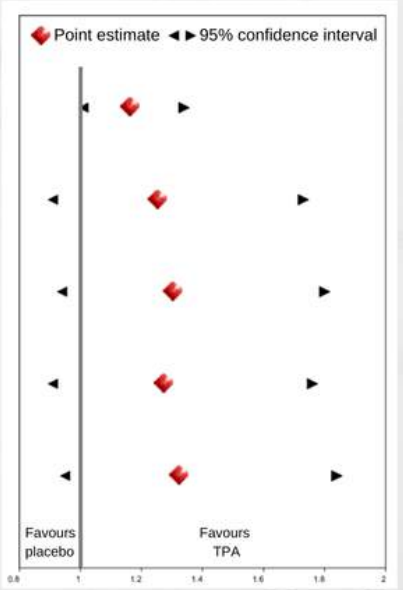
Patient-level reanalysis of multicentre placebo-controlled RCT, Europe

Patients 18-80y >=30 min of acute ischemic stroke symptoms presenting 3-4.5h after onset, no significant improvement

Excl: ICH, rapid improvement, NIHSS >25, seizure at onset, stroke/serious head trauma in last 3m, prev stroke + DM, heparin last 48h with raised APTT, platelet <100,000, SBP>185, DBP>110, blood glucose <50 or >400mg/dL, ?SAH, oral anticoag, major surgery/severe trauma in last 3m, major bleeding disorder

Relative risk of mRS 0-1 at 90 days
TPA (n=418) vs placebo (n=403)

Unadjusted		1.16 (1.01 to 1.34)
Adjusted: Baseline NIHSS, onset to treatment time, smoking, prior hypertension	Missing data imputed	1.25 (0.91 to 1.73)
	Missing data excluded	1.30 (0.94 to 1.80)
Adjusted: Baseline NIHSS, age, weight, onset to treatment time, SBP, DBP, dose/ bodyweight, smoking, previous stroke, diabetes, atrial fibrillation, hypertension, previous antiplatelet drugs, sex	Missing data imputed	1.27 (0.91 to 1.76)
	Missing data excluded	1.32 (0.95 to 1.84)



Alper BMJ EBM 2020 10.1136/bmjebm-2020-111386

mRS: modified Rankin Scale

SGEM #297

298 WHAT'S THE SIGNS AND THE SYMPTOMS OF PNEUMONIA?

Clinical Question:

What is the accuracy of individual signs adn symptoms for diagnosing community acquired pneumonia?

Bottom Line:

Reanalysis of the original ECASS III data does not support the potential benefit of TPA given between 3-4.5h after onset of stroke symptoms and confirms the known potential harm.

Guest:

Dr. Justin Morgenstern is an emergency physician and the creator of the excellent #FOAMed project called First10EM.com. He has a great new blog post about increasing diversity in medicine using something called the BSAP approach and an interesting Broome Doc podcast with Dr. Casey Parker called EBM 2.0.

Case Overview

Case: A 67-year-old woman with no previous health problems presents with fever, cough, and myalgias. You are working with a medical student on their very first rotation, and you want to spend some time teaching them about the history and physical exam. However, being an evidence-based medicine enthusiast, you wonder what aspects of the patient's presentation are going to be truly helpful in making a diagnosis.

Background: Depending on the time of year, fever and cough can be one of the most common presentations seen in the emergency department. It is important not to miss pneumonia in the sea of viral illnesses. We have covered various aspects of this issue a number of times on the SGEM:

- SGEM#287: Difficult to Breathe – It Could Be Pneumonia
- SGEM#286: Behind the Mask – Does it need to be an N95 mask?
- SGEM#263: Please Stop, Prescribing – Antibiotics for Viral Acute Respiratory Infections
- SGEM#216: Pump It Up – Corticosteroids for Patients with Pneumonia Admitted to Hospital
- SGEM#120: One Thing or Two for Community Acquired Pneumonia?

Antibiotic overuse is a significant problem, and ordering chest x-rays (CXR) on everyone is inefficient, expensive, and adds potentially unnecessary risk from radiation. Thus, it is important to know how accurate the history and physical exam is for identifying patients with pneumonia.

A prior meta-analysis demonstrated that the combination of normal vital signs and normal lung exam effectively rules out pneumonia (Marchellow eat al JABFM 2019), and that a physician's overall clinical impression is moderately accurate (Dale et al BrJGP 2019).

However, there has not been a meta-analysis looking at the evidence for individual signs and symptoms for pneumonia in the last decade.

Reference: Ebell et al. Accuracy of Signs and Symptoms for the Diagnosis of Community-acquired Pneumonia: A Meta-analysis. AEM July 2020

Population: Adolescents and adults presenting with symptoms of respiratory infection or clinically suspected pneumonia in the outpatient setting

Intervention: Any clinical sign or symptom (including vital signs) for pneumonia

Outcomes: Radiologically confirmed pneumonia (using CXR as the gold standard)

Authors' Conclusions

"While most individual signs and symptoms were unhelpful, selected individual signs and symptoms are of value for diagnosing CAP. Teaching and performing these high value elements of the physical examination should be prioritized, with the goal of better targeting chest radiographs and ultimately antibiotics."

Quality Checklist for Systematic Review Diagnostic Studies

- [?] 1. The diagnostic question is clinically relevant with an established criterion standard.
- [✓] 2. The search for studies was detailed and exhaustive.
- [✓] 3. The methodological quality of primary studies were assessed for common forms of diagnostic research bias.
- [✓] 4. The assessment of studies were reproducible
- [✓/✗] 5. There was low heterogeneity for estimates of sensitivity or specificity.
- [✗] 6. The summary diagnostic accuracy is sufficiently precise to improve upon existing clinical decision-making models.

Case Outcomes

Key Results:
They identified 16 studies that met their inclusion and exclusion criteria. Seven studies were based in the emergency department and nine in a primary care setting. The number of participants ranged from 52 to 2850. The mean age ranged from 32 to 62 years, and between 48% and 60% of the participants were female.

No individual sign or symptom was good enough to independently rule in or rule out pneumonia.

A CXR was used as the gold standard in all studies. The risk of bias was assessed as low in 12 studies and moderate in five. The prevalence of pneumonia was 10% in the primary care studies and 20% in emergency department studies.

The most helpful indicator was “overall clinical impression”, with a positive likelihood ratio of 6.32 (the highest of any finding) (95% CI 3.58-10.5) and a negative likelihood ratio of 0.54 (95% CI 0.46-0.64).

Although a number of symptoms and signs were associated with pneumonia, the low positive likelihood ratios – generally less than 2 – mean that none of these factors are even close to diagnostic on their own. Examples include subjective fever, dyspnea, chest pain, dullness to percussion, crackles, confusion, and toxic or ill appearance. The negative likelihood ratios were even less helpful. We will include a full table with the results in the show notes.

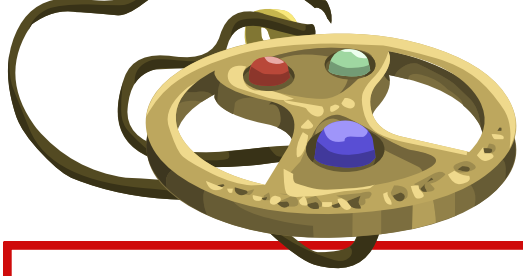
Case Outcomes

Key Results:

The finding with the best test characteristic to rule in pneumonia was egophony, with a positive likelihood ratio of 6.17 (95% 1.34-18.0) when present, although the negative likelihood ratio was only 0.96 (0.93-0.99) The absence of any abnormal vital sign was the best finding for ruling out pneumonia, with a negative likelihood ratio of 0.25 (95% CI 0.11-0.48)

Sign or symptom	Studies (patients)	Sensitivity (95% CI)	Specificity (95% CI)	LR+ (95% CI)	LR− (95% CI)	Diagnostic odds ratio (95% CI)	AUROCC
Overall clinical impression	7 (5081)	0.50 (0.39-0.61)	0.92 (0.84-0.96)	**6.32 (3.58-10.5)**	**0.54 (0.46-0.64)**	**11.5 (6.7-18.5)**	0.741
Medical history							
Chronic obstructive pulmonary disease	3 (748)	0.19 (0.13-0.27)	0.91 (0.86-0.95)	**2.37 (1.21-4.33)**	**0.88 (0.78-0.97)**	**2.74 (1.24-5.51)**	
Previous pneumonia	3 (1245)	0.13 (0.02-0.47)	0.90 (0.63-0.98)	1.32 (0.81-2.00)	0.96 (0.81-1.02)	1.39 (0.79-2.21)	
Any comorbidity	3 (3904)	0.44 (0.33-0.55)	0.63 (0.50-0.75)	1.19 (0.99-1.48)	0.90 (0.80-1.01)	1.34 (0.98-1.80)	
Alcohol use disorder	3 (988)	0.06 (0.02-0.23)	0.96 (0.93-0.98)	NC	NC	NC	
Smoking (current)	4 (3425)	0.32 (0.13-0.59)	0.69 (0.54-0.81)	1.06 (0.53-1.78)	0.97 (0.66-1.22)	1.18 (0.44-2.73)	
Male sex	4 (3539)	0.46 (0.39-0.54)	0.57 (0.52-0.61)	1.08 (0.93-1.23)	0.94 (0.83-1.06)	1.15 (0.88-1.47)	
Smoking (ever)	3 (1434)	0.50 (0.30-0.69)	0.52 (0.36-0.67)	1.03 (0.78-1.28)	0.97 (0.75-1.18)	1.09 (0.66-1.70)	
Symptoms							
Pleuritic chest pain	3 (1245)	0.32 (0.26-0.39)	0.87 (0.65-0.96)	2.76 (0.97-7.133)	0.81 (0.70-1.02)	3.56 (0.95-9.77)	
Fever (subjective)	8 (4907)	0.63 (0.50-0.74)	0.55 (0.38-0.71)	**1.47 (1.26-1.71)**	**0.68 (0.58-0.80)**	**2.10 (1.48-2.87)**	0.623
Chills	7 (2453)	0.55 (0.43-0.67)	0.62 (0.50-0.72)	**1.44 (1.26-1.65)**	**0.73 (0.63-0.83)**	**2.00 (1.58-2.49)**	0.610
Coryza and rhinorrhea absent	4 (1106)	0.60 (0.40-0.77)	0.57 (0.22-0.66)	**1.43 (1.11-2.00)**	**0.71 (0.56-0.86)**	**2.07 (1.31-3.13)**	
Sputum (bloody)	4 (1582)	0.13 (0.06-0.27)	0.90 (0.84-0.94)	1.33 (0.80-2.06)	0.96 (0.84-1.02)	1.41 (0.78-2.47)	
Dyspnea	10 (5626)	0.63 (0.48-0.75)	0.51 (0.31-0.71)	**1.30 (1.07-1.65)**	**0.75 (0.66-0.85)**	**1.75 (1.28-2.34)**	0.598
Sore throat absent	3 (782)	0.60 (0.49-0.70)	0.52 (0.28-0.75)	1.29 (0.75-1.77)	0.81 (0.57-1.34)	1.78 (0.65-3.83)	
Chest pain	8 (5031)	0.51 (0.33-0.69)	0.58 (0.37-0.76)	**1.21 (1.05-1.42)**	**0.86 (0.78-0.94)**	**1.41 (1.13-1.74)**	0.549
Headache	3 (1188)	0.65 (0.46-0.81)	0.42 (0.21-0.65)	1.19 (0.93-1.49)	0.85 (0.67-1.08)	1.35 (0.90-1.94)	
Sputum (any)	6 (4441)	0.71 (0.60-0.81)	0.35 (0.21-0.51)	1.11 (0.96-1.32)	0.84 (0.63-1.11)	1.37 (0.87-2.07)	
Myalgias	3 (1424)	0.49 (0.41-0.56)	0.57 (0.45-0.68)	1.10 (0.91-1.45)	0.92 (0.77-1.10)	1.26 (0.82-1.86)	
Sputum (purulent)	3 (1365)	0.52 (0.35-0.70)	0.52 (0.39-0.65)	1.09 (0.90-1.26)	0.92 (0.73-1.08)	1.21 (0.83-1.71)	
Cough	7 (1866)	0.88 (0.82-0.93)	0.16 (0.07-0.34)	1.07 (0.97-1.27)	0.77 (0.41-1.37)	1.57 (0.71-3.01)	
Signs							
Egophony	3 (1116)	0.05 (0.03-0.10)	0.99 (0.95-0.99)	**6.17 (1.34-18.0)**	**0.96 (0.93-0.99)**	**6.46 (1.36-18.9)**	
Dullness to percussion	7 (1932)	0.14 (0.10-0.19)	0.94 (0.88-0.97)	**2.62 (1.14-5.30)**	**0.92 (0.87-0.98)**	**2.89 (1.17-5.90)**	NC
Confusion	4 (1596)	0.11 (0.08-0.15)	0.95 (0.92-0.97)	**2.15 (1.36-3.34)**	**0.94 (0.90-0.98)**	**2.29 (1.39-3.63)**	
Crackles	12 (5898)	0.42 (0.32-0.52)	0.79 (0.68-0.86)	**2.00 (1.54-2.58)**	**0.74 (0.66-0.82**	**2.70 (1.95-3.63)**	0.611
Decreased breath sounds	6 (4322)	0.25 (0.20-0.32)	0.87 (0.78-0.92)	**1.96 (1.23-3.02)**	**0.87 (0.79-0.95)**	**2.29 (1.31-3.73)**	
Abnormal lung exam (any finding)	8 (2875)	0.60 (0.40-0.78)	0.67 (0.42-0.85)	**1.90 (1.26-2.91)**	**0.61 (0.47-0.75)**	**3.18 (1.83-2.08)**	0.669
Rhonchi	5 (2375)	0.23 (0.16-0.32)	0.87 (0.78-0.92)	**1.76 (1.26-2.41)**	**0.89 (0.83-0.95)**	**1.99 (1.35-2.81)**	
Toxic or ill appearance	5 (4162)	0.42 (0.22-0.65)	0.70 (0.43-0.88)	**1.46 (1.08-2.15)**	**0.83 (0.71-0.94)**	**1.77 (1.17-2.64)**	
Pleural rub	5 (1885)	0.07 (0.04-0.11)	0.97 (0.91-0.992)	3.02 (0.74-8.02)	0.96 (0.91-1.02)	3.20 (0.72-8.81)	
Wheeze (any)	8 (2519)	0.25 (0.19-0.32)	0.75 (0.68-0.92)	1.00 (0.82-1.22)	1.00 (0.94-1.07)	1.00 (0.77-1.30)	
Vital signs							
Temp>=37.7-38.0	10 (5490)	0.34 (0.25-0.56)	0.87 (0.79-0.92)	**2.52 (2.02-3.20)**	**0.77 (0.70-0.83)**	**3.30 (2.60-4.16)**	0.637
O2 saturation < 95%	3 (1089)	0.36 (0.22-0.53)	0.83 (0.78-0.87)	**2.12 (1.47-2.71)**	**0.77 (0.61-0.92)**	**2.83 (1.61-4.39)**	
Heart rate> 100 bpm	8 (5172)	0.33 (0.23-0.44)	0.84 (0.74-0.90)	**2.04 (1.59-2.62)**	**0.80 (0.73-0.86)**	**2.55 (1.93-3.31)**	0.606
Respiratory rate> 20-25 bpm	3 (3638)	0.53 (0.25-0.79)	0.84 (0.44-0.91)	**2.02 (1.34-3.02)**	**0.65 (0.45-0.84)**	**3.14 (2.08-4.51)**	
Any abnormal vital sign	3 (604)	0.93 (0.74-0.98)	0.30 (0.12-0.59)	**1.37 (1.10-1.84)**	**0.25 (0.11-0.48)**	**6.01 (3.03-10.6)**	

Where the positive likelihood ratio (LR+), negative likelihood ratio (LR−) or diagnostic odds ratio differed significantly from 1.0, the value is shown in bold face.
NC, not calculable from data; AUROCC = area under the receiver operating characteristic curve.



Time to Talk Nerdy

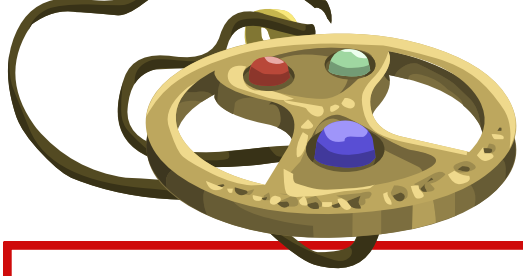
1. Exclusions: You excluded patients from skilled nursing facilities, with chronic lung disease, and immunosuppressed patients. From a pure diagnostic standpoint, that makes sense. However, these are probably the patients in whom it's most important not to miss a diagnosis of pneumonia. Based on your results, how do you approach the diagnosis in these patients?

2. Other Databases: You limited your search to the Medline databases, whereas we often see systematic reviews search multiple databases to ensure the results aren't biased by missing published studies. Can you explain for the listeners why a researcher might decide to search one database versus multiple, and whether you think it could significantly affect the results?

3. Imperfect Gold Standard: The signs and symptoms were compared to CXR. We know that a CXR is less accurate in diagnosing CAP than a CT scan. How do you think that could have impacted the results?

4. Prevalence and Possible Selection Bias: Perhaps it is just the community I work in, where everyone wants their viral illness checked in the emergency department, but a 20% prevalence of pneumonia in the emergency department seems quite high to me. Could this represent selection bias, and if so how might that impact the results?

5. Spectrum Bias: In general, these studies included patients in whom the clinician suspected pneumonia, and so presumably are a sicker cohort than all comers with cough. The negative likelihood ratios would probably look better if we included all comers, and we might be misled into over-testing if we try to apply these results to every patient presenting with a cough.



