The Skeptics' Guide to Emergency Medicine

SEASON #4

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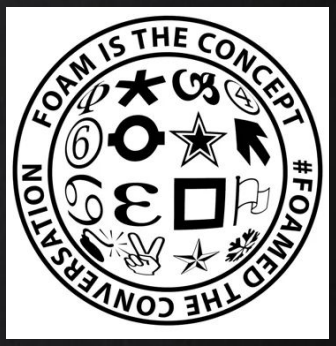
Remember to be skeptical of anything you learn, even if you learned it from the Skeptics' Guide to Emergency Medicine

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 being 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.

The SGEM was inspired by the KT project started by Dr. Andrew Worster from McMaster University. He called his project Best Evidence in Emergency Medicine (BEEM). BEEM has a process that is a reliable and validated method of selecting relevant emergency medicine articles. You can get the BEEM critical appraisal tools as part of the Free Open Access to Meducation movement. FOAM – Medical education for anyone, anywhere, anytime.

> "FOAM should not be seen as a teaching philosophy or strategy, but rather as a globally accessible crowd-sourced educational adjunct providing inline (contextual) and offline (asynchronous) content to augment traditional educational principles".



The SGEM consists of a weekly podcast on iTunes and blog. It also has a Facebook page, active Twitter feed, Google+ and YouTube channel.

So stop practicing medicine from over ten years ago and start practicing medicine based on the best evidence.

Listen to the podcast and turn your car into a classroom.

Remember to be skeptical of anything you learn,
even if you learned it from the Skeptics' Guide to Emergency Medicine.

To Access the SGEM Click on any Social Media Icon:

DISCLAIMER

The Skeptics' Guide to Emergency Medicine (SGEM) and this material produced is produced in Canada and is intended for emergency medicine and critical care providers. A goal of the SGEM is to disseminate the best evidence so you can provide patients with the best care.

The provider of this educational material may discuss commercial products and/or devices as well as the approved/investigative use of commercial products/devices.

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The SGEM makes a reasonable effort to supply accurate information but does not assume any liability for errors or omissions. Because of the nature of the program and its format, it is not recommended that they serve as the sole basis for patient evaluation and treatment.

Remember to be skeptical of anything you learn,
even if you learned it from the Skeptics' Guide to Emergency Medicine.

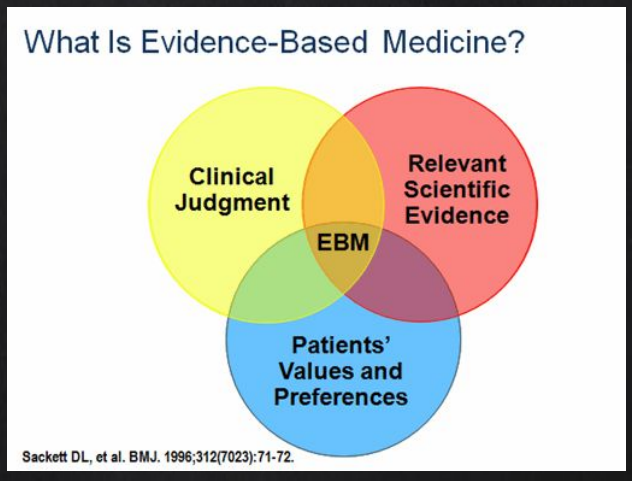
Evidence-Based Medicine

The year was 1992. Dr. David Sackett's mentee Dr. Gordon Guyatt coined the term "Evidence Based Medicine"(EBM)[1] and a new philosophy of transforming clinical care was born. As with most paradigm shifts, opponents argued that EBM was neither novel nor a panacea for the imperfections of medical science, particularly since EBM was inherently contradictory lacking any evidence of effectiveness compared with centuries of medical tradition.[2] Early pundits criticized EBM as a cult-like phenomenon in which groupthink reduced the complexities of medical research to a single step while confusing statistics with scientific method. In particular, EBM opponents criticize the EBM hierarchy of evidence, which is believed to minimize clinician's expertise and imply that every medical question requires and is ethically appropriate for randomized controlled trial answers.[3]

EBM supporters readily acknowledge that the structured approach to finding, appraising, and acting upon research evidence outlined by Dr. Guyatt's Evidence Based Medicine Working Group is imperfect, will require continual methodological upgrades, often hijacked by entities with ulterior motives, and merits rigorous investigation like any other "intervention". [4,5] Yet EBM mirrors the perspective of democracy, which is frequently viewed as the worst type of government … except for every other alternative. Indeed, EBM is the worst form of (research-enhanced) medicine, except for every other approach! While nurses, physician extenders, and physicians await a better approach to find practice-ready evidence and translate that research into bedside care, EBM remains a lighthouse to guide all of us towards the best approximation of truth in a sea of chaos, noise, and competing influences.