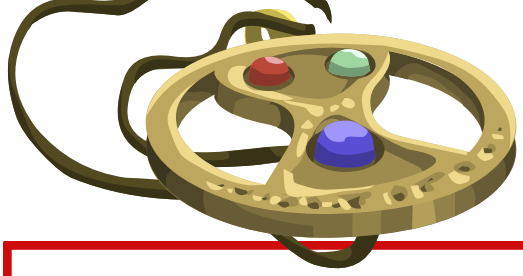
Time to Talk Nerdy

6. Verification Bias: You mention in your methods that you only included studies in which imaging was either performed on all patients, or all high-risk patients with a random sampling of low risk patients, in order to avoid verification bias. Can you explain verification bias to our listeners, and why it might be important when considering this type of literature?

7. Sensitivity vs. Specificity: The only finding with a moderate sensitivity for ruling out pneumonia was the absence of any abnormal vital signs. I worry that people will hear that result and interpret it as if the patient has an abnormal vital sign, they must get imaging. However, the specificity is going to be pretty low – basically every influenza patient is mildly tachycardic. Can you talk about sensitivity, specificity, and how these numbers actually drive your clinical practice?

8. Limited Utility vs. No Utility: It would be pretty easy to look at these numbers and get a little nihilistic. Is the physical exam even necessary? However, there is a difference between a single criterion having limited impact independently, and it having no impact at all. Presumably, the overall clinician's impression – which was the most accurate finding – included many of these individual findings, so they may add up to more than the sum of their parts.

9. Clinically Significance : A positive CXR does not mean a patient has a bacterial pneumonia. Prescribing antibiotics to a patient with a viral pneumonia is unlikely to have a patient-oriented outcome (POO). Do you think this disease-oriented outcome (DOO) and not a POO is a problem?



Time to Talk Nerdy

10. Are All Clinicians the Same? Overall clinical judgement was the most accurate for diagnosing pneumonia, but I wonder whether all clinicians are equally good. First, do we know what level of training the participants in these studies were. Second, do you think there are ways that we can improve our own clinical judgement when it comes to pneumonia?

Comment on Authors' Conclusion Compared to SGEM Conclusion: We agree with the authors' conclusion that most individual signs and symptoms are unhelpful on their own, but there are a few high value findings, like normal vital signs, or egophony. These findings can be used to teach the physical exam and may help make better decisions about imaging and antibiotic use.

Clinical Application: Depending on where you are in your career, reviewing these numbers may help you develop the expertise required to accurately diagnose pneumonia, although clinical diagnosis alone will never be perfect.

What Do I Tell My Patient? Based on the symptoms you have, your normal vital signs, and the fact that your lung exam is normal, I think it is very unlikely that you have a pneumonia today, so we don't have to expose you to an CXR. However, we can never be 100% certain, so if you are getting worse, please come back so we can recheck you.

Case Resolution: You review the entire history and physical exam with your student, as everyone needs to learn the basics. You explain to the patient that based on your clinical expertise, you think it is unlikely that they have a pneumonia, and so they don't need to be exposed to CXR at this time. However, you explain to the patient that no test is perfect, so if she is getting worse and is worried that you may have missed a pneumonia, she should come back for a recheck.

Episode End Notes

You Retweeted

Dr. Ken Milne - EBM and Rural @TheSGEM · Jul 21

What sign or symptom has the greatest likelihood ration associated with pneumonia? #SGEMHOP #EBM onlinelibrary.wiley.com/doi/abs/10.111... @First10EM @markebell @AcademicEmerMed @SAEMonline @AliRaja_MD @klinelab

Fever	27.9%
Cough	21.4%
Egophony	**32.5%**
Rhonchi	18.2%

280 votes · Final results

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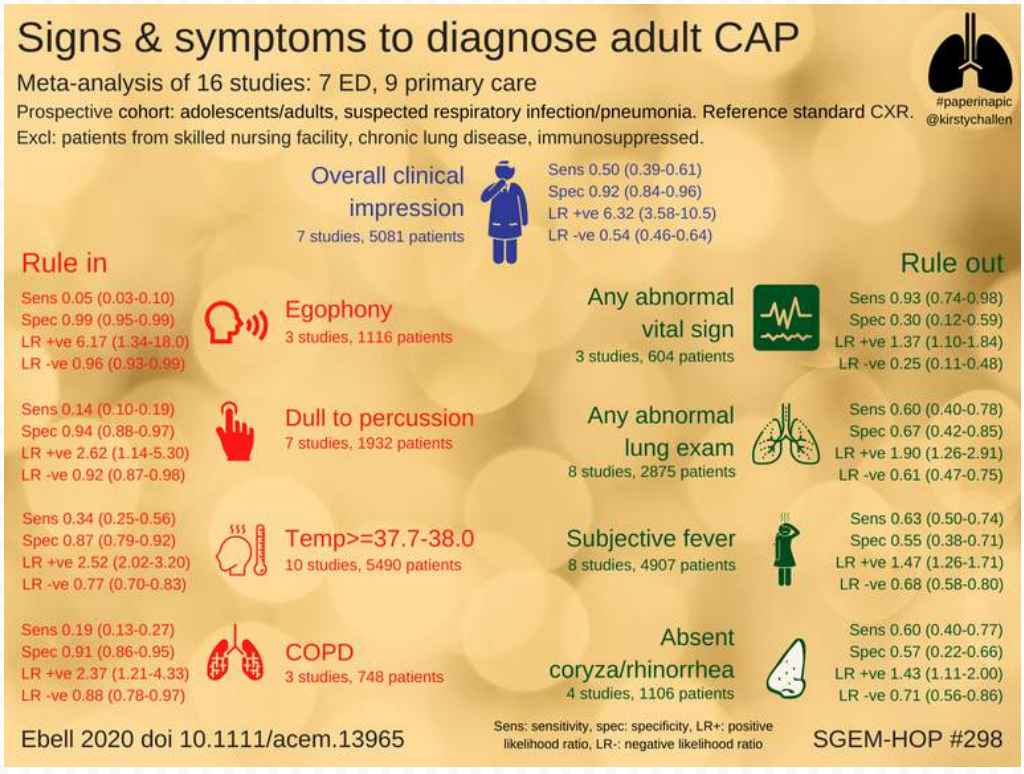

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LEARNING TO TEST FOR COVID19

Clinical Question:

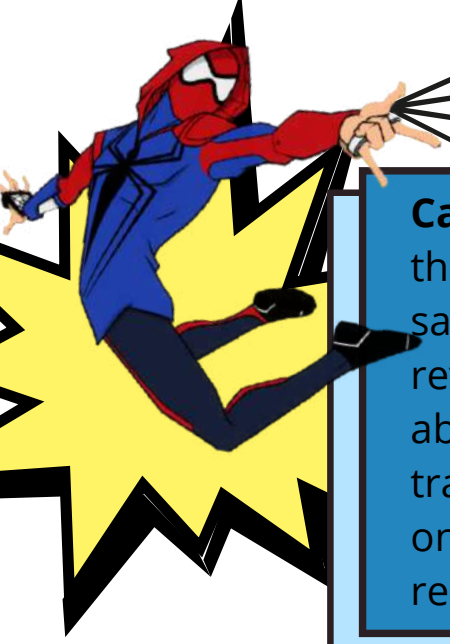
What is the diagnostic accuracy of history, clinical examination, routine labs, RT-PCR, immunology tests, and imaging tests for the Emergency Department diagnosis for COVID19?

Bottom Line:

The limitations for diagnostic testing for COVID-19 must be understoof. Current PCR tests have a fairly high false negative rate, so serial testing should be performed. There may be a role for imaging in suspected patients, but there are no pathognomonic findings for COVID-19.

Guest:

Dr. Corey Heitz is an emergency physician in Roanoke, Virginia. He is also the CME editor for Academic Emergency Medicine.



Case Overview

Case: You are working in the emergency department during the COVID-19 outbreak, and you see a patient with oxygen saturations of 75% on room air, a fever, and a cough. Upon review of systems, you learn that she lost her sense of taste about two days ago. Your hospital performs COVID reverse transcriptase polymerase chain reaction (rt-PCR) nasal swabs on suspected patients, so you order this test and await the results.

Background: In early 2020, a pandemic broke out with origins thought to be in the Wuhan region of China. A novel coronavirus, SARS-Co-V-2, commonly called COVID-19, rapidly spread around the world, overwhelming hospitals and medical systems, causing significant morbidity and mortality.

The speed with which the outbreak occurred made identification of cases difficult, as the disease exhibited a variety of symptoms, and testing lagged spread. The US Federal Drug Administration (FDA) allowed for emergency development and use of rt-PCR assays, and dozens of companies released assay kits.

I consciously have tried to avoid contributing to the COVID-19 information overload. However, I did do a CAEP Town Hall on therapeutics (SGEM Xtra: Be Skeptical) with Dr. Sean Moore and a friendly debate on mandatory universal masking in public with Dr. Joe Vipond (SGEM Xtra: Masks4All).

This review discusses the diagnostic accuracy of rt-PCR for COVID-19, as well as signs, symptoms, imaging, and other laboratory tests.

Reference: Carpenter et al. Diagnosing COVID-19 in the Emergency Department: A Scoping Review of Clinical Exam, Labs, Imaging Accuracy and Biases. AEM August 2020

Population: Original research studies describing the frequency of history, physical findings, or diagnostic accuracy of history/physical findings, lab test, or imaging tests for COVID-19

Intervention: None

Comparison: None

Outcomes: Diagnostic accuracy (sensitivity, specificity, and likelihood ratios)

This is an SGEMHOP episode which means we have the lead author on the show. Dr. Chris Carpenter is Professor of Emergency Medicine at Washington University in St. Louis and a member of their Emergency Medicine Research Core. He is a member of the SAEM Board of Directors and the former Chair of the SAEM EBM Interest Group and ACEP Geriatric Section. He is Deputy Editor-in-Chief of Academic Emergency Medicine where he is leading the development of the "Guidelines for Reasonable and Appropriate Emergency Care" (GRACE) project. He is also Associate Editor of Annals of Internal Medicine's ACP Journal Club and the Journal of the American Geriatrics Society, and he serves on the American College of Emergency Physician's (ACEP) Clinical Policy Committee. Dr. Carpenter also wrote the book on diagnostic testing and clinical decision rules.

Authors' Conclusions

"With the exception of fever and disorders of smell/taste, history and physical exam findings are unhelpful to distinguish COVID-19 from other infectious conditions that mimic SARS-CoV-2 like influenza. Routine labs are also non-diagnostic, although lymphopenia is a common finding and other abnormalities may predict severe disease. Although rRT-PCR is the current criterion standard, more inclusive consensus-based criteria will likely emerge because of the high false-negative rate of polymerase chain reaction tests. The role of serology and CT in ED assessments remains undefined."

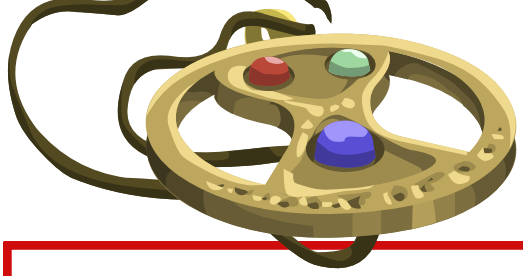
Quality Checklist for Systematic Review Diagnostic Studies

- [/] 1. The diagnostic question is clinically relevant with an established criterion standard.
- [x] 2. The search for studies was detailed and exhaustive.
- [✓] 3. The methodological quality of primary studies were assessed for common forms of diagnostic research bias.
- [✓] 4. The assessment of studies were reproducible
- [x] 5. There was low heterogeneity for estimates of sensitivity or specificity.
- [x] 6. The summary diagnostic accuracy is sufficiently precise to improve upon existing clinical decision-making models.

Case Outcomes

Key Results:
The authors screen 1,907 citations and 87 were included in the review. None adhere to the Standards for Reporting of Diagnostic Accuracy (STARD) or the updated reporting framework for history and physical examination. Rt-PCR was used as the criterion standard for many of the studies, but none explored the possibility of false negatives.

	Frequency	Sense & Spec	LR+	LR-
Clinical Exam				
• Fever	84-87%			
• Hyposmia			5.3	0.61
• Hypogeusia			7.1	0.38
• Anosmia	47-73%			
• Cough	58%			
Routine Labs				
• Lymphopenia	>50%			
Rt-PCR				
• Single Test		Sn 60-78%		
• Two Tests		Sn 86%		
• Five Tests		Sn 98%		
Serology				
• IgM or IgG >20d		Sn 82-100%, Sp 87-100%		
Imaging				
• Chest X-Ray		Sn 33-60%		
• CT Scan		Sn 72-94%, Sp 24-100%		



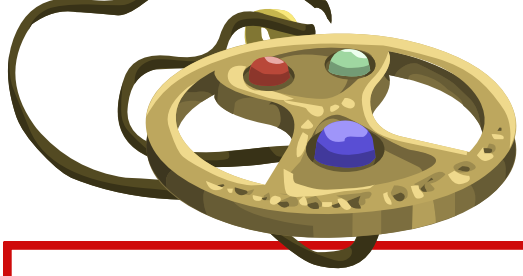
Time to Talk Nerdy

1) PRISMA-ScR (Scoping Review): What are the differences between PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) and the PRISMA-ScR guidelines?

"PRISMA provides a reproducible reporting framework for systematic review and meta-analysis authors. Multiple PRISMA extensions exist (acupuncture, harms, health equity, network meta-analysis) and in 2018 PRISMA published "scoping review" reporting methods. A scoping review differs from a systematic review in that formal quality assessment of individual diagnostic studies with QUADAS-2 is not performed. PRISMA-ScR still requires a reproducible search strategy and synthesis of research findings. We selected a scoping review rather than a systematic review because we had limited time to find and synthesize the studies amidst our own institution's COVID-19 chaos, yet we wanted to draw a line in the sand for diagnostic accuracy quality reporting because we were seeing the same research biases occurring repeatedly."

2) Search: Why did you decide to exclude non-English language studies? Would there not be a benefit to the experience out of other countries (especially China), even if not published in English-language journals?

"This was simply for expediency because we lacked time to find/fund a translator. You will see from the articles that we the majority of the studies were from China. This was because it was early May and there was little experience or research published from Europe or US at that time. As described in Figure 2, we did not exclude any studies for the purpose of language. This probably reflects a bias of our search engines (PubMed and EMBASE) for Asian language journals, as well as the fact that English is increasingly the universal language for scientific reporting."

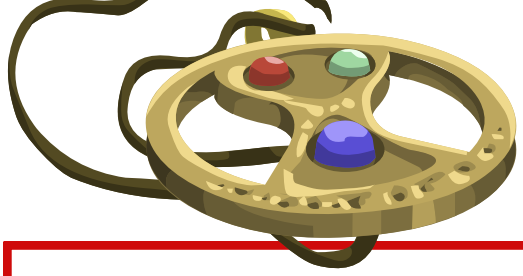


Time to Talk Nerdy

3) STARD: Can you tell us more about the Standards for Reporting of Diagnostic Accuracy (STARD) guidelines. None of the included studies adhered to the STARD guidelines. Why are these guidelines so important to follow?

"Over two decades ago, journal editors and publishers convened to create mutually agreeable reporting standards that would transcend specialities beginning with the CONSORT criteria for randomized controlled trials. These reporting standards continue to multiple (nearly 400 now!) and are warehoused at the EQUATOR Network. Like PRISMA for systematic reviews, STARD is the EQUATOR Network reporting standard for diagnostic studies. Unfortunately, as demonstrated in our COVID-19 scoping review, uptake of these reporting standards has been slow in emergency medicine. In 2017, Gallo et al reporting on behalf of the Best Evidence in Emergency Medicine (BEEM) team that ~80% of a randomly selected portion of diagnostic studies from eight EM journals report about half of STARD criteria (Gallo et al 2017). Some elements of STARD that were commonly omitted included reporting the time interval between the index test and the criterion standard, the reproducibility of the index test, harms associated with the test, 2×2 contingency tables, and test performance variability across clinicians, labs, or test interpreters. EQUATOR Network reporting standards like STARD are imperfect, but provide a minimal basement quality standard to ensure that diagnostic investigators evaluate essential features of their research design and that journal reviewers/editors analyze those elements of the study (Carpenter and Meisel AEM 2017) ."

4) Diagnostic Biases: A core papers resident and clinicians should be familiar with is the one on various diagnostic biases (Kohn et al AEM 2013). Let's go through some of the common diagnostic biases and how they can impact results and specifically COVID19 testing?

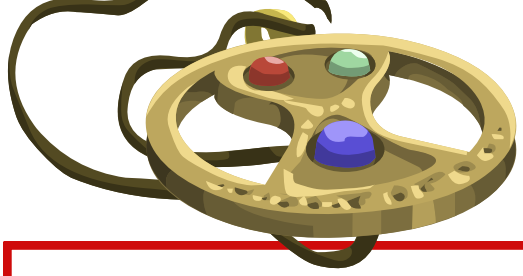


Time to Talk Nerdy

- **Spectrum Bias (Effect):** Sensitivity depends on the spectrum of disease, while specificity depends on the spectrum of non-disease. So, you can falsely raise sensitivity if the clinical practice has lots of very sick people. Specificity can look great if you have no sick patients in the cohort (the worried well). How could spectrum bias impact COVID19 testing?

"This is difficult to ascertain using the data provided in the research reporting of the early COVID-19 era. Investigators rarely reported distribution of disease severity (% ICU admissions, APACHE-2 scores) or baseline risk profile (frailty score, comorbid illness score) in COVID-19 positive patients nor the distribution of alternative diagnoses in COVID-19 negative patients. Washington University is participating in a study that includes fifty emergency departments across the United States to derive a PERC-like rule that identifies patients at low-risk of COVID-19 when testing is delayed or unavailable. With the variability in COVID-19 prevalence compounded by fluctuating availability of criterion standard testing resources, we have noted a skew towards testing very low risk or no-risk patients, which will skew specificity upwards and leave sensitivity relatively unaffected. Future COVID-19 diagnostic investigators (whether evaluating history, physical exam, labs, imaging, or decision-aids) need to report sufficient detail to permit stratification of accuracy estimates by disease severity in order to understand the impact of spectrum bias."