WHAT IS EBM?

The label "EBM" implies that evidence is the sole ingredient. On the contrary, the philosophy of EBM seeks to incorporate and weigh equally patient preferences/priorities, clinician expertise, and the least biased research evidence to deliver the highest quality medical care to patients when faced with diagnostic, prognostic, or therapeutic scenarios.



EBM provides a structured approach to find, appraise, and begin to apply research.[6] The EBM approach diverges from the more passive approach relied upon by investigators, which relied upon publishing alone to disseminate innovations. One problem with complete reliance upon publication is that most published research erroneously asks the wrong questions on misrepresentative patients and thereby misguides clinicians without improving patient outcomes.[7] Another logical flaw of relying upon publications as a vehicle for widespread permeation into clinical practice is that clinicians are bombarded with over 3800 new biomedical publications on PubMed daily, yet residency training in finding and critically appraising research is haphazard.[8]

Evidence-Based Medicine

The EBM approach involves starting with a focused clinical question followed by five-steps to finding an answer that accommodates clinical expertise, patient perspectives, and the highest quality research.

Step 1: Develop an answerable and focused PICOT question

- P = population (including age, gender, ethnicity, disease process and severity, if appropriate)
- I = intervention (treatment, risk factor exposure – note this is not pertinent for most diagnostic accuracy queries)
- C = control (comparator population to whom the intervention group is assessed)
- O = outcomes (rate of occurrence, progression of disease, accuracy of test)
- T = timing of the intervention to affect outcome(s)

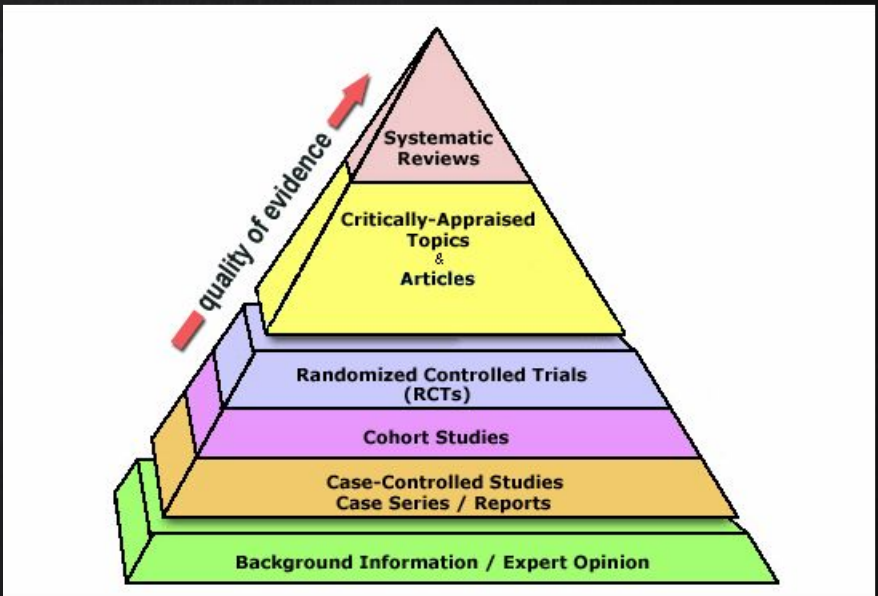
The PICOT question focuses subsequent steps to achieve the most pertinent results for the patients typically encountered.[9]

Step 2: Devise a Search Strategy

Numerous open access electronic databases exist, including PubMed (https://www.ncbi.nlm.nih.gov/pubmed/) and Google Scholar (https://scholar.google.com/). Both resources often provide access to the full manuscript as well. The Turning Research Into Practice (TRIP) database is an extremely useful EBM resource that permits users to develop search strategies using a PICOT question (https://www.tripdatabase.com/). Alternatively, some sites like the Washington University in St. Louis Journal Club (http://emed.wustl.edu/Journal-Club) provide search strategies for common emergency medicine scenarios, along with User's Guide to the Medical Literature critical appraisals.[6]