- **Incorporation Bias:** This occurs when results of the test under study are actually used to make the final diagnosis. This makes the test appear more powerful by falsely raising the sensitivity and specificity. Incorporation bias is particularly prevalent when the index test is part of the composite group of findings that determine whether the disease was present of absent.



Time to Talk Nerdy

"In the case of COVID-19, viral cultures were not commonly evaluated (or ever reported as a comparative criterion standard in the research we synthesized). In fact, we did not find any recommendations for a more preferable criterion standard by authors, commentators, or governmental websites like the CDC – so we proposed one that includes a downstream evaluation of exposure history, symptoms at the time of testing, laboratory tests including rRT-PCR, imaging, serology, and viral cultures as an optimal criterion standard for COVID-19. Of course, our recommended criterion standard would also be at risk for incorporation bias when evaluating history and physical exam, labs, or imaging but seems to have more face validity than using PCR as the criterion standard for PCR in which case PCR can never be wrong!"

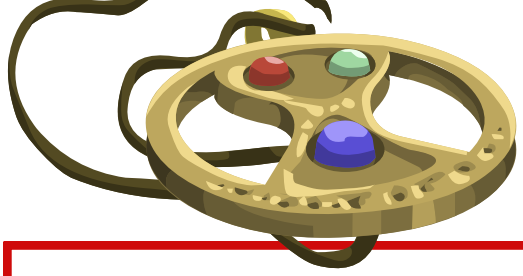
Table 2
Proposed COVID-19 Criterion Standard

Expert consensus months after acute illness, including
• Exposure history
• Symptoms
• Laboratory tests
• rRT-PCR
• Imaging
• Serology
• Viral cultures

rRT-PCR = real-time reverse transcription–polymerase chain reaction.

- **Differential Verification Bias (Double Gold Standard):** This occurs when the test results influence the choice of the reference standard. So, a positive index test gets an immediate/gold standard test whereas the patients with a negative index test get clinical follow-up for disease. This can raise or lower sensitivity/specificity.

"This is likely to occur in COVID-19 when the results of one test (CT demonstrating typical viral pneumonia findings of COVID-19) prompt clinicians or researchers to obtain additional COVID-19 testing such as repeat rRT-PCR or bronchoalveolar lavage specimens for COVID-19 testing. Differential verification bias is associated with increased specificity (and to a lesser extent sensitivity) for diseases that resolve spontaneously. On the other hand, for diseases that only become detectable during follow-up (like repeat rRT-PCR or serology testing) observed specificity and sensitivity are decreased."



Time to Talk Nerdy

- **Imperfect Criterion Standard (Copper Standard Bias):** This is what can happen if the *"gold"* standard is not that good of a test. False positives and false negatives can really mess up results.

"If errors on the index and criterion standard are correlated (i.e. usually incorrect at the same time or correct at the same time), observed sensitivity and specificity are falsely increased compared with what we would observe in the real world. On the other hand, if errors on the index and criterion standard do not correlate (are independent), observed sensitivity/specificity are lower than real world settings. Since a "gold standard" for COVID-19 does not yet exist, we proposed one as a starting point (see Table 2 above)."

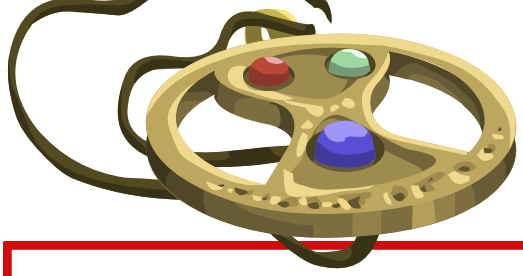
5a) False-Negatives: What are the implications of false negatives?

"Patient perspective: I don't have COVID-19! No need for face mask or social isolation for me! Time to party like it's 1999!"

Hospital perspective: This individual does not have COVID-19, so we can put them in a hospital room with another patient who does not have COVID-19. Also, nurse/physician do not need personal protective equipment with this patient."

In Figure 3 (see below), we also demonstrated the association between baseline COVID-19 prevalence and false positive/false negative results for three antibody tests.

One approach to reduce false negative rates due to imperfect (or unavailable) rRT-PCR testing was to evaluate every patient with PCR + CT. However, CT is also an imperfect COVID-19 diagnostic test and has additional negative consequences (Rapits et al 2020). The first unwanted side effects of CT are the cost to patient/society and the medical radiation exposure to the patient. The second consequence is potential contamination of CT technicians or subsequent patients in the scanner.



Time to Talk Nerdy

Recommendations to deep clean the scanner for an hour after every COVID-19 patient exist, but this delays access to the CT scanner for every patient in the ED. Consequently, the British Society of Thoracic Imaging issues guidelines for which suspected COVID-19 patients would benefit from CT evaluation (Nair et al 2020).

5b) False-Positives: What are the Implications of False-Positives?
"False positives for rRT-PCR are likely uncommon if labs follow CDC testing recommendations. On the other hand, false positives for antibody testing are largely unknown and rarely contemplated. We provided an algebraic manipulation of Bayes Theorem that provides a threshold COVID-19 prevalence at which the likelihood of a true positive is equal to a false positive:

Using this equation and the results reported from one serology study (Bendavid et al 2020), we estimate that threshold to be 0.62% prevalence, but using the results from yet another study (Whitman et al 2020) that threshold to be ~10%. In other words, if regional prevalence is <10% than a positive test is more likely to be a false positive than to be a true positive.

The implications of a false positive test could include unnecessary isolation of individuals (including restriction from work and lost income further increasing health disparities) and the expense of additional diagnostic testing.

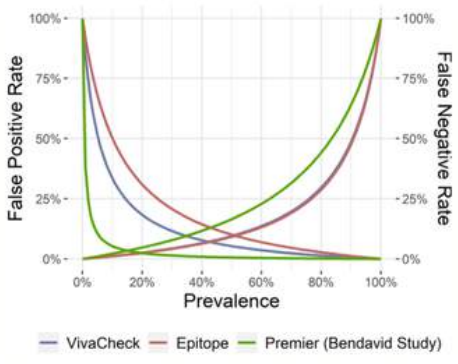


Figure 3. False-positive and false-negative rates as a function of pretest probability (or prevalence for surveillance studies) for serologic tests for SARS-CoV-2 antibodies. The left side of the graph illustrates the false-positive rate, and the right illustrates the false-negative rate.

We also provide clinicians with a resource to help patients and families to understand the imperfections of rRT-PCR in Figure 4. These Cates plots can be adapted as diagnostic investigators better understand the sensitivity/specificity of rRT-PCR (or antigen/serology tests)."

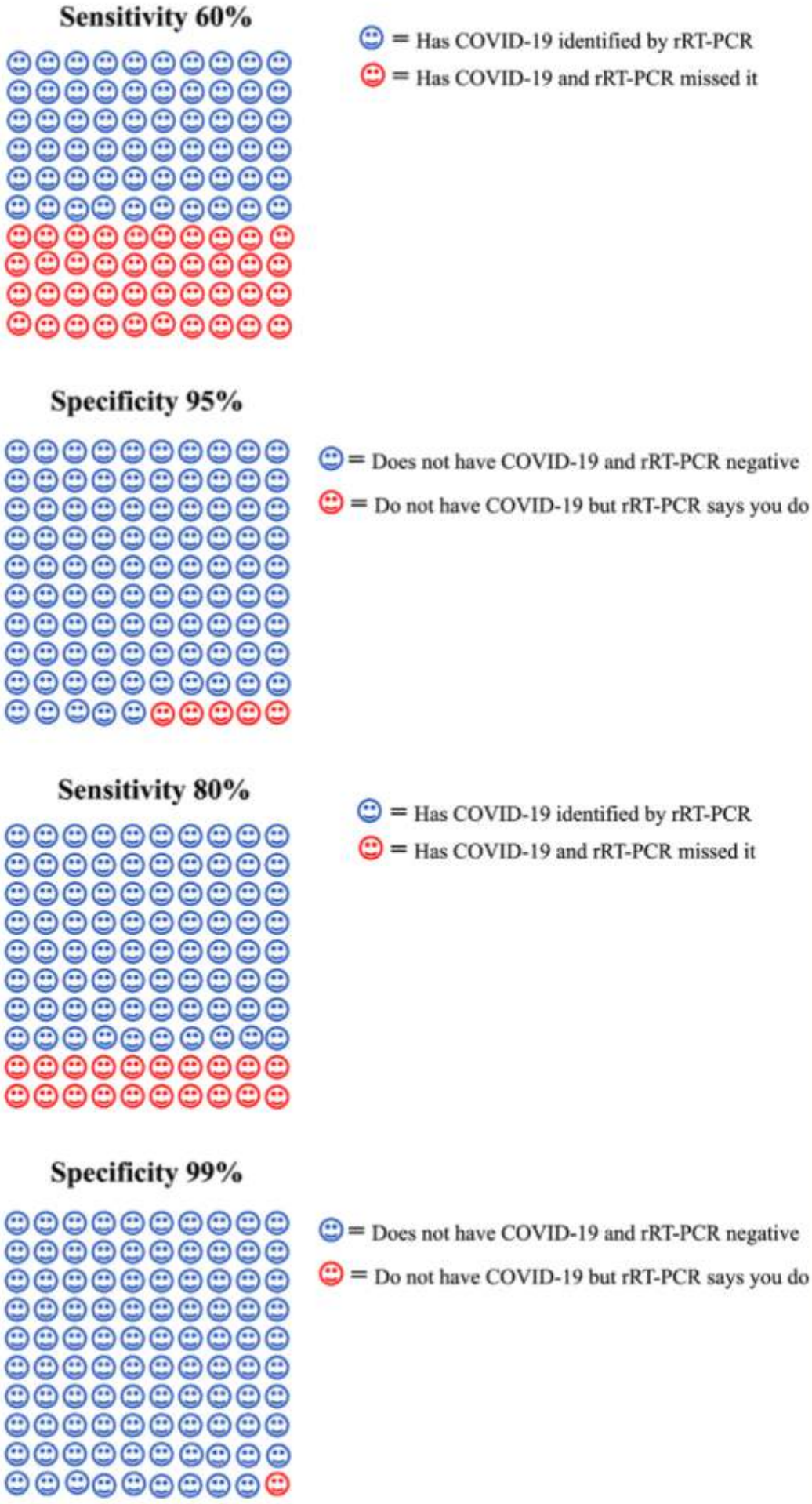
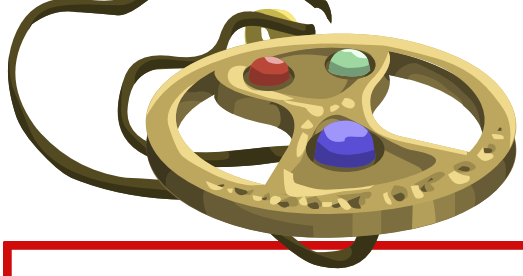


Figure 4. Cates plot for patients. rRT-PCR = real-time reverse transcription–polymerase chain reaction.



Time to Talk Nerdy

What do you think the implications are for future research in the diagnostic accuracy of COVID19?

1. *Diagnostic investigators must adhere to STARD reporting standards or clinicians/policy-makers risk devolving into a confusing Tower of Babel with rampant miscommunication and preventable repetition of research error.*
2. *Journal editors and reviewers should hold researchers to STARD standards by seeking additional data or clarifications when elements of diagnostic testing (such as accuracy among patient subsets, explicit 2×2 contingency table reporting, and inter-rater test reproducibility) are missing.*
3. *Contemplate the harms of testing, including quantification of false-negatives and false-positives and the associated adverse consequences for patients, hospitals, and communities.*
4. *Consider reporting interval likelihood ratios for continuous data.*
5. *Beyond the elementary Cates plots we propose, develop formal shared decision-making resources for patients/families to aid meaningful discussions around the interpretation of signs/symptoms, imaging, labs, and rRT-PCR (Hess et al AEM 2015).*

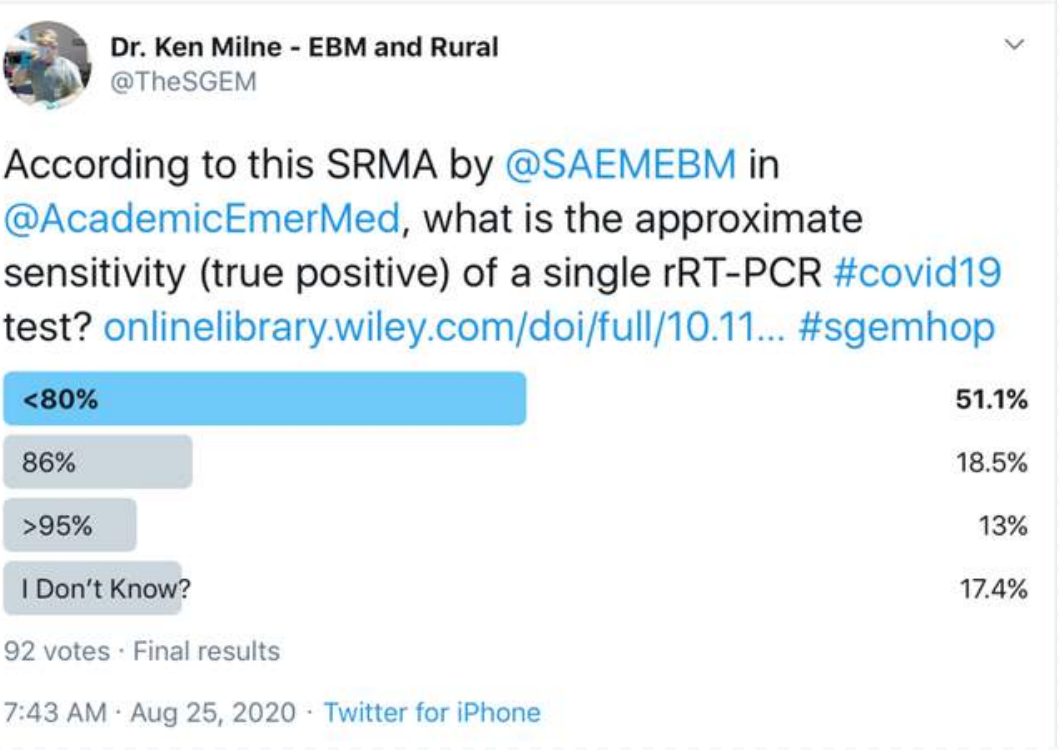
Comment on Authors' Conclusion Compared to SGEM Conclusion: We agree with the authors' conclusions.

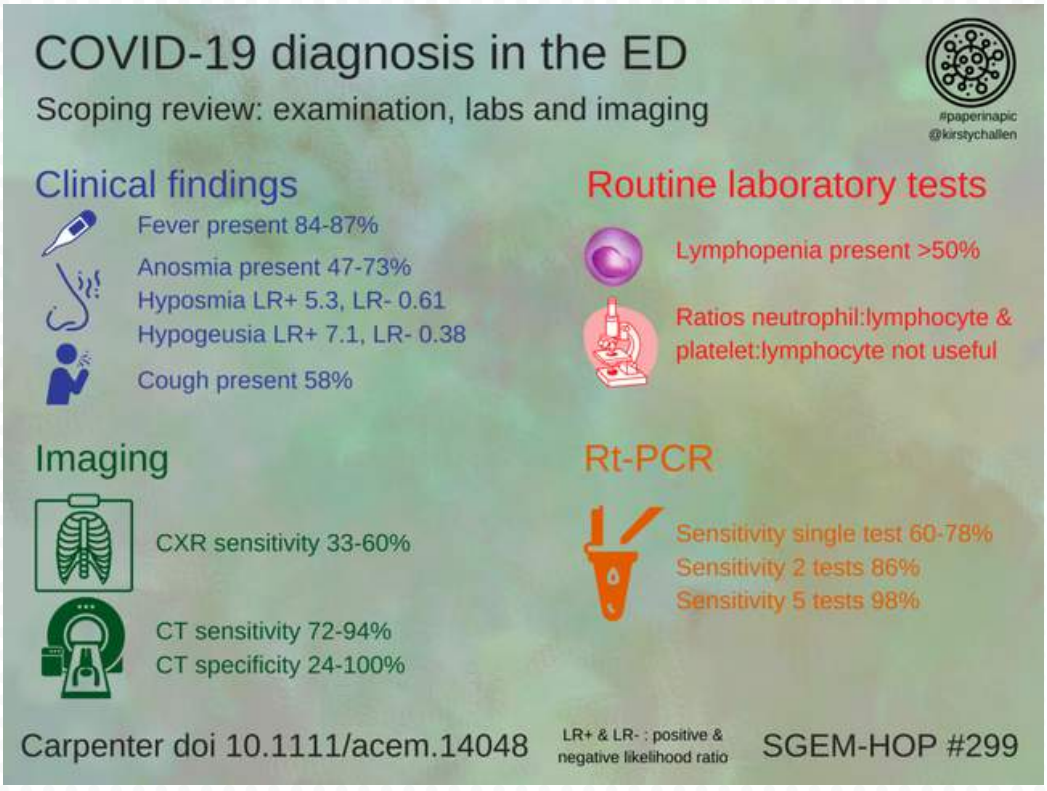
Clinical Application: Be aware of high false negative rates for rt-PCR testing and maintain a high level of suspicion in high-risk patients.

What Do I Tell My Patient? Your initial COVID test came back negative. However, given the suspicion we have, we are going to continue to protect ourselves, staff and other patients, and are going to care for you as if you have the virus.