Step 3: Find and Select the Least Biased Research

EBM describes a hierarchy of evidence depicting less biased research towards the top. Expert opinion and case reports site at the bottom of the hierarchy because they are more prone to spurious observations via unconscious interpretation, small sample sizes and statistical chance then are masked controlled trials and systematic reviews of multiple trials. However, this hierarchy does not imply that the more bias prone forms of evidence are worthless or that systematic reviews are consistently free of bias or worthy of changing practice. Sufficiently large, high-quality observational research can inform healthcare delivery, while meta-analyses can be skewed by industry influence, ignorant of methodological standards, and overly duplicative.[10]



Evidence-Based Medicine

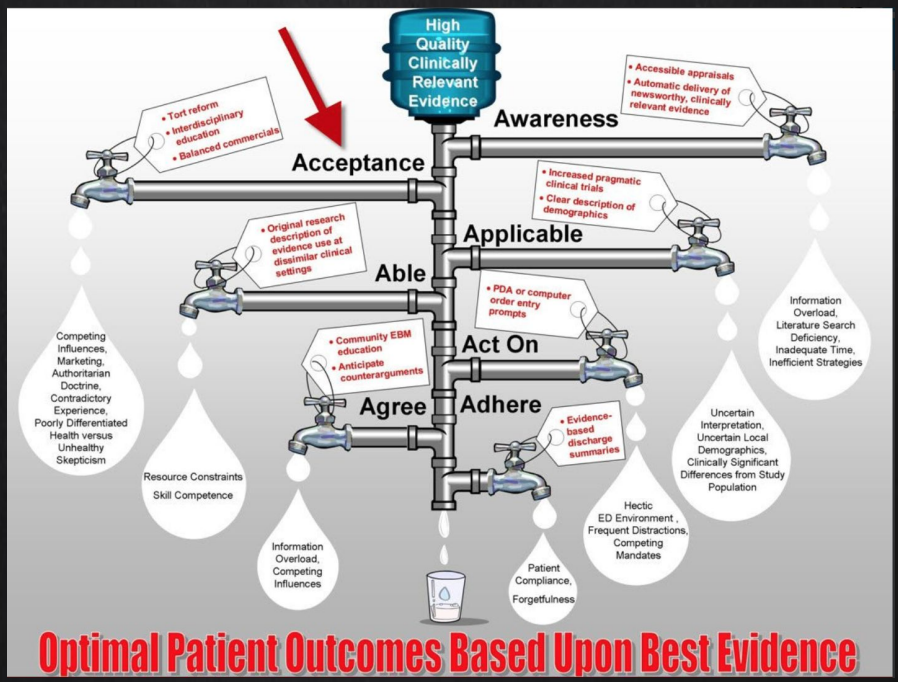
Step 4: Critically Appraise the Study

Not all research is created equal. Reviewing each relevant manuscript identified requires time and (just like inserting a central line or emergently intubating the crashing patient's airway) a bit of mentorship.[8] Critically appraising a randomized controlled trial, for example, consists of a series of questions:

1. Does the study population apply to your patient?
2. Were the patients adequately randomized?
3. Was the randomization process concealed (to patients, clinicians, outcome assessors)?
4. Were the patients analyzed in the groups to which they were randomized (Intention to Treat)?
5. Were the patients recruited consecutively to minimize selection bias?
6. Were patients in both groups similar with respect to pertinent prognostic factors?
7. Were all groups managed similarly except for the intervention?
8. Was follow-up complete?
9. Were all patient-important outcomes considered?
10. Was the treatment effect large enough and precise enough to be clinically significant?