Case Resolution: Your patient tests negative for the virus. Despite this, your suspicion is high, so you continue to use appropriate personal protection equipment (PPE) when entering the room.

Episode End Notes



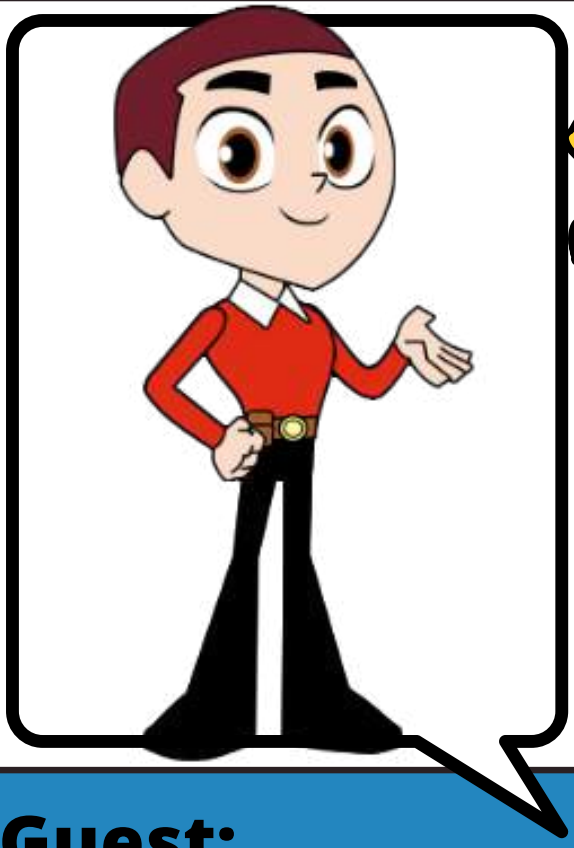


300

THE LUNG IS UP WHERE IT BELONGS - WITH OR WITHOUT A CHEST TUBE

Clinical Question:

Does everyone with a large first-time spontaneous pneumothorax need a chest tube?

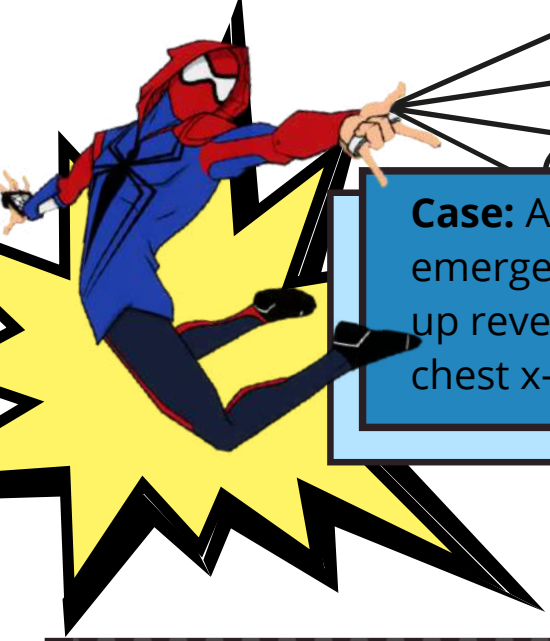


Bottom Line:

It is reasonable to provide conservative management in a patient with large first-time spontaneous pneumothoraxes as long as you can ensure close follow-up.

Guest:

Dr. Malthaner is the Chair/Chief of the Division of Thoracic Surgery, Director of Thoracic Surgery Research and Simulation, and Professor in the Departments of Surgery, Oncology, and Epidemiology and Biostatistics at the Schulich School of Medicine and Dentistry and Western University. Rick is also the founder of Western University's Department of Surgery Journal Club and runs The Skeptik Thoracik Journal Club.



Case Overview

Case: A 49-year-old healthy male electrician presents to the emergency room with right chest pain and dyspnea. The work-up reveals a diagnosis of a right pneumothorax confirmed by chest x-ray (CXR). What do you do?

Background: A patient with a pneumothorax is a common presentation to the emergency department. Pneumothoraxes can be broken down into either primary or secondary. Primary pneumothorax occurs in healthy people. Secondary pneumothoraxes are associated with underlying lung disease.

There is considerable heterogeneity in the management of primary spontaneous pneumothoraxes, but the most common treatment is interventional drainage, sometimes progressing to surgical intervention.

However, the insertion of a chest tube is often painful and can cause organ injury, bleeding, and infection. An alternative approach is conservative management, with intervention reserved for patients for whom the pneumothorax becomes physiologically significant. I covered in the Skeptik Thoracik Journal Club which can be viewed on YouTube.

Reference: Brown et al. Conservative versus Interventional Treatment for Spontaneous Pneumothorax. NEJM 2020

Population: Patients 14 to 50 years of age with a unilateral primary spontaneous pneumothorax of 32% or more on chest radiography according to the Collins method.

Exclusion:

- Previous primary spontaneous pneumothorax on the same side
- Secondary pneumothorax (defined as occurring in the setting of acute trauma or underlying lung disease including asthma with preventive medications or symptoms in the preceding two years)
- Coexistent hemothorax
- Bilateral pneumothorax
- "Tension' pneumothorax" (systolic BP <90 mmHg, mean arterial pressure <65 mmHg, or shock index HR/SBP ≥1)
- Pregnancy at time of enrolment
- Social circumstances (inadequate support after discharge to re-attend hospital if required or unlikely to present for study follow up)
- Planned air travel within the following 12 weeks

Intervention: A small chest tube (≤12 French) was inserted and attached to an underwater seal, without suction and a CXR was obtained one hour later.

- If the lung had re-expanded and the underwater drain no longer bubbled, the drain was closed with the use of a three-way stopcock. Four hours later, if the patient's condition was stable and a repeat CXR showed that the pneumothorax had not recurred, the drain was removed, and the patient was discharged.
- If the initial drain insertion did not result in resolution on CXR or if the pneumothorax recurred under observation, the stopcock was opened, the underwater seal drainage was recommenced, and the patient was admitted.
- Subsequent interventions were at the discretion of the attending clinician.

Comparison: Patients were observed for a minimum of four hours before a repeat CXR was obtained.After observation, if patients did not receive supplementary oxygen and were walking comfortably, they were discharged with analgesia and written instructions.

- Interventions were allowed in the conservative-management protocol under five conditions:
    i. Clinically significant symptoms persisted despite adequate analgesia;
    ii. Chest pain or dyspnea prevented mobilization;
    iii. Patient was unwilling to continue with conservative treatment;
    iv. Patient's condition became physiologically unstable (systolic blood pressure of <90 mm Hg, heart rate in beats per minute greater than or equal to systolic blood pressure in millimeters of mercury, respiratory rate of >30 breaths per minute,
    v. Spo2 of <90% while the patient was breathing ambient air or a repeat chest radiograph showed an enlarging pneumothorax along with physiological instability.
- In these situations, subsequent interventions were at the discretion of the attending clinician.

Outcomes:

- **Primary Outcome:** Complete radiographic resolution of primary spontaneous pneumothorax (full lung re-expansion), as determined by the treating physician, within eight weeks after randomization.
- **Secondary Outcomes:** Per-protocol analysis of the primary outcome. Time to radiographic resolution. Time to symptom resolution of symptoms. Pneumothorax recurrence 24 hours or later after chest tube removal. Adverse events. Length of stay (LOS) in the hospital in the first eight weeks. Number of invasive procedures. Number of radiologic investigations. Number of days off from work. Chest-tube drainage for equal to or greater than 72 hours. Patient satisfaction. Two sensitivity analyses of the primary outcome.

Figure S1: Graphic of Collins Method for determining the 'sum of interpleural distances", from which pneumothorax size is estimated. %Collins = 4.2 +4.7(A+B+C)

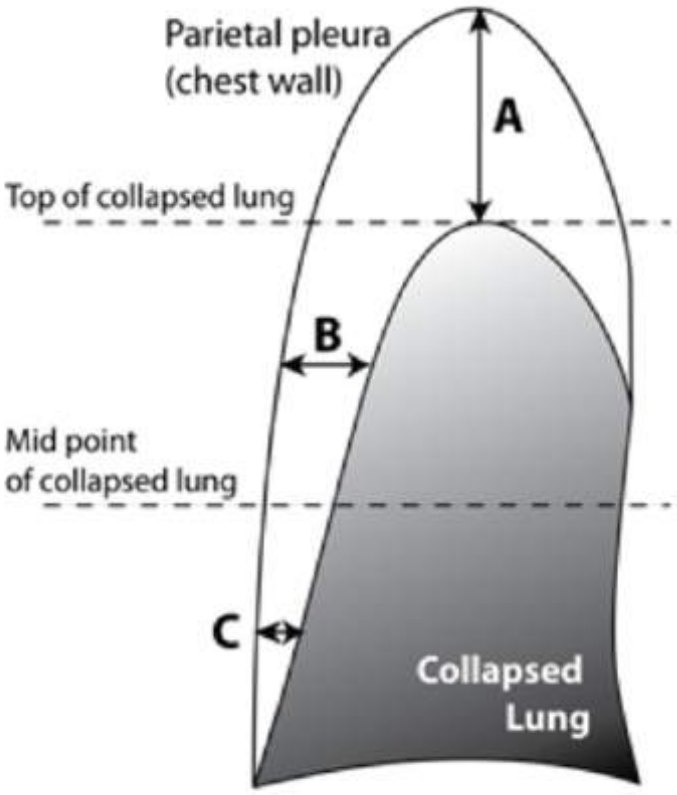


Figure modified from Collins et al. Quantification of Pneumothorax Size on Chest Radiographs Using Interpleural Distances: Regression Analysis Based on Volume Measurements from Helical CT. American Journal of Roentgenology. 1995;165:1127-130.

Authors' Conclusions

"Although the primary outcome was not statistically robust to conservative assumptions about missing data, the trial provides modest evidence that conservative management of primary spontaneous pneumothorax was noninferior to interventional management, with a lower risk of serious adverse events."

Quality Checklist for Randomized Clinical Trials

- ✓ 1. The study population included or focused on those in the emergency department.
- ✓ 2. The teams were adequately randomized.
- ✓ 3. The randomization process was concealed.
- ✓ 4. The teams were analyzed in the groups to which they were randomized.
- ? 5. The study teams were recruited consecutively (i.e. no selection bias).
- ✓ 6. The teams in both groups were similar with respect to prognostic factors.
- ✗ 7. All participants (patients, clinicians, outcome assessors) were unaware of group allocation.
- ✗ 8. All groups were treated equally except for the intervention.
- ✓ 9. Follow-up was complete (i.e. at least 80% for both groups).
- ✓ 10. All patient-important outcomes were considered.
- ? 11. The treatment effect was large enough and precise enough to be clinically significant.

Case Outcomes

Key Results:
The cohort of patients analyzed was 256 (154 intervention group and 162 conservative group). The mean age was 26 years and the mean pneumothorax size was about 65% based on the Collins formula.

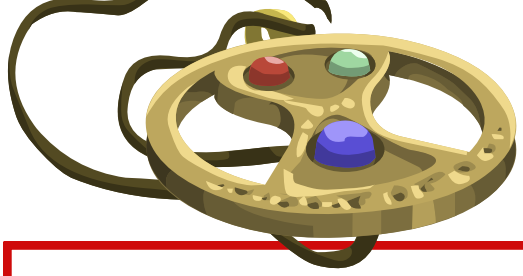
Conservative management was shown to be non-inferior to placing a chest tube in a patient with a large first-time spontaneous pneumothorax.

- **Primary Outcome:** Re-Expansion within Eight Weeks
  - Intervention Group 98.5% vs. Conservative Group 94.4%
  - Risk Difference -4.1% (95% CI; -8.6% to 0.5%) p=0.02 which meets the pre-specified non-inferiority margin of -9%

- **Secondary Outcomes:**

	Intervention Group	Conservative Group	RR, HR (95% CI)
Time to CXR resolution (median)	16 days	30 days	HR 0.49 (0.39-0.63)
Time to Symptom Resolution (median)	93.4%	94.6%	RR 1.1% (-4.4-6.7)
Pneumothorax Recurrence	16.8%	8.8%	RR 1.9 (1.03-3.52)
Serious Adverse Events	12.3%	3.7%	RR 3.3 (1.37-8.1)
Hospital LOS (mean)	6.1 days	1.6 days	RR 2.8 (1.8-3.6)
One or More Procedures	94.2%	15.4%	RR 6.1 (4.24-8.77)
Days off Work (mean)	10.9 days	6.0 days	RR 2.0 (1.0-3.0)
Chest-tube drainage for ≥72 hours	51.0%	9.3%	RR 41.7 (32.6-50.8)
Patient Satisfied or Very Satisfied	89.3%	94%	

- **Sensitivity Analysis: Worst Case**
  - Intervention Group 93.5% vs. Conservative Group 82.5%
  - Risk Difference -11.0% (95% CI; -19.4% to -1.5%) which does not meet pre-specified non-inferiority margin of -9%



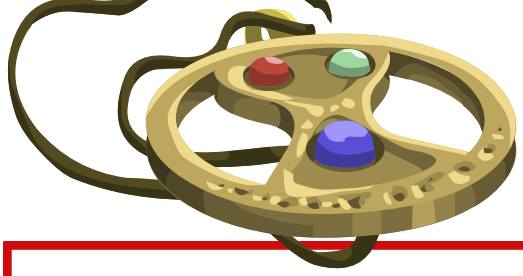
Time to Talk Nerdy

1. Missing Data: An important thing to look at when critically appraising a study is how did the authors manage missing data? In this study, what happened when the data on patients in whom the 8-week visit occurred after 56 days? Were treated as missing, unless a later CXR showed a persisting pneumothorax, thereby confirming treatment failure.

Two sensitivity analyses were undertaken in this trial. In one analysis, the 8-week window was extended to 63 days and data on patients in whom the 8-week visit occurred after 63 days were treated as missing, unless a later CXR showed a persisting pneumothorax, thereby confirming treatment failure. In the other analysis, data on patients in whom the 8-week clinic visit occurred after 56 days were imputed as failure (worst case scenario).

2. Per-Protocol vs. Intention-to-Treat (ITT) Analysis: Their primary outcome used an ITT analysis. It is better in non-inferiority trials to use a per-protocol analysis. This is because the ITT will bias towards finding non-inferiority while a per-protocol is a more conservative approach. Their secondary outcomes did include a per-protocolanalysis of the primary outcome (complete lung re-expansion within 8 weeks, as reviewed by two radiologists who were unaware of the trial-group assignments).
In the per-protocol analysis, 98.4% in the intervention group had resolution within 8 weeks as compared with 94.6% in the conservative group (RD, −3.8% [95% CI; −8.3 to 0.7]).

3. Satisfaction Scale: They used a 6- point Likert scale to assess patient satisfaction at eight weeks. While the scale has face validity, we are not aware that this specific instrument has been validated in this disease specific condition. I don't think one exits and this may be a minor nerdy point.



Time to Talk Nerdy

4. Adaptive Biased-Coin Randomization: The urn randomization is the most widely known type of the adaptive biased-coin randomization. They are a compromise between designs that yield perfect balance in treatment assignments and complete randomization which addresses experimental bias. The urn design forces a small-sized trial to be balanced but approaches complete randomization as the size of the trial (n) increases (Wei and Lachin 1988).

In an adaptive biased-coin randomization the probability of being assigned to a group decreases if the group is overrepresented and increases if the group is underrepresented. This special less common method of randomization is thought to be less affected by selection bias than permuted-block randomization.

We talked about Cluster Randomization on SGEM#:247. Rather than randomizing the individual patients, it randomizes groups of patients to the intervention or control. There are strengths and weaknesses to any trial design.

5. Non-Inferiority Margin: How do you determine what is considered non-inferior? That authors stated in the methods there was not any previously established noninferiority margin. As such, the steering committee of respiratory and emergency physicians reasoned that a success rate of 90% in the conservative-management group as compared with an anticipated 99% success rate in the intervention group after 8 weeks would be acceptable to both doctors and patients. While I think this was a reasonable margin based their expert opinion and assumptions.

It would have been interesting to ask patients what they would consider "*reasonable*" for non-inferiority? Ultimately, the data showed their assumptions were pretty good with the success rate in the intervention group being 98.5% vs. 94.4% in the conservative group. This gave a difference of -4.1% (95% CI; -8.6% to 0.5%) p=0.02 which met the pre-specified non-inferiority margin of -9%.

Comment on Authors' Conclusion Compared to SGEM Conclusion: We agree with the authors conclusions but are not sure if they apply to our patients. In Canada we don't admit spontaneous pneumothoraxes with chest tubes. We send these patients home with Heimlich valves and follow-up in Thoracik clinic. I sleep better knowing they won't develop the dreaded tension pneumothorax.

Clinical Application: This new evidence provides give us more confidence to our practice of treating some of these patients with patients with a first large spontaneous pneumothoraxes conservatively.

What Do I Tell My Patient? You have a collapse of your lung. This can happen randomly is some people. It seems to be stable and not getting worse. We going to keep an eye on you and not put a tube in your chest. These tubes have been used before to let the lung re-inflate. While a chest tube is a very safe procedure there are always some risks. New research shows more than 90% of patients will be fine without a tube in their chest. If the repeat CXR in about four hours is ok, we will send you home with follow-up with your friendly Thoracik surgeon. You can come back to the emergency department at any time if you are feeling worse or are concerned.

Case Resolution: You enter a shared decision-making process with the patient on whether or not to place a chest tube. Part of that is to support whatever decision he chooses. He decides to go with conservative management and will follow-up in the clinic.