Step 5: Apply the Evidence Using Shared Decision Making

In 1999 the Institute of Medicine estimated an average delay of 17-years for 14% of research evidence to penetrate into bedside practice. The Knowledge Translation Pipeline developed at the 2007 Academic Emergency Medicine Consensus Conference illustrates the "leaks" that occur between the research "lab" and real-world bedside application.[11]



FOAMed (Free Open Access Medical Education) secondary peer review resources like Skeptics Guide to Emergency Medicine and Best Evidence in Emergency Medicine reduce many of these leaks by raising awareness of potentially practice-enhancing research in an era of information overload, while discussing potential biases and pragmatic issues associated with application of the evidence. In addition, the last two Knowledge Translation Pipeline leaks involve patients and patients' families, so discussing important diagnostic, prognostic, and therapeutic applications of research with the patients when more than one reasonable choice exists is essential.[12]

Evidence-Based Medicine

So it seems that the intent of EBM is admirable, while the realities of applying EBM are rife with challenges. SGEM Season 4 is an invaluable resource for physicians, nurses, and students aspiring to implement new knowledge and de-implement outdated dogma in an increasingly time and resource-constrained clinical context. These pages include humor, tears, personal strife, occasional disagreement, and a steady stream of empathy for our patients and clinical colleagues. Enjoy – and carpe diem.

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Best Evidence in Emergency Medicine

The Best Evidence in Emergency Medicine (BEEM) is an international, emergency medicine, knowledge translation project created by emergency physicians for emergency physicians It was started by Dr. Andrew Worster of McMaster University in 2005. It provides up to 12 hours of continuing medical education per course. BEEM does not have any financial or other affiliation with any commercial organization.

BEEM Mission: To provide emergency physicians with the best clinical evidence to optimize patient care.

BEEM Vision: The vision of BEEM is to be the most valid, reliable, and unbiased global source of current clinically-relevant patient-centered research for Emergency Physicians.

BEEM Validation: BEEM has the only validated audience rating tool in emergency medicine continuing medical education.

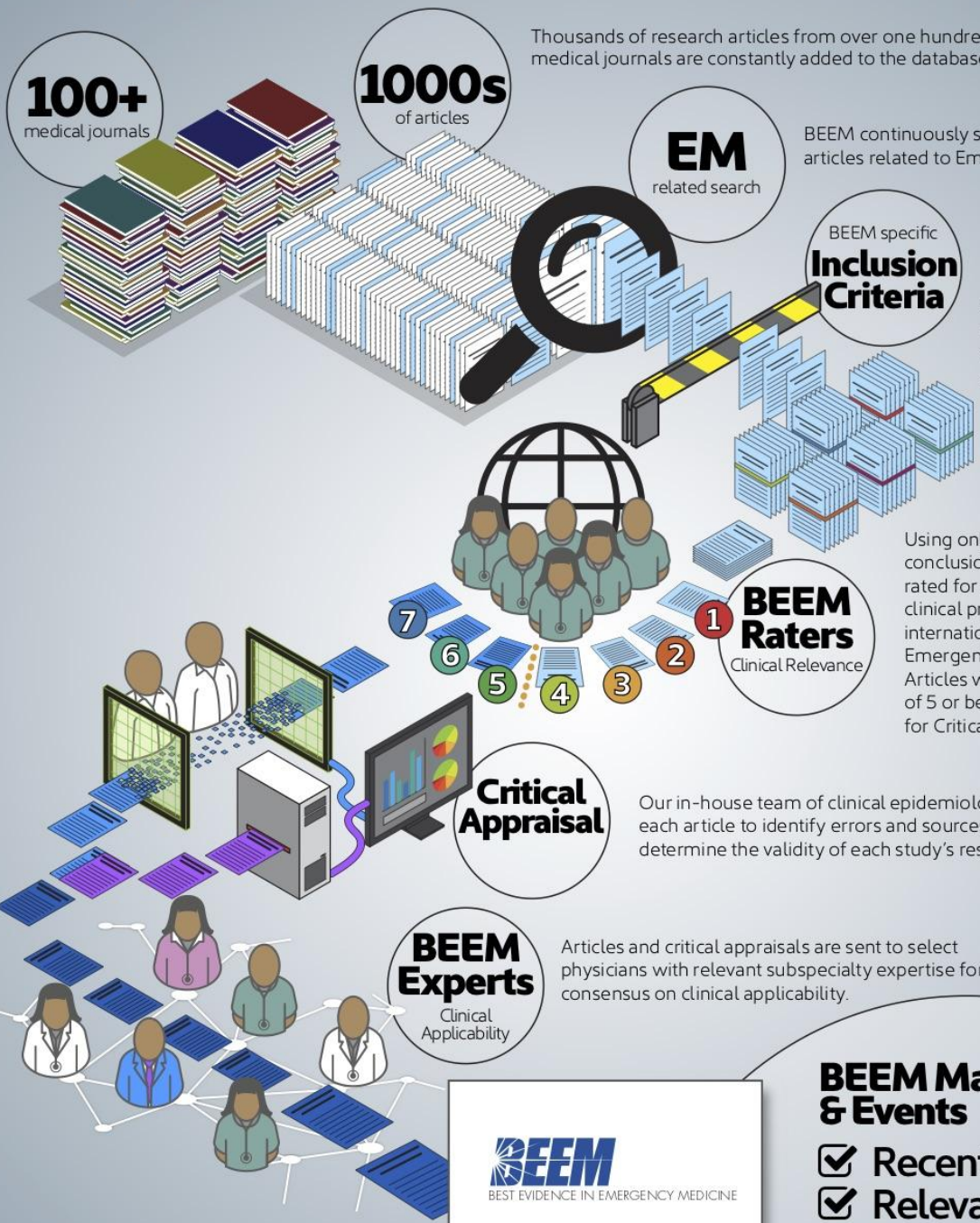
Worster et al. Consensus Conference Follow-up: Inter-rater Reliability Assessment of the Best Evidence in Emergency Medicine (BEEM) Rater Scale, a Medical Literature Rating Tool for Emergency Physicians. Acad Emerg Med Nov 2011.

BEEM Rater Score: The BEEM rater score, to the best of our knowledge, is the only known measure of clinical relevance. It has a high interrater reliability and face validity and correlates with future citations.

Carpenter et al. Best Evidence in Emergency Medicine (BEEM) Rater Scores Correlate With Publications' Future Citations. Acad Emerg Med Oct 2013.

The BEEM Process

Identifying the Best Evidence



BEEM Manual & Events

- ☑ Recent
- ☑ Relevant
- ☑ Valid
- ☑ Applicable
- ☑ Unbiased

The best evidence-based guidance for clinical practice in Emergency Medicine

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127 Suspicious Minds vs. Clinical prediction rule in children with trauma

Case Scenario:
A 10-year-old girl is a restrained rear-seat passenger in a MVA. The car was "T-boned" on her side of the vehicle at low city speeds. She presents via EMS with a c-spine collar and on a spine board. She is alert, appropriate and in no distress. Her exam is normal; no evidence of abdominal wall trauma, tenderness or nausea/vomiting. Given the mechanism of the injury you are concerned about blunt abdominal trauma.

Clinical Question:
How well do clinicians identify children with blunt torso trauma with intra-abdominal injuries compared to an established clinical prediction rule?

Bottom LINE

Clinicians do reasonably well at predicting which children with blunt torso trauma require investigations for intra-abdominal injuries requiring intervention. Nothing can be said at this time about the clinical decision instrument.

Comparison of clinical suspicion versus a clinical prediction rule in identifying children at risk for intra-abdominal injuries after blunt torso trauma.

Mahajan P et al. AEM. Sept 2015

P Children < 18 years old with blunt torso trauma presenting to an ED

I Clinical suspicion of intra-abdominal injury [ordinal scale (<1%, 1-5%, 6-10%, 11-50%, > 50%)]

C Intra-abdominal injury undergoing acute intervention

O Descriptive statistics using clinician gauged risk < 1% as cut-off (Sensitivity, Specificity, +/- LR)

Authors' Conclusion:

"A clinical prediction rule had a significantly higher sensitivity than clinician suspicion for identifying intra-abdominal injury undergoing acute intervention, but a lower specificity. The higher specificity of clinician suspicion, however, did not translate into clinical practice, as clinicians frequently obtained abdominal computed tomography scans in patients they considered to be at very low risk. If validated, this clinical prediction rule can assist in clinical decision-making around computed tomography use after blunt abdominal trauma in children by limiting computed tomography scan use in low-risk patients."

Background

The leading cause of death in children is trauma. Blunt torso trauma makes up a significant portion of the mortality statistics. CT scanning has become a routine method for identifying children with intra-abdominal injuries. The amount of radiation being delivered to these vulnerable patients and the risks of developing radiation-induced malignancy has raised concern. There is evidence that clinical suspicion is not accurate in identifying children with intra-abdominal injuries. In addition, there is wide variation on the use of abdominal CT and over utilization in children with low pre-test probability of clinically important injuries.