Episode End Notes

Other FOAMed:

- First10EM: Conservative Treatment for Primary Spontaneous Pneumothorax
- St. Emlyn's Blog: JC – Conservative Management of Pneumothoraces
- EM Literature of Note: Put an End to Routine Chest Tubes
- The Bottom Line: Primary Spontaneous Pneumothorax (PSP) Trial
- REBEL EM https://rebelem.com/spontaneous-pneumothorax-stand-there-and-do-nothing/

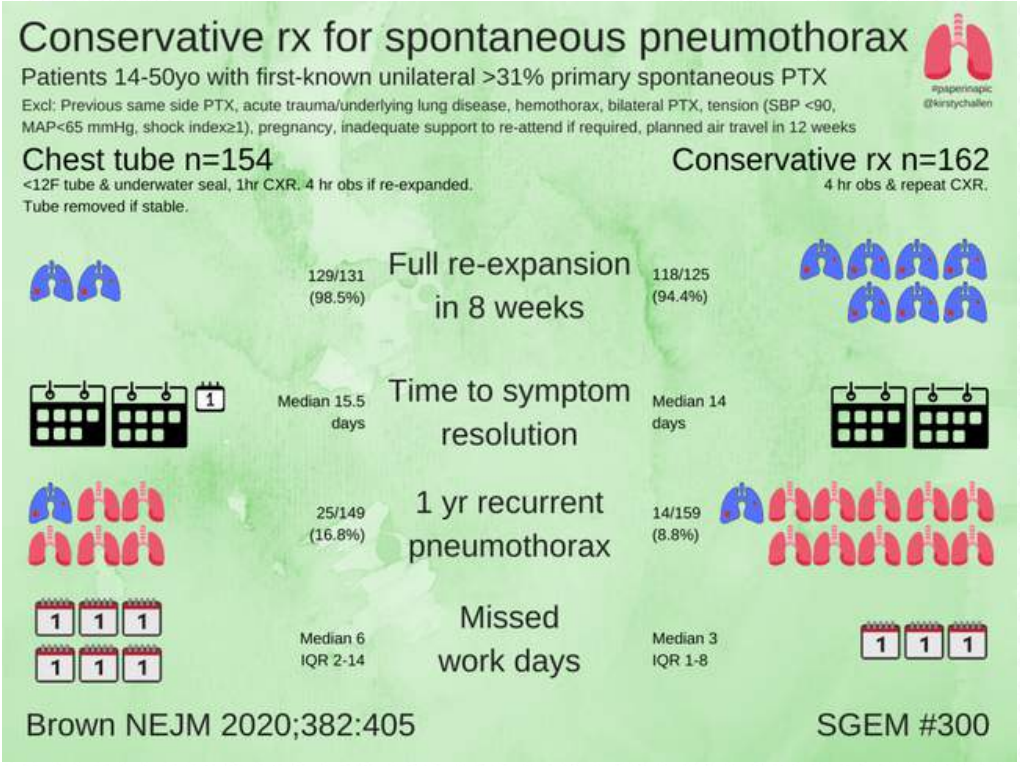
Will this RCT showing non-inferiority of conservative management vs chest tube for spontaneous pneumothorax change your clinical practice? #EBM #FOAMed

thesgem.com/2020/09/sgem30...

.@ACEPNow .@CAEP_Docs .@SRPCanada .@ThoracikRick

No - Don't accept results	8%
No - Already doing	19%
Yes- Might change	**63%**
Yes - Definitely change	10%

48 votes · Final results



301

YOU CAN'T STOP GI BLEEDS WITH TXA

Clinical Question:

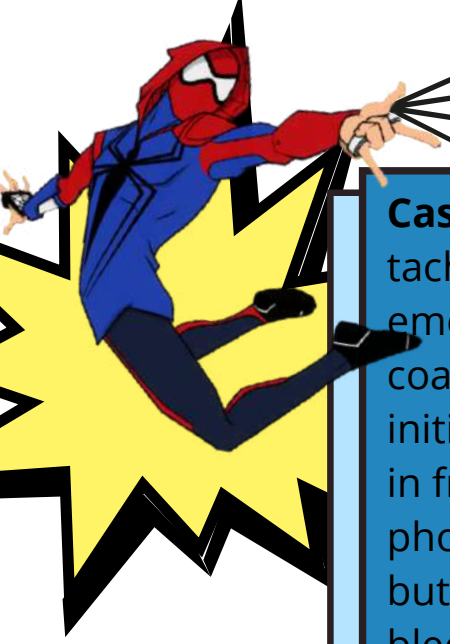
Does treatment with TXA reduce the mortality of patients with upper or lower GI bleeds?

Bottom Line:

The latest evidence does not support the use of TXA in GI bleeds.

Guests:

Dr. Robert Goulden and Dr. Audrey Marcotte are Chief Residents from the Royal College of Emergency Medicine Program at McGill University. Robert's academic interests include research and evidence-based medicine. Alongside his EM residency, he is doing a PhD in epidemiology. Audrey's academic interests include trauma and resuscitation. Outside of medicine, Audrey likes to play rugby and run.



Case Overview

Case: A 58-year-old man presents with hypotension, tachycardia, and pallor. He vomits a large amount of bloody emesis and has epigastric discomfort. He is not taking any anti-coagulants. He remains hemodynamically unstable despite initial resuscitation and has another episode of hematemesis in front of you. While waiting for your consultant to answer the phone, you consider treating him with tranexamic acid (TXA), but wonder if it will prevent death from gastrointestinal (GI) bleeding.

Background: We have covered the use of TXA a number of times on the SGEM. TXA is an anti-fibrinolytic agent that inhibits clot breakdown and has demonstrated mixed results in different clinical settings.

The CRASH-2 trial showed a 1.5% absolute mortality benefit with TXA in adult trauma patients compared to placebo (SGEM#80). TXA also seems to improve patient-oriented outcomes in epistaxis (SGEM#53 and SGEM#210).

However, TXA did not show a statistically significant difference for the primary outcome in post-partum hemorrhage (SGEM#214) WOMAN Trial, hemorrhagic stroke (SGEM#236) or traumatic intracranial hemorrhage (SGEM#270) CRASH-3.

A Cochrane systematic review and meta-analysis of eight smaller trials (n=1,701) using TXA in gastrointestinal bleeding suggested a large (40%) risk reduction in all-cause mortality (Bennett et al 2014). However, even a meta-analysis is prone to bias and is only as good as the quality of the included trials. When all participants in the intervention group with missing outcome data were included as treatment failures, or when the analysis was limited to trials with low risk of attrition bias the mortality benefit of TXA disappeared.

Reference: Roberts et al. Effects of a high-dose 24-h infusion of tranexamic acid on death and thromboembolic events in patients with acute gastrointestinal bleeding (HALT-IT): an international randomised, double-blind, placebo-controlled trial. The Lancet 2020

Population: Adult patients (16 years of age or 18 years of age and older depending on country) with significant upper or lower GI bleed. Significant bleed was defined clinically (judged at risk of bleeding to death, hypotension <90 mmHg systolic, tachycardia, signs of shock, needing transfusion, urgent endoscopy or surgery).

Intervention: Intravenous TXA, 1g loading dose over 10 minutes followed by 3g maintenance over 24 hours

Exclusion: Any patient whom the clinician felt had a clear indication or clear contraindication for TXA

Comparison: Matching placebo (Sodium chloride 0.9% IV)

Outcomes:

- **Primary Outcome:** Death due to gastrointestinal (GI) bleeding within five days
- **Secondary Outcomes:**
  - Death due to gastrointestinal bleeding within 24h and within 28 days
  - All-cause and cause specific mortality at 28 days
  - Rebleeding within 24h, 5 days, 28 days
  - Surgical or radiological intervention
  - Blood product transfusion
  - Thromboembolic events (deep vein thrombosis, pulmonary embolism, stroke, myocardial infarction)
  - Seizures and other complications (sepsis, pneumonia, renal and liver failure, cardiac event)
  - Days in intensive care unit
  - Functional status (Katz index of Independence in activities of daily living)

Authors' Conclusions

"We found that tranexamic acid did not reduce death from gastrointestinal bleeding. On the basis of our results, tranexamic acid should not be used for the treatment of gastrointestinal bleeding outside the context of a randomised trial."

Quality Checklist for Randomized Clinical Trials

- ☑ 1. The study population included or focused on those in the emergency department.
- ☑ 2. The teams were adequately randomized.
- ☑ 3. The randomization process was concealed.
- ☑ 4. The teams were analyzed in the groups to which they were randomized.
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- ☑ 7. All participants (patients, clinicians, outcome assessors) were unaware of group allocation.
- ☑ 8. All groups were treated equally except for the intervention.
- ☑ 9. Follow-up was complete (i.e. at least 80% for both groups).
- ☑ 10. All patient-important outcomes were considered.
- ☒ 11. The treatment effect was large enough and precise enough to be clinically significant.

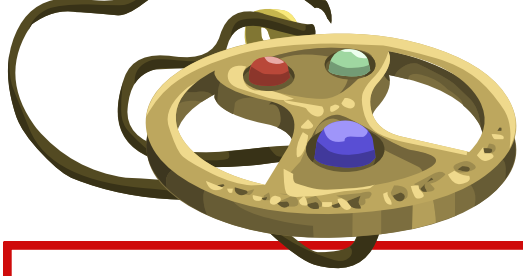
Case Outcomes

Key Results:
Mean age 58 years, two-thirds male, nine out of ten were upper GI bleeds, half were thought to be due to varices and about 9% were known to be on anti-coagulants.

No statistically significant difference in mortality from GI bleed.

- **Primary Outcome:** Mortality from GI bleed within five days
  - 3.7% (TXA) vs. 3.8% (placebo), RR 0·99 (0·82–1·18)

- **Secondary Outcomes:**
  - No significant difference in all-cause mortality at 28 days, 9.5% (TXA) vs. 9.2% (Placebo), RR 1·03 (95% CI; 0·92–1·16)
  - Statistically significant increase in venous thromboembolism (VTE), 0.8% (TXA) vs. 0.4% (Placebo). RR 1.85 (95% CI; 1.15-2.98). This effect was more marked in those with suspected variceal bleeding than in those with non-variceal bleeding (p=0.035 for heterogeneity).
  - No significant difference in all other secondary outcomes including rebleed and death due to rebleed at multiple time points, need for additional interventions, and other safety outcomes.



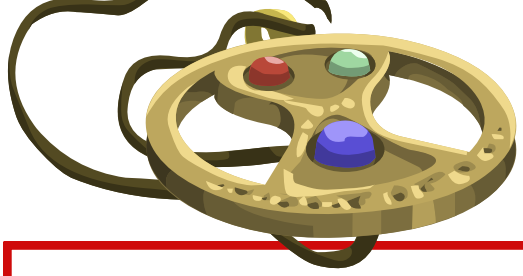
Time to Talk Nerdy

1) Consistency in Results: This trial is definitively and unambiguously "*negative*" – it's actually rare that we get a trial result that is so clear cut. All of the different outcomes lined up as showing no statistical benefit, and there were no subgroups in which that differed. In contrast, think of CRASH-3 (TXA for intracranial hemorrhage) or PARAMEDIC-2 (epinephrine for out-of-hospital cardiac arrest), other well-conducted large RCTs, where the fact that some outcomes were "*positive*" and others "*negative*" have left people still debating how to interpret them.

2) Changing the Primary Outcome: Switching the outcome midway through a trial is a *red flag* for potential statistical shenanigans, as there is a risk that investigators are aware of partial results and are switching from a non-significant to a significant outcome. However, in this case the decision to switch was made and published with a justification before unblinding.

However, they did shift from a reliable, unambiguous, patient-centred outcome – all-cause mortality at 28 days – to a much less patient and clinically important outcome – mortality from GI bleeding at five days. Patients (and clinicians) don't usually care what they die of – they care whether they die or not. It's also much more challenging to reliably determine the cause of death as compared to determining *if* someone is dead or not. Imagine if TXA decreased GI bleeding death by 2% but increased VTE death by 4%. Should that be considered a positive trial?! In the end, it doesn't matter as the original primary outcome of all-cause mortality at 28 days – which I think should be the outcome we are most interested in – was also not significantly different.

- *"The sample size calculation was initially based on all cause mortality as the primary outcome since we expected that most deaths would be due to bleeding. However, while the trial was underway, we observed that over half of all deaths were due to nonbleeding causes. Accumulating evidence from other large trials of tranexamic acid showed no apparent effect on non-bleeding deaths."*



Time to Talk Nerdy

- *"The primary outcome was therefore changed to death due to bleeding within 5 days of randomisation on Nov 21, 2018. Based on the amended primary outcome, assuming a risk of death due to bleeding of 4%, a study with 12000 patients has about 85% power (two-sided α of 5%) to detect a clinically important 25% relative reduction in death due to bleeding from 4% to 3%".*

3) Secondary Outcomes: The finding of increased VTE risk is interesting. It may be a chance finding since there were lots of secondary analyses and by random chance alone, we would expect a few to be statistically different. However, this was a safety outcome for which there was a reasonable prior belief in potential harm, and their point estimate (RR 1.85) was almost identical to the point estimate from the prior Cochrane review (RR 1.86). Arguably a 0.4% absolute increase in VTE (0.8% vs. 0.4%, NNH = 250) is not that clinically important, but given there is no evidence of benefit here, it strengthens the case against using TXA for this indication.

4) Selection Bias: As with CRASH-3 and the WOMAN trials, patients whom clinicians felt there was a clear indication or contraindication to TXA were excluded. We don't have a clear idea how many patients were excluded for these reasons. As such, we must consider the possibility of selection bias.

5) Large RCT vs. SRMA of Small Studies: The prior Cochrane meta-analysis of RCTs showed a statistically significant 40% relative reduction in mortality with TXA in GI bleeds. This trial refutes the finding of a large reduction and suggests we should be careful in putting too much faith in meta-analyses of methodologically flawed small trials. However, it does not rule out a small or modest reduction.

Comment on Authors' Conclusion Compared to SGEM Conclusion: We agree with the authors conclusion, though we would emphasize that all-causemortality was also unaffected by TXA.

Clinical Application: When it comes to GI bleeding, it is time to put aside TXA from your treatment toolbox and focus on basic volume resuscitation while liaising with your consultants for definitive hemorrhage control.

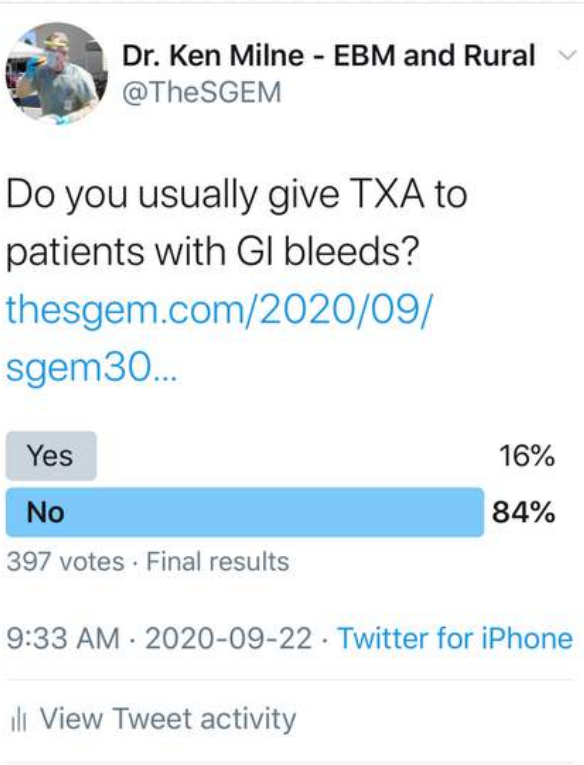
What Do I Tell My Patient? We have no specific medication that directly stops the bleeding, but we will stabilize you with blood transfusions to prepare you for definitive treatment with endoscopy.

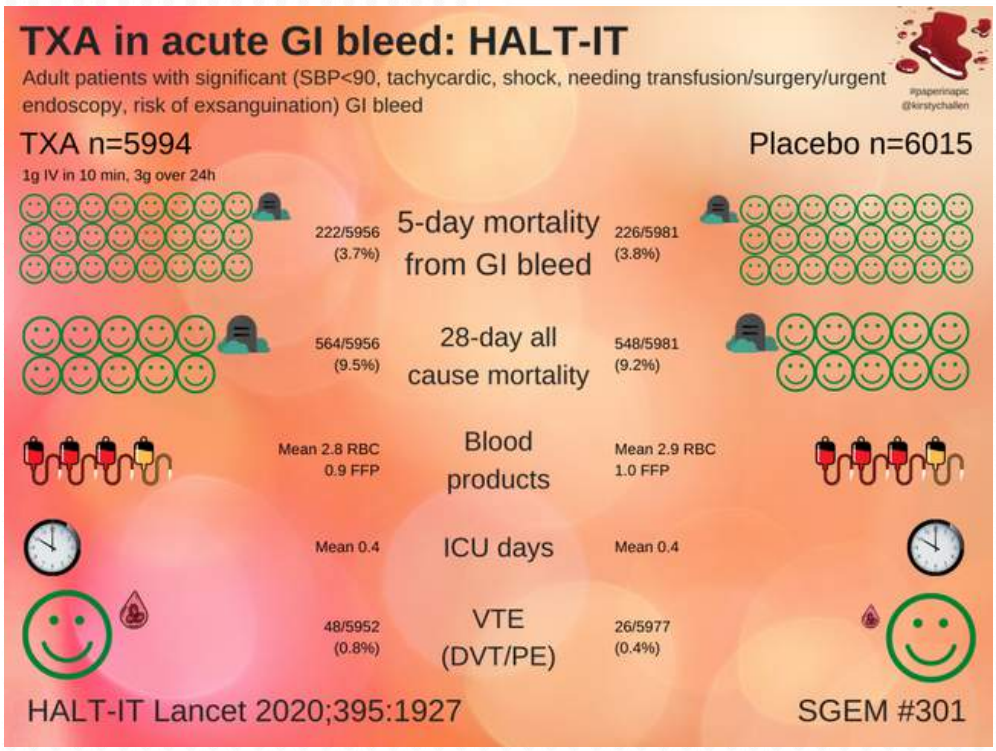
Case Resolution: You decide not to give TXA based on the results of HALT-IT. You continue to resuscitate the patient and organize for urgent endoscopy. He has two esophageal varices that are successfully ligated.

Episode End Notes

Other FOAMed:

- First10EM – TXA for GI bleeds: No benefit (The HALT-IT trial)
- The Bottom Line – HALT-IT
- REBEL EM – The HALT-IT Trial: TXA in Acute GI Bleeds
- St. Emlyn's – Halt! It's not time for TXA! Or is it? HALT-IT results at St Emlyn's





302

WE DIDN'T START THE FIRE BUT CAN ANTACID MONOTHERAPY STOP THE FIRE?

Clinical Question:

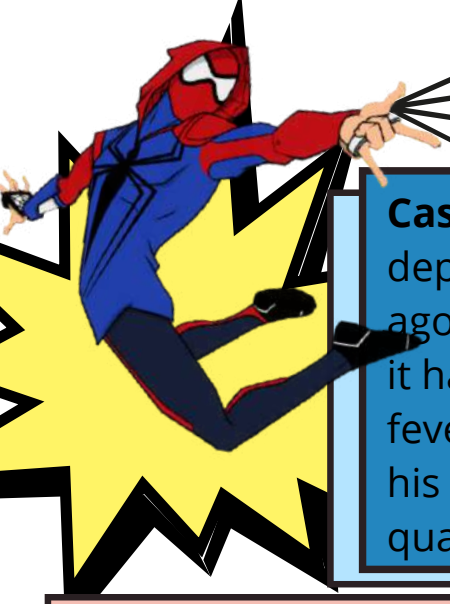
Is antacid monotherapy more effective in relieving epigastric pain than in combination with lidocaine?

Bottom Line:

Consider using antacid monotherapy in place of lidocaine/anatacid combination therapy for patients with dyspepsia.

Guest:

Dr. Chris Bond is an emergency medicine physician in Calgary. He is also an avid FOAM supporter/producer through various online outlets including TheSGEM.



Case Overview

Case: A 34-year-old male presents to the emergency department with burning epigastric pain after eating two hours ago. He says he gets this from time to time but this is the worst it has ever been. He denies chest pain, shortness of breath, fever and vomiting. His vital signs are within normal limits and his abdominal exam reveals mild epigastric and left upper quadrant tenderness with no peritonitis.

Background: Patients presenting to emergency departments (EDs) with epigastric pain are typically treated with an antacid, either alone or combined with other medications. Such medications include viscous lidocaine, an antihistamine, a proton pump inhibitor, or an anticholinergic (1,2). In Canada we often use an antacid plus viscous lidocaine referred to as a “Pink Lady”. This is different than the alcoholic cocktail called a Pink Lady. In the US, combination treatment is often called a “GI Cocktail”.

There are mixed results from studies with varying methodological quality looking at acute dyspepsia management in the ED. One single-blind study comparing 30 mL of antacid with or without 15 mL of viscous lidocaine found the addition of lidocaine significantly increased pain relief, decreasing patient pain score by 40 mm compared to 9 mm with antacid monotherapy (3). Another single-blind RCT comparing antacid plus either benzocaine solution or viscous lidocaine found no statistical difference between the two interventions, however, there was no antacid monotherapy group (4).

A larger, double-blind RCT of 113 patients compared 30 mL of antacid monotherapy, antacid with 10 mL of an anticholinergic, and antacid with anticholinergic and 10 mL of 2% viscous lidocaine. This study found all treatments had clinical efficacy and there was no statistical difference in pain relief between the three treatment groups. The conclusion from Berman et al was to recommend antacid monotherapy (5).

Reference: Warren et al. Antacid monotherapy is more effective in relieving epigastric pain than in combination with lidocaine. A randomized double-blind clinical trial. AEM Sept 2020.

Population: Adult patients with epigastric pain or dyspepsia presenting to the emergency department.

Excluded: Patients unable to consent or under 18 years of age.

Intervention:

- Arm 1 (Viscous): Received 10 mL oral lidocaine 2% viscous gel plus 10 mL antacid (traditional antacid/lidocaine mixture)

Comparison:

- **Arm 2 (Solution):** Received 10 mL lidocaine 2% solution plus 10 mL antacid
- **Arm 3 (Antacid):** Received 20 mL antacid alone

Outcome:

- **Primary Outcome:** Change in pain scores on 100mm visual analog scale (VAS) at 30 minutes after treatment.
- **Secondary Outcomes:** Medication palatability (taste, bitterness, texture, and overall acceptability) using a VAS, change in pain score 60 minutes post administration and adverse events.

This is an SGEMHOP episode which means we have the lead author on the show, Dr. Jaimee Warren. She is a first-year doctor at the Royal Melbourne Hospital and an aspiring emergency and retrieval physician. She hopes to one day work in rural and extreme environments.

Authors' Conclusions

"A 20 mL dose of antacid alone is no different in analgesic efficacy than a 20 mL mixture of antacid and lidocaine (viscous or solution). Antacid monotherapy was more palatable and acceptable to patients. A change in practice is therefore recommended to cease adding lidocaine to antacid for management of dyspepsia and epigastric pain in the ED."

Quality Checklist for Randomized Clinical Trials

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- ☑ 2. The teams were adequately randomized.
- ☑ 3. The randomization process was concealed.
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- ☒ 5. The study teams were recruited consecutively (i.e. no selection bias).
- ? 6. The teams in both groups were similar with respect to prognostic factors.
- ☒ 7. All participants (patients, clinicians, outcome assessors) were unaware of group allocation.
- ☑ 8. All groups were treated equally except for the intervention.
- ☑ 9. Follow-up was complete (i.e. at least 80% for both groups).
- ☑ 10. All patient-important outcomes were considered.
- ☑ 11. The treatment effect was large enough and precise enough to be clinically significant.

Case Outcomes

Key Results:
The trial enrolled 94 patients and 89 could be analyzed (30 viscous, 31 solution and 28 antacid group). The mean age was in the early 40's, with around 2/3 female and 80% of patients were discharged with a gastrointestinal diagnosis.

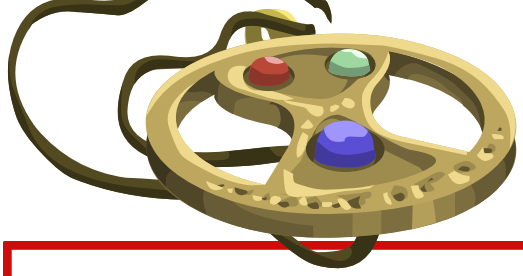
All three treatments (viscous, solution, or antacid monotherapy) worked and there was no statistical difference between groups.

- **Primary Outcome:** The lidocaine solution with antacid and antacid monotherapy provided clinically important (>13 mm) analgesia at 30 minutes (17mm and 20mm), viscous lidocaine with antacid did not (9mm). However, this still did not result in a statistically significant difference between treatments.

- **Secondary Outcomes:** At 60 minutes, all treatment groups (viscous, solution and antacid monotherapy) experienced additional pain relief. The change in median pain scores was clinically significant (>13 mm) for all three arms (21mm, 26mm, and 32mm).

The most frequent adverse effect was oral numbness (lidocaine viscous 20% and lidocaine solution 26%). Two patients in the viscous arm reported dizziness and tiredness (7%), and four patients in the solution arm reported cough, nausea, and dizziness (13%). One patient in the antacid arm reported a dry mouth (4%).

Participants found antacid monotherapy to be the most palatable solution, with statistically significant differences in taste, bitterness, and overall acceptability.



Time to Talk Nerdy

Listen to the podcast on iTunes to hear Jaimee's responses to our ten nerdy questions.

1. Inclusion Criteria: Patients were enrolled prospectively based on the clinician providing an antacid therapy. This resulted in a large group of patients having non-GI causes of pain. Why not enroll patients for whom the final diagnosis was dyspepsia or epigastric pain after ED workup?

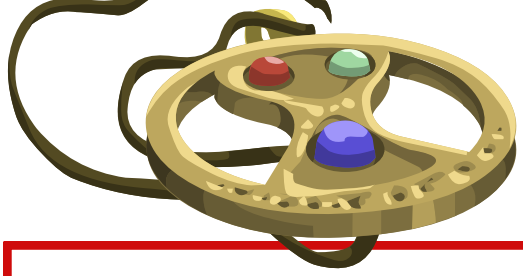
2. Selection Bias: Why were patients that presented overnight excluded from enrolment (funding for research staff 24/7)? Are these patients potentially different (eg. more severe presentations of alcohol related gastritis, large meals for dinner followed by lying down or other reasons)?

3. Unbalanced Groups: In Table 1, it appears that more patients in the lidocaine arms had prior proton pump inhibitor (PPI) use and more prior upper GI related diagnoses (eg. Peptic ulcer disease/gastritis/gastroesophageal reflux disease). It also appears the viscous group received more rescue analgesics in the ED. Can you confirm these are all non-statistically significant differences between groups as the p-values are not documented?

4. Blinding of Staff: The solutions were not made to look identical. This could have unblinded the trial to the nursing staff. Do you think that could have impacted the results and did you consider asking the nurses which group they felt the participant was randomized?

5. Placebo Effect: The patients may also have been unblinded and susceptible to a placebo effect. Lidocaine has a bitter taste and can cause oral numbness. It has been demonstrated that bitter tasting treatments can increase the placebo effect.

- Wright et al. If it Tastes Bad it Must Be Good: Consumer Naïve Theories and the Marketing Placebo Effect. Intern. J. of Research in Marketing 2013



Time to Talk Nerdy

- Kihlstrom. Placebo: Feeling Better, Getting Better, and the Problems of Mind and Body. Mcgill J Med. 2008
- Evans FJ. The placebo response in pain reduction. In: Bonica JJ, editor. Advances in Neurology. New York: Raven; 1974

6. Diagnosis: Do you think that the effectiveness of antacid monotherapy is the same whether the diagnosis is dyspepsia vs. GERD vs. gastritis vs. PUD?

7. Primary Outcome: Your primary outcome was a change in 100mm VAS at 30 min. While that is an important patient-oriented outcome (POO) what about length of relief? Your secondary outcome was 60min. What about a longer time frame or return to ED within 24hrs?

8. Other Comparisons: Can you comment on how use of these medications compares with H2 receptor antagonists and PPIs in terms of efficacy for treating dyspepsia and epigastric pain in the ED?

9. Down Under: This was a single centre study conducted in Melbourne, Australia. Patient expectations can be different depending on the country. What are your thoughts to the external validity to other countries (UK, USA, Canada, Europe, etc)? Do you think you would find similar results?

10. Anything Else: Is there anything else you'd like to comment on about your paper that we have not asked, or you think is important for the SGEMers to know?

Comment on Authors' Conclusion Compared to SGEM Conclusion: We generally agree with the authors' conclusions but would say that a change in practice should be "considered" rather than "recommended".

Clinical Application: Give antacid monotherapy for dyspepsia in the emergency department.

What Do I Tell My Patient? We have given you some medication to treat your stomach pain. This is usually related to eating and sometimes to reflux or in rare cases an ulcer. If you are having recurrent pain you can use over the counter antacid medications. If it is persistent and frequent, you may need to see your family doctor to start a daily medication and perhaps have more investigations.

Case Resolution: You give your patient 20 mL of antacid and his epigastric pain improves. You suggest he try antacids in the future if he has recurrent post prandial pain and follow-up with his family physician.

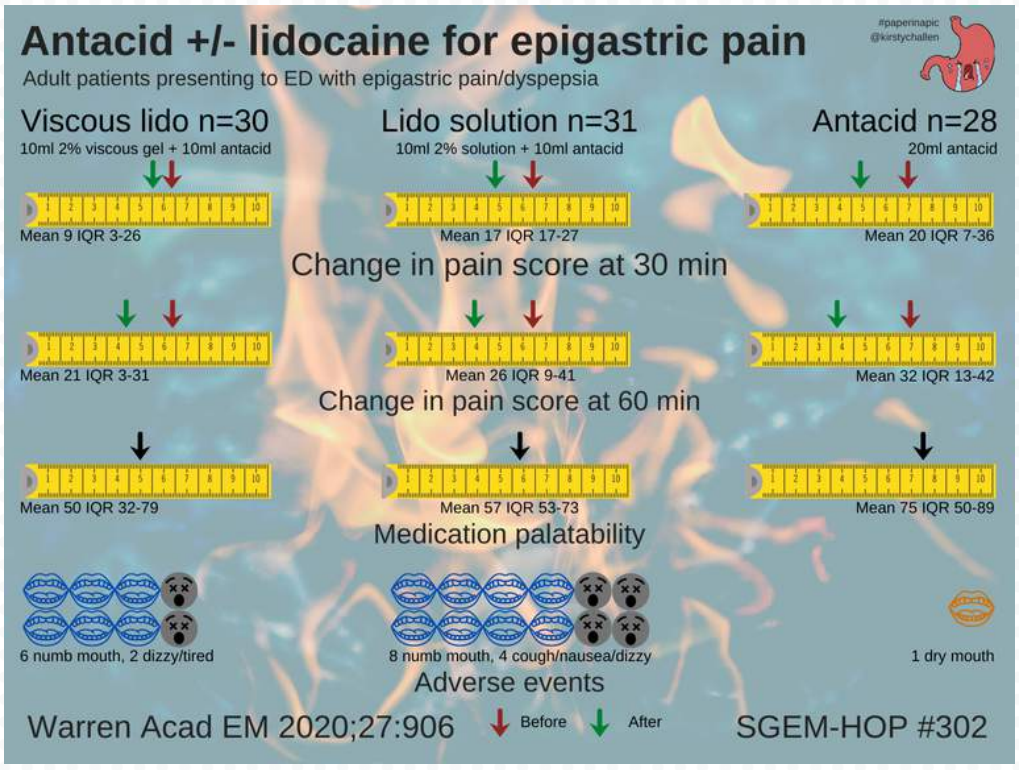
Episode End Notes

What do you use to treat patients presenting to the ED with epigastric pain? #EBM #FOAMed #SGEMHOP onlinelibrary.wiley.com/doi/10.1111/ac... @socmobem @SAEMonline @AcademicEmerMed

Antacid Alone	**51.1%**
Antacid+Lodocaine Viscus	25.2%
Antacid+Lidocaine Sol'n	10.4%
Other (please provide)	13.3%

135 votes · Final results

8:21 AM · Sep 29, 2020 · Twitter Web App



303

TWO CAN MAKE IT - LESS LIKELY TO HAVE ANOTHER STROKE BUT MORE LIKELY TO HAVE A BLEED (THALES TRIAL)

Clinical Question:

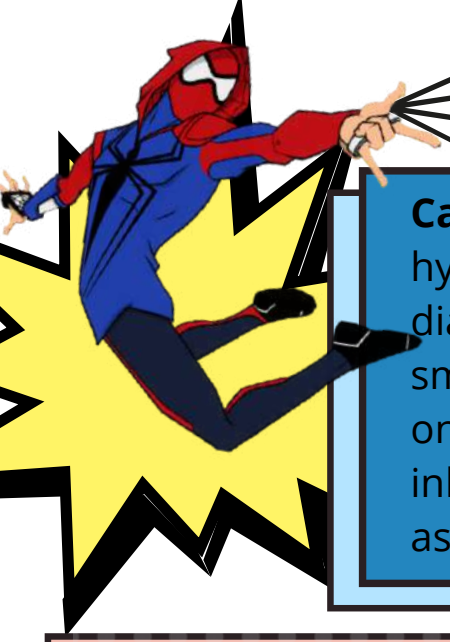
Is the combination of ticagrelor and aspirin superior to aspirin alone in reducing the risk of subsequent stroke or death among patients with acute non-cardioembolic cerebral ischemia?

Bottom Line:

Ticagrelor in combination with aspirin cannot be routinely recommended at this time. The decrease in subsequent strokes comes at a cost of increased serious bleeding and no increase in a good neurologic outcome. A risk assessment and shared decision making is encouraged.

Guest:

Dr.Barbra Backus is an emergency physician at the Emergency Department of the Erasmus University Medical Center in Rotterdam, the Netherlands. She is the creator of the HEART Score and an enthusiastic researcher.



Case Overview

Case: A 65-year-old man with a history of well controlled hypertension presents to the emergency department and is diagnosed with a mild stroke (NIHSS score 3). He is a non-smoker, not diabetic and has never had a stroke before. The only medicine he takes is an angiotensin converting enzyme inhibitor. You are wondering if he should be discharged on just aspirin or aspirin plus another antiplatelet agent like ticagrelor.

Background: Acute ischemic strokes are the leading cause of disability in our society and the third most common cause of death.

Aspirin has been used to prevent a subsequent stroke in patients who suffered an acute ischemic stroke (AIS) or transient ischemic attack (TIA), which occur in approximately 5-10% of patients in the first few months after their primary event.

Trials have shown mixed results with the combination of aspirin with clopidogrel in this population. SGEM#24 reviewed a randomized controlled trial (RCT) of aspirin vs. aspirin + clopidogrel in patients with recent symptomatic lacunar infarcts identified by MRI (Benavente et al NEJM 2012). Adding clopidogrel to aspirin did not reduce recurrent strokes but did increase risk of bleed and death. The study was stopped early due to harm and lack of efficacy.

An RCT done in China on patients with minor strokes or TIAs who were treated within 24 hours after the onset of symptoms showed that aspirin plus clopidogrel is superior to aspirin alone for reducing the risk of stroke in the first 90 days and does not increase the risk of hemorrhage (Wang et al NEJM 2013).

A third RCT assigned patients with minor ischemic stroke or high-risk TIA to ASA alone or the combination of both aspirin and clopidogrel. This trial was also stopped early because of lower risk of major ischemic events but higher risk of major hemorrhage with the combination therapy compared to aspirin alone (Johnston et al NEJM 2018).