Results

Key Results: Clinicians predicted 168/203 (83%) intra-abdominal injuries requiring intervention and predicted 9217/11716 (79%) negative patients.

Sensitivity= 82.8% (76.9 – 87.7)	Specificity= 78.7% (77.9 – 79.4)
PPV= 6.3% (5.4 – 7.3)	NPV= 99.6 % (99.5 – 99.7)
+LR= 3.9 (3.6 – 4.2)	-LR= 0.22 (0.16 – 0.30)

Commentary

Five questions for Dr. Mahajan about his research study. Listen to the podcast for his responses.

1. There usually is some backstory about how a research project got started. So what was the inspiration for doing this project?
2. Your title does not specify that the standard which you are comparing the physicians performance metrics is an un-validated instrument which may mislead the reader into using this instrument prematurely. You mention the fact the instrument is unvalidated later in the text, but I worry that the message is lost.
3. The literature has many examples where the results of a derivation study were not echoed in the validation studies. Are there plans to take this clinical prediction instrument and attempt to validated it in a future study?
    a. We have to remember that before a CDI is ready for prime-time, it should go through three steps. The first is derivation – where the researchers try to see amongst a number of various variables, which ones appear to have predictive value. Unfortunately, just by chance alone, some variables may appear significant when they are not. This is why the second stage, validation, is so important. At this stage the researchers work to confirm the significance of the predictive variables from the derivation study. There are examples of seemingly awesome derived CDIs that, when it came time to validation, did very poorly.

Commentary cont'd

4. The rates of CT scans based on physician behavior was 5318/11919 = 45%. The rates of CT using the un-validated decision instrument would have been 7004/12044 = 58%. The un-validated instrument appears to significantly increase CT rates.

5. We like to see patient oriented outcomes as the primary outcome. Although the study title describes the outcome *being "children at risk for intra-abdominal injuries"*, really the results are describing children with intra-abdominal injuries requiring intervention.

Clinical Application

No change for now.

STUDY QUALITY CHECKLIST

The clinical problem is well-defined	👍
The study population represents the target population (ie no spectrum bias)	👍
The study population included or focused on those in the ED	👍
The study patients were recruited consecutively (ie no selection bias)	👍
The diagnostic evaluation was comprehensive and applied equally to all patients (ie verification bias)	👎
All diagnostic criteria were explicit, valid, reproducible (ie no incorporation bias)	👍
The reference standard was appropriate (ie no imperfect gold-standard bias)	👍
All undiagnosed patients underwent sufficiently long/comprehensive follow-up (ie no double gold-standard bias)	👍
The L.R.(s) of the test(s) in presented or can be calculated from the information provided	👍
The precision of the measure of diagnostic performance is satisfactory	👍

CONCLUSION VS COMMENTARY

COMPARISON

Until the decision instrument is validated, there is limited value in comparing clinicians' judgment to it.

WHAT DO I TELL MY PATIENT?

I'M A BIT WORRIED THAT YOUR CHILD HAS A SIGNIFICANT ABDOMINAL INJURY. WE WILL NEED TO DO SOME MORE TESTS TO FIND OUT IF THERE ARE INTERNAL INJURIES. ONE THE TESTS THAT CAN HELP US IDENTIFY IMPORTANT ABDOMINAL INJURIES IS A CT SCAN.

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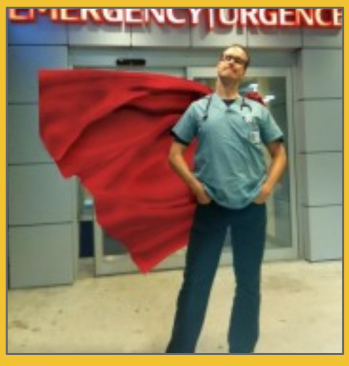


GUEST SKEPTIC: Dr. Anthony G. Crocco
Medical Director & Division Head of the Division of Pediatric Emergency at McMaster's Children's Hospital

128 One Hour AMI Rule Out / Rule In (Harder, Better, Faster?)

Case Scenario:
A 53 year-old man presents with left-sided chest pain that started 90 minutes, radiates to his left arm, associated with nausea without vomiting. The pain began while he was doing yard work. He has never had pain like this before.