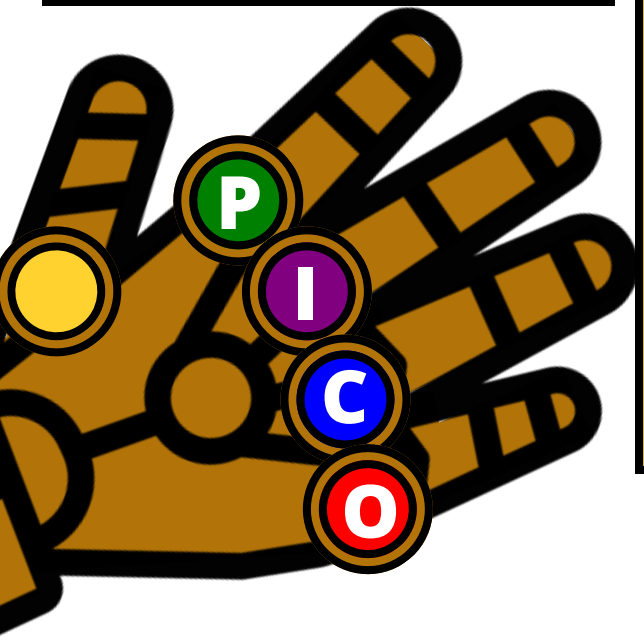
As an antiplatelet agent that blocks the P2Y12 receptor, clopidogrel requires hepatic conversion to its active form through a pathway that is ineffective in 25% of white and 60% of Asian patients; efficacy is therefore uncertain in these patients (Pan et al Circulation 2017).

Ticagrelor is a direct-acting antiplatelet agent that does not depend on metabolic activation. A trial of ticagrelor alone did not show a benefit over aspirin in preventing subsequent cardiovascular events (Johnston et al NEJM 2016). The effect of the combination of ticagrelor and aspirin on prevention of stroke has not been well studied.

Reference: Claiborne Johnston S et al. Ticagrelor and Aspirin or Aspirin Alone in Acute Ischemic Stroke or TIA. NEJM July 2020

Population: Patients 40 years and older who experience a mild-to-moderate acute noncardioembolic ischemic stroke (NIHSS score of 5 or less), or high-risk TIA (ABCD2>5) or symptomatic intracranial or extracranial arterial stenosis (>50% lumen narrowing accounting for the TIA)

Intervention: 30-day regimen of ticagrelor (180-mg loading dose followed by 90 mg twice daily) plus aspirin (300 to 325 mg on the first day followed by 75 to 100 mg daily).



Excluded: Thrombolysis or EVT was planned <24 hours before randomization or if there was planned use of anticoagulation or specific anti-platelet therapy other than ASA. Patients were also not eligible if they had "hypersensitivity to ticagrelor or ASA, a history of atrial fibrillation or ventricular aneurysm or a suspicion of a cardioembolic cause of the TIA or stroke, planned carotid endarterectomy that required discontinuation of the trial medication within 3 days after randomization, a known bleeding diathesis or coagulation disorder, a history of intracerebral hemorrhage, gastrointestinal bleeding within the past 6 months, or major surgery within 30 days before randomization."

Comparison: 30-day regimen of matching placebo plus aspirin.

Outcomes:

- **Primary Outcome:** Composite of stroke or death within 30 days.
- **Secondary Outcomes:** First subsequent ischemic stroke, incidence of disability within 30 days and adverse events.

Authors' Conclusions

"Among patients with a mild-to-moderate acute noncardioembolic ischemic stroke (NIHSS score ≤5) or TIA who were not undergoing intravenous or endovascular thrombolysis, the risk of the composite of stroke or death within 30 days was lower with ticagrelor–aspirin than with aspirin alone, but the incidence of disability did not differ significantly between the two groups. Severe bleeding was more frequent with ticagrelor."

Quality Checklist for Randomized Clinical Trials

- [?] 1. The study population included or focused on those in the emergency department.
- [✓] 2. The teams were adequately randomized.
- [✓] 3. The randomization process was concealed.
- [✓] 4. The teams were analyzed in the groups to which they were randomized.
- [?] 5. The study teams were recruited consecutively (i.e. no selection bias).
- [✓] 6. The teams in both groups were similar with respect to prognostic factors.
- [✓] 7. All participants (patients, clinicians, outcome assessors) were unaware of group allocation.
- [✓] 8. All groups were treated equally except for the intervention.
- [✓] 9. Follow-up was complete (i.e. at least 80% for both groups).
- [✗] 10. All patient-important outcomes were considered.
- [✓] 11. The treatment effect was large enough and precise enough to be clinically significant.

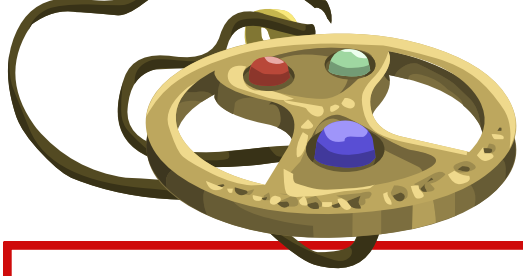
Case Outcomes

Key Results:
11,016 patients underwent randomization (5,523 to ticagrelor-aspirin and 5,493 to placebo plus aspirin). The average participant was 65 years old, more than 60% were male, more than 75% had a history of hypertension and 91% presented with ischemic strokes. Thirteen percent of the patients were taking aspirin before the initial index stroke or TIA.

Less strokes and more bleeds in the combination group with no statistical difference between the two groups for a good neurologic outcome.

- **Primary Outcome:** Stroke or death within 30 days
  - 5% in combo group vs. 6.6% in aspirin alone (HR, 0.83; 95% CI, 0.71 to 0.96) p=0.02

- **Secondary Outcomes:**
  - Subsequent ischemic stroke 5.0% vs. 6.3% (HR, 0.79; 95% CI, 0.68 to 0.93) P=0.004
  - Incidence of disability was not statistically different 23.8 vs. 24.1% (P=0.61)
  - Severe bleeding was greater in the combo group: 5% vs. 0.1% in the aspirin group (P=0.001)



Time to Talk Nerdy

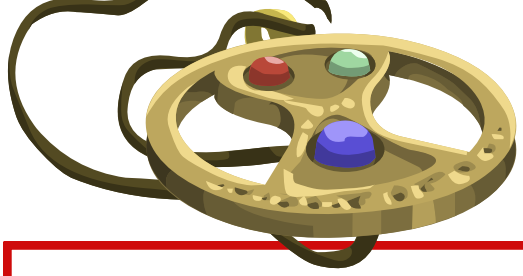
1) Industry Funded: This trial was sponsored by the maker of ticagrelor and multiple authors reported financial conflicts of interest. A Cochrane SRMA has reported that industry funded studies have more favorable efficacy results and conclusions compared to non-industry funded studies. These differences cannot be explained by standard risk of bias assessment tools (Lundh et al 2017).

2) Low AIS and High TIAs: These are a very select group of patients with many exclusion criteria. This makes it difficult to apply the results to all low AIS and high-risk TIA patients.

3) Composite Outcome: There can be only one...primary outcome. Their primary outcome was stroke or death within 30 days. While they did find a statistical difference between the combination therapy and aspirin alone, the difference was driven by stroke. There was no statistical difference in death between the two groups 6% vs 0.5% (HR 1.33, 95% CI, 0.81 to 2.19).

4) Relative vs. Absolute Reduction: They demonstrated a 17% relative reduction in their composite primary outcome or a 1.1% absolute reduction. This gives an NNTB of 90 for a disease-oriented outcome (DOO) of stroke because there was no difference in death or disability which are patient oriented outcomes (POO). For serious adverse events there as a 500% relative increase in severe bleeding which as only a 0.4% absolute increase. This gives a NNTH of 250 for a POO.

5) Length of Treatment: They only looked at 30 days for their outcomes. Patients with small strokes or high risk TIAs are going to be on antiplatelet drugs indefinitely. It would have been helpful to see longer term outcomes of at least 90 days like many stroke studies or even better years.



Time to Talk Nerdy

Questions include: Does the efficacy continue? Would mortality benefit become statistically significant? Would the severe adverse event rate increase with time? It is interesting that the premature discontinuation rate was four times higher in the combination group (2.6% vs 0.6%) due to bleeding. This does not address the additional cost of ticagrelor ($360/month vs $1/month).

Comment on Authors' Conclusion Compared to SGEM Conclusion: We agree with the authors' conclusions.

Clinical Application: With antiplatelet drugs and anticoagulants there is always a trade-off. While adding another antiplatelet drug to aspirin has the potential to increase efficacy it also increases the potential harm. I will be more likely to prescribe dual therapy for patients who are at high risk of coronary artery disease (CAD) and low bleeding risk while less like to prescribe dual therapy for patients at low risk of CAD and high risk of bleeding.

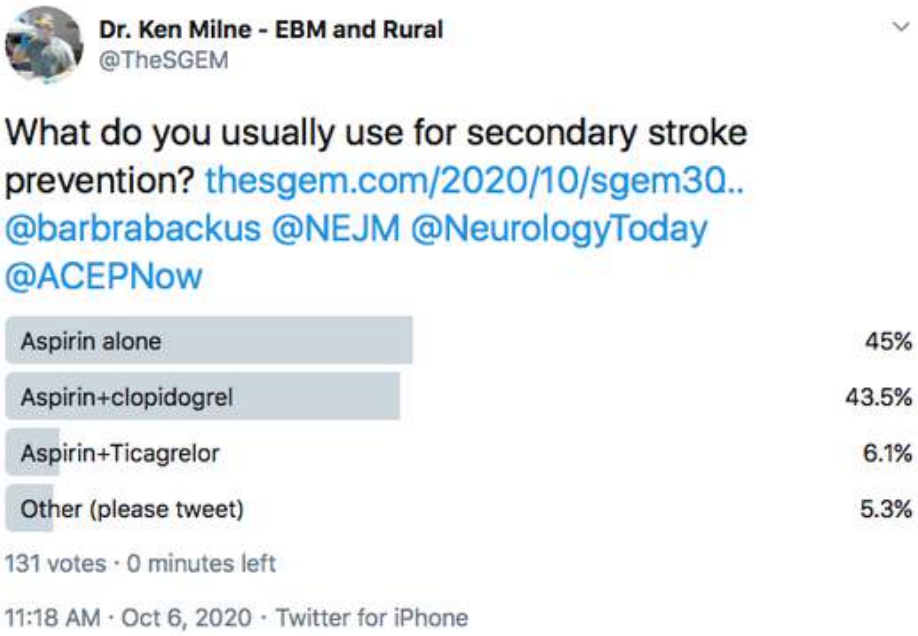
What Do I Tell My Patient? You have had a mild stroke. I would recommend taking low dose of aspirin a day. This can lower your risk of having another stroke. We could also add another drug. It is can lower your risk of having another stroke even more. However, it can increase your risk of having a serious bleed. The combination of the two drugs has not been shown to improve your function and is more expensive.

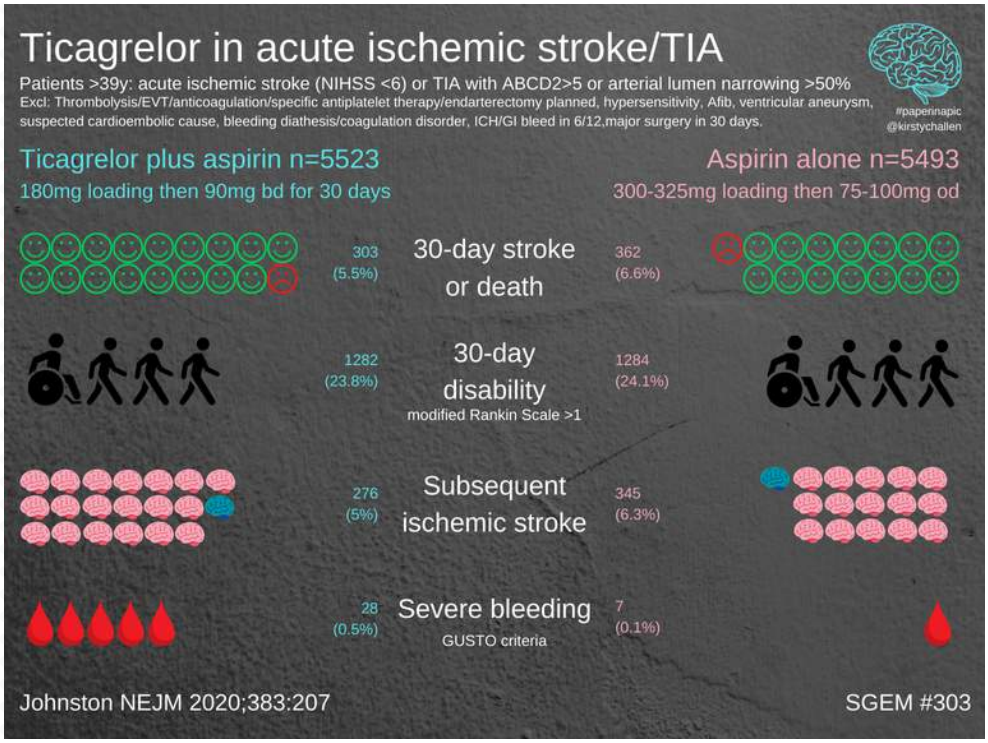
Case Resolution: You discharge the patient home with aspirin alone with an Urgent TIA/Stroke Clinic follow-up in the next 24 to 48 hours.

Episode End Notes

Other FOAMed:

- REBEL EM – The THALES Trial: Ticagrelor and Aspirin vs Aspirin Alone in Acute Ischemic Stroke or TIA



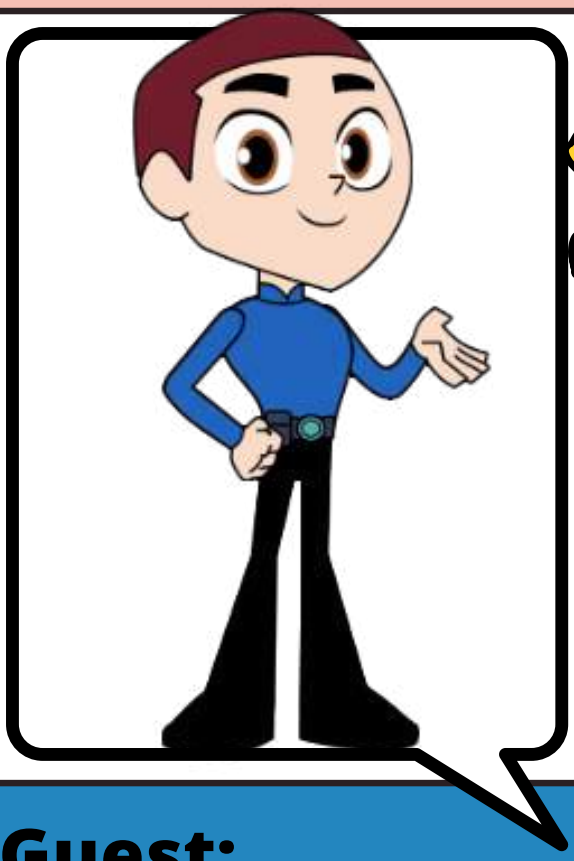


304

TREATING ACUTE LOW BACK PAIN - IT'S TRICKY, TRICKY, TRICKY

Clinical Question:

Is the addition of acetaminophen to ibuprofen better than ibuprofen alone in treating ED patients with acute, non-traumatic, non-radicular low back pain?

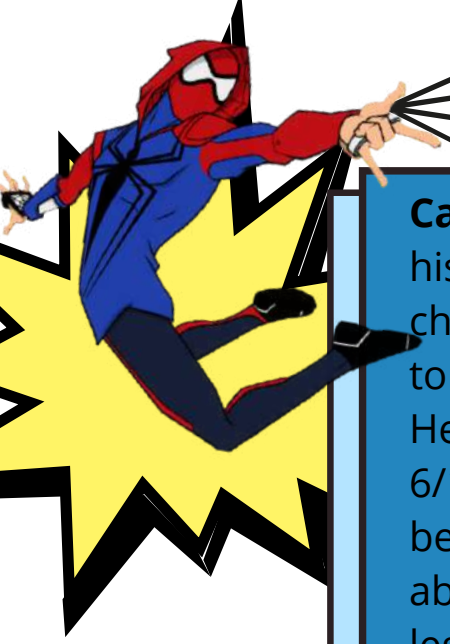


Bottom Line:

We cannot recommend the addition of acetaminophen to ibuprofen for adult patients presenting to the ED with acute, non-traumatic, non-radicular low back pain.

Guest:

Dr. Sergey Motov is an Emergency Physician in the Department of Emergency Medicine, Maimonides Medical Center in New York City. He is also one of the world's leading researchers on pain management in the emergency department, specifically the use of ketamine. His twitter handle is @PainFreeED.



Case Overview

Case: A 41-year-old man without a significant past medical history presents to the emergency department (ED) with a chief complaint of lower back pain that started 48 hours prior to the ED visits after attempting to move a couch in his house. He describes the pain as sharp, constant, non-radiating, and 6/10 in intensity. Pain gets worse with movement and minimal bending. The pain is limiting his usual activities included his ability to go to work. He denies weakness or numbness of the legs as well as bowel or bladder dysfunctions. You perform a physical exam and note prominent tender area to palpation at the right lumbar region. You explain to the patient the most likely diagnosis is a muscle strain. Your usual approach is to treat this type of case scenario with Ibuprofen. The patient asked you if Ibuprofen alone will be strong enough to control his pain.

Background: Pain is one of the most frequent reasons to attend an ED. Low back pain (LBP) is responsible for 2.3% of all ED visits resulting in 2.6 million visits each year in the USA (Friedman et al Spine 2010). We have covered back pain a number of times on the SGEM.

- SGEM#87: Let Your Back Bone Slide (Paracetamol for Low-Back Pain)
- SGEM#173: Diazepam Won't Get Back Pain Down
- SGEM#240: I Can't Get No Satisfaction for My Chronic Non-Cancer Pain

The SGEM bottom line from SGEM#240 was:
There appears to be no long-term analgesics benefits from prescribing opioids for chronic non-cancer pain (nociceptive and neuropathic). However, their use is associated with increased adverse events.

The American College of Emergency Physicians (ACEP) has updated their clinical policy on prescribing opioids for adult ED patients. There are no Level A recommendations, one Level B recommendation and multiple Level C recommendations (ACEP June 2020)

- In adult patients experiencing opioid withdrawal, is emergency department-administered buprenorphine as effective for the management of opioid withdrawal compared with alternative management strategies?
    - **Level B Recommendations:** When possible, treat opioid withdrawal in the emergency department with buprenorphine or methadone as a more effective option compared with nonopioid-based management strategies such as the combination of α2-adrenergic agonists and antiemetics

Many other pharmaceutical treatments besides opioids have been tried to address acute LBP pain with limited success. These include: acetaminophen (Williams et al Lancet 2014), muscle relaxants (Friedman et al JAMA 2015), NSAIDs (Machado et al Ann Rheum Dis 2017), steroids (Balakrishnamoorthy et al Emerg Med J 2014) and benzodiazepines (Friedman et al Ann Emerg Med 2017).

Pain outcomes for patients with LBP are generally poor; One week after an ED visit in an unselected LBP population, 70% of patients report persistent back pain–related functional impairment and 69% report continued analgesic use (Friedman et al AEM 2012).

There are a number of non-pharmaceutical treatment modalities that have also been tried to treat low back pain. They include: CBT and mindfulness (Cherkin et al JAMA 2016), chiropractic (Paige et al JAMA 2017), physical therapy (Paolucci et al J Pain Research 2018) and acupuncture (Colquhoun and Novella Anesthesia and Analgesia 2013). None of these other treatments has high-quality evidence supporting their use.

Nonsteroidal anti-inflammatory drugs (NSAIDs) are recommended as first-line medication therapy for patients with acute LBP. Acetaminophen is often used for acute LBP, although it is unlikely to be effective when used as monotherapy. Whether or not combining an NSAID with acetaminophen can improve patient outcomes is unknown.

Reference: Friedman et al. Ibuprofen Plus Acetaminophen Versus Ibuprofen Alone for Acute Low Back Pain: An Emergency Department-based Randomized Study. AEM 2020.

Population: Adults aged 21 to 69 years who presented to the ED primarily for management of acute non-traumatic, non-radicular, musculoskeletal LBP with Roland Morris Disability Questionnaire (RMDQ)score of >5.

- The RMDQ is a 24-item questionnaire commonly used to measure LBP and related functional impairment. The scale goes from 0 (no impairment) to 24 (maximum impairment).

Intervention: Combination ofibuprofen 600mg plus acetaminophen 500 to 1000n orally, every 6 hours.

Exclusions:
"non- musculoskeletal etiology of low back, such as urinary tract infection or influenza-like illness; radicular pain, defined as pain radiating below the gluteal folds in a dermatomal distribution; pain duration > 2 weeks (336 hours); or a baseline LBP frequency of once per month or more frequently. Patients with substantial, direct trauma to the back within the previous month were excluded as were those who were unavailable for follow-up, those who were pregnant or breastfeeding, patients with a chronic pain syndrome defined as use of any analgesic medication on a daily or near-daily basis, and those who were allergic to or intolerant of the investigational medications."

Comparison: Monotherapy of Ibuprofen 600mg plus placebo,orally, every 6 hours.

Outcomes:

- **Primary Outcome:** Improvement of LBP on the RMDQ between ED discharge and the 7-day telephone follow-up.

- **Secondary Outcomes:** 1 week and 48 hours after ED discharge were as follows: 1) participants' worst LBP during the previous 24 hours, using a four-item ordinal scale (severe, moderate, mild, or none); 2) the frequency of LBP during the previous 24 hours using a five-item scale (not at all, rarely, sometimes, usually, always); 3) the frequency of any analgesic or LBP medication use during the previous 24 hours; 4) satisfaction with treatment, as measured by response to the question, "The next time you have back pain, do you want to take the same medications you've been taking this past week?"; 5) the day post–ED discharge the participant was able to return to usual activities; and 6) the frequency of visits to any health care provider.

Authors' Conclusions

"Among ED patients with acute, nontraumatic, non-radicular LBP, adding acetaminophen to ibuprofen does not improve outcomes within 1 week."

Quality Checklist for Randomized Clinical Trials

- [x] 1. The study population included or focused on those in the emergency department.
- [x] 2. The teams were adequately randomized.
- [x] 3. The randomization process was concealed.
- [x] 4. The teams were analyzed in the groups to which they were randomized.
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- [x] 8. All groups were treated equally except for the intervention.
- [x] 9. Follow-up was complete (i.e. at least 80% for both groups).
- [x] 10. All patient-important outcomes were considered.
- [x] 11. The treatment effect was large enough and precise enough to be clinically significant.

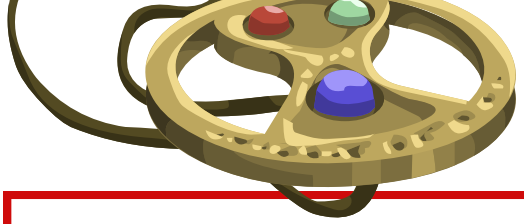
Case Outcomes

Key Results:
They screened 605 patients for eligibility and were able to randomize 120. The mean age was 41 years, 52% were men, mean duration of symptoms was 48 hours and 80% were working at least 30 hours a week.

No statistical difference between ibuprofen plus acetaminophen and ibuprofen alone in back pain improvement at one week.

- **Primary Outcome:** Mean improvement of RMDQ (+/-SD) at 1 week
  - Combo 11.1 (+/- 10.7) vs Mono 11.9 (+/- 9.7)
  - Between group difference 0.8 (95% CI -3.0 to 4.7)

- **Secondary Outcomes:**
  - Participants' worst LBP during the previous 24 hours, using a four-item ordinal scale (severe, moderate, mild, or none): No statistical difference
  - Frequency of LBP during the previous 24 hours using a five-item scale (not at all, rarely, sometimes, usually, always): More frequent in combination group
  - Frequency of any analgesic or LBP medication use during the previous 24 hours: No statistical difference
  - Satisfaction with treatment, as measured by response to the question, "The next time you have back pain, do you want to take the same medications you've been taking this past week?" No statistical difference
  - How many days post–ED discharge the participant was able to return to usual activities: No statistical difference
  - Frequency of visits to any health care provider: No statistical difference



Time to Talk Nerdy

1. Ibuprofen Dosing: They used 600mg of ibuprofen in this trial rather than 400mg. Unlike opioid analgesics, NSAID dosing is limited by their "analgesic ceiling", meaning there is a dose-analgesic response. Above certain doses, NSAIDs produce more side effects or harms without providing additional analgesia. Our team has published evidence supporting this on both ibuprofen (Motov et al Ann Emerg Med 2019) and ketorolac (Motov et al Ann Emerg Med 2017). The ketorolac paper was covered on SGEM#175.

2. External Validity: This study was conducted in two urban EDs serving a socioeconomically depressed population. Socioeconomic factors have been shown to be associated with an increased risk of pain (Poleshuckand Green Pain 2008). It is unclear if this data could be applied to other populations.

3. Exclusion Criteria: Patients were excluded if they had LBP greater than two weeks. The mean duration of LBP varied from 12 to 96h prior to enrollment in the study. We could not find if patients were patients taking any medications prior to enrollment. They also listed a number of other exclusion criteria including patients who were "intolerant of the investigational medications." The authors did not explicitly state if patients were excluded if they had renal/hepatic insufficiency or co-medications such as coumadin, aspirin, direct oral anti-coagulants, etc.

4 Concordance: The loss to follow-up was less than the quality indicator of 20%. However, more than one-third of both groups did not take their study medication as instructed 24 hours prior to the 1-week phone call. Similarly, about one-fifth of patients did not take their study medications as instructed 24 hours prior to 48h phone call.

5. Other Medication: It was not stated in the manuscript that patients were told/advised not to take any other medications other than those used in the trial. While this would be pragmatic, it could mask any difference between the ibuprofen plus acetaminophen compared to the ibuprofen alone group.

Comment on Authors' Conclusion Compared to SGEM Conclusion: We agree with the authors' conclusion

Clinical Application: There still appears to be no great treatment options for patients presenting with acute low back pain. Evidence for individual pharmaceutical therapies are limited and this trial provides evidence that a combination therapy of acetaminophen and ibuprofen is not better than ibuprofen alone. This agrees with the previous SGEM episode looking at a combination of diazepam and naproxen (SGEM#173). We also don't have high-quality evidence that non-pharmacological treatments work well.

One final thing that is important is to discuss expectations with the patient. They need to know that their pain might not be completely relieved in the ED. The goal should be about about limiting suffering, not eliminating pain. Most patients will have persistent symptoms a week after presentation and many will have continued pain and functional impairment months after symptom onset (Itz et al 2013 , Donelson et al 2012 and Costa et al 2012). We need to be supportive and realistic when discussing the natural history of acute low back pain with patients.

What Do I Tell My Patient? You have a muscle strain in your back. This is a very common problem and can be very painful. Ibuprofen can help lower your pain, but it is unlikely get rid of your pain completely. Adding medications like acetaminophen or even a benzodiazepam has not shown to be more effective. People have tried many other medications and non-medications to try and help. One thing we know is that opioids are not usually recommended. Unfortunately, you may have pain over the next few weeks or months. Try to stay active and, if your pain is getting worse, you can't function, or are otherwise worried please return to the ED for re-assessment.

Case Resolution: You recommend ibuprofen 400mg as a first line agent and try to set reasonable expectations.

Episode End Notes

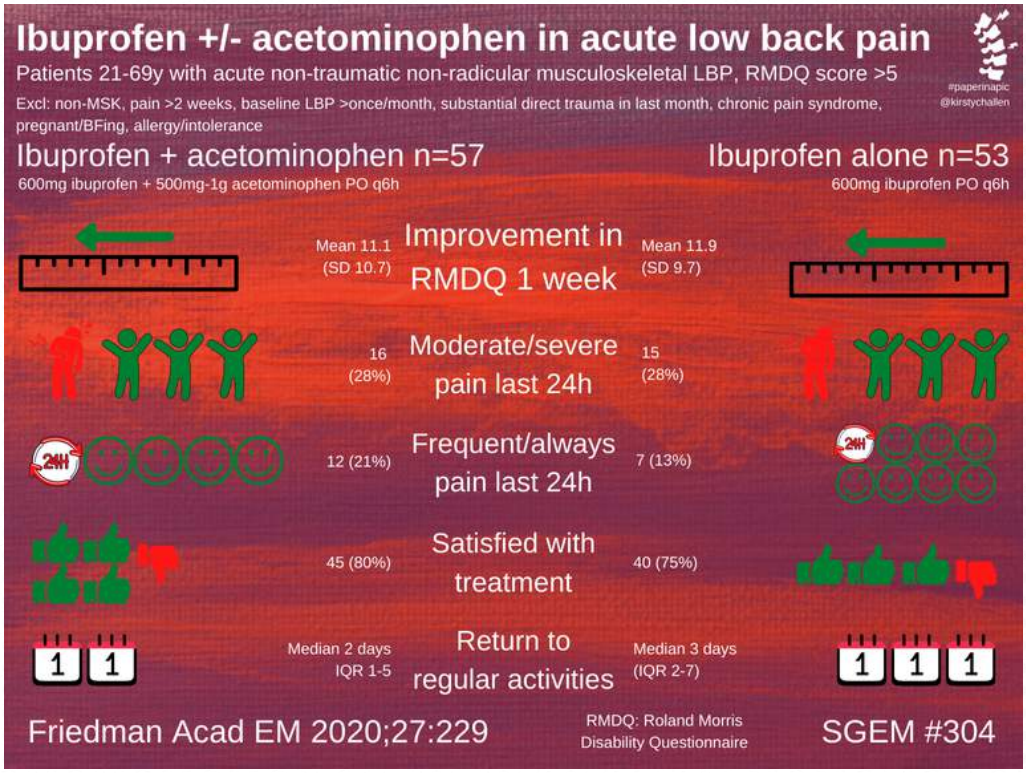
Dr. Ken Milne - EBM and Rural
@TheSGEM

What is your usual first line treatment for ED patients with acute, non-traumatic, non-radicular low back pain? thesgem.com/2020/10/sgem30... @painfreeED @Rick_Pescatore @meganranney @AliRaja_MD @KirstyChallen

Acetaminophen	11.1%
Ibuprofen	34.7%
Combo of both	**47.1%**
Other (please tweet)	7.1%

539 votes · Final results

9:17 AM · Oct 13, 2020 · Twitter Web App



PLAYLIST

SGEM Season#8

The Skeptics' Guide to EM • 4 likes • 44 songs, 2 hr 59 min

#	TITLE	ALBUM	DATE ADDED	
1	Learning To Fly Tom Petty and the Heartbreakers	Into The Great Wide Open	Aug 30, 2020	4:02
2	The Changingman Paul Weller	Stanley Road	Aug 30, 2020	4:02
3	Time of the Season - Mono Version The Zombies	Odessey and Oracle	Aug 30, 2020	3:34
4	Never Gonna Give You Up Rick Astley	Whenever You Need Somebody	Aug 30, 2020	3:33
5	Life in a Northern Town The Dream Academy	The Dream Academy	Aug 30, 2020	4:19
6	pointer sister - (She's Got) The Fever		Aug 30, 2020	6:14
7	Slick Rick - Teacher Teacher (Music Video)		Aug 30, 2020	4:57
8	Blood Pressure Mutemath	Odd Soul (Deluxe Version)	Aug 30, 2020	3:03
9	Back In The U.S.S.R. - Remastered 2009 The Beatles	The Beatles (Remastered)	Aug 30, 2020	2:43
10	With Or Without You - Remastered U2	The Joshua Tree (Super Deluxe)	Aug 30, 2020	4:55
11	Who's Gonna Drive You Home Tonight Bennie Carl	Who's Gonna Drive You Home Tonight	Aug 30, 2020	3:50

SCAN HERE FOR PLAYLIST

12	 9 to 5 Dolly Parton	9 To 5 And Odd Jobs	Aug 30, 2020		2:42
13	I Want a Dog - Pet Shop Boys		Aug 30, 2020		6:17
14	Pink Floyd - Breathe		Aug 30, 2020		3:58
15	That Was A Crazy Game of Poker		Aug 30, 2020		8:42
16	 Behind the Mask Michael Jackson	Michael	Aug 30, 2020		5:01
17	 She Blinded Me With Science Thomas Dolby	Retrospectacle - The Best Of Thomas Dolby	Aug 30, 2020		3:41
18	 True Colors Cyndi Lauper	True Colors	Aug 30, 2020		3:47
▶	 Bloody Well Right Supertramp	Crime Of The Century (Remastered)	Aug 30, 2020	♡	4:32 •••
20	 Jump Van Halen	Best of Volume 1	Aug 30, 2020		3:59
21	 Absolutely Right Five Man Electrical Band	Absolutely Right - The Best Of Five Man E...	Aug 30, 2020		2:18
22	 All About That Bass E Meghan Trainor	Title (Deluxe)	Aug 30, 2020		3:07
23	 Papa's Got A Brand New Bag James Brown	Star Time	Aug 30, 2020		2:08
24	The Isley Brothers This Old Heart Of Mine		Aug 30, 2020		2:50
25	 Do You Really Want To Hurt Me Culture Club	This Time	Aug 30, 2020		4:24
26	 Come Together - Remastered 2009 The Beatles	Abbey Road (Remastered)	Aug 30, 2020		4:19
27	 (No Matter If I'm) Wet or Dry Sesame Street's Chrissy And The Alphabeats	Sesame Street: Sesame Road, Vol. 1	Aug 30, 2020		1:38
28	Cream - Strange Brew		Aug 30, 2020		2:50
29	The Replacements - Seen Your Video (REMAS...		Aug 30, 2020		3:08
30	Ariana Grande - Focus		Aug 30, 2020		3:45
31	 The Living Years Mike & The Mechanics	Living Years	Aug 30, 2020		5:30
32	 Tenth Avenue Freeze-Out Bruce Springsteen	Born To Run	Aug 30, 2020		3:10
33	Focus - Hocus Pocus		Aug 30, 2020		6:42
34	 Take The Money And Run Steve Miller Band	Fly Like An Eagle	Aug 30, 2020		2:50
35	My Buddy (Buddies) - Anne Murray		Aug 30, 2020		4:12
36	 Boogie Wonderland Earth, Wind & Fire, The Emotions	I Am	Aug 30, 2020		4:48
37	Gary Numan - Crash		Aug 30, 2020		3:40

38		Be A Dentist Lisa Daniel, Barbara Jaeson, Peter McNally	Little Shop Of Horrors (Original UK Cast R...	Aug 30, 2020	2:30
39		The Gories - Nitroglycerine		Aug 30, 2020	3:47
40		Graduation (Friends Forever) Vitamin C	Vitamin C	Aug 30, 2020	5:40
41		DeBarge - Rhythm Of The Night (Official Musi...		Aug 30, 2020	3:52
42		New York State of Mind Billy Joel	Turnstiles	Aug 30, 2020	6:02
43		Old Man - 2009 Remaster Neil Young	Harvest (2009 Remaster)	Aug 30, 2020	3:22
44		Total Eclipse of the Heart Bonnie Tyler	The Very Best of Bonnie Tyler	Aug 30, 2020	4:27