His initial ECG is unremarkable.

Clinical Question:
Is it possible to rule in / rule out acute myocardial infarction in the ED with high sensitivity troponin T and ECG in one hour?

Bottom LINE

Due to the biases / other factors mentioned below, a one-hour protocol utilizing high sensitivity troponin T cannot be recommended at this time. External validation of this protocol and an explicit discussion of how the diagnosis of AMI is arrived at might allow for a rapid rule out in the future

Prospective validation of a 1-hour algorithm to rule-out and rule-in acute myocardial infarction using a high-sensitivity cardiac troponin T assay

Reichlin T et al. CMAJ. May 2015.

P Patients presenting to the ED within 12 hours of onset of non-traumatic chest pain or symptoms suggestive of AMI. This was part of an ongoing study in Switzerland, Spain and Italy (Advantageous Predictors of Acute Coronary Syndrome Evaluation (APACE) study)

Excluded: Kidney failure requiring dialysis or STEMI.

I High sensitivity Troponin T at time zero and one hour with ECG

C Two independent cardiologists (ED presentation to 90-day follow-up, including patient history, physical exam, coronary angiography, echocardiography, follow-up data, and serial high sensitivity troponin T measurements

O Acute myocardial infarction (NPV, PPV, and AUC)

Authors' Conclusion:

This rapid strategy incorporating high-sensitivity cardiac troponin T baseline values and absolute changes within the first hour substantially accelerated the management of suspected acute MI by allowing safe rule-out as well as accurate rule-in of acute MI in 3 out of 4 patients.

Background

Only about 5% of all consecutive patients presenting with acute chest pain will have a ST elevated myocardial infarction (STEMI) (Apple et al). These are the easy ones to diagnose and manage. This leaves the other 95% of chest pain patients. These are the hard ones.

We need to figure out who will rule-in vs. rule-out for acute myocardial infarction (AMI). This is where cardiac biomarkers play a major role.There have been many biomarkers used over the last 60 years to try to identify patients with acute myocardial infarction.

The first practical test utilized, as a cardiac marker was serum glutamic oxaloacetic transaminase (SGOT) that is now called aspartate amino-transferase (AST). Since the late 1990's the cardiac marker of choice has changed from CK-MB to Troponin. A limitation of current troponin assays is that they can take 3-4 hours to rise. This means the diagnosis of Non-STEMI can take many hours of continued monitoring with serial blood sampling.

Ruling out AMI takes time, uses resources, contributes to overcrowding, and causes patient anxiety. High sensitivity troponin assays are all the rage now and used in many emergency departments. They offer very high sensitivity but are less specific than prior troponin assays. There is limited evidence from studies that the use of high sensitivity troponins may allow for the safe discharge of patients more rapidly from the emergency department than what is possible with traditional troponin assays.

Results

Key Results: 1,320 patients who presented to the emergency department within twelve hours of onset of non-traumatic chest pain or other symptoms suggestive of AMI. The median age was 60 years and 69% were men. Acute MI was the final diagnosis in 17% of patients. They divided patients into three different categories:

1. *Rule-Out of Acute MI:* Base- line high sensitivity troponin T level <12 ng/L *and* an absolute change within the first hour of less than 3 ng/L. Sixty percent (786/1320) ruled out for AMI.
2. *Rule-In of Acute MI:* Either a baseline high sensitivity troponin T value of 52 ng/L or greater, *or* an absolute change within the first hour of 5 ng/L or greater. Sixteen percent (216/1320) ruled in for AMI.
3. *Observation Zone:* Patients fulfilling neither criteria for rule-in or rule-out were classified as being in the *"observational zone."* Twenty-four percent (318/1320) were in the observation zone.

One-hour Algorithm Test Characteristics for Acute MI:

- Area under the curve 0.96 (95%CI 0.95 to 0.97)
- *Rule-Out Zone:* Sensitivity of 99.6% (95% CI 97.6% to 99.9%) and Negative Predictive Value 99.9% (95% CI 99.3 to 100%)
- *Rule-In Zone:* Specificity of 95.7% (95% CI 94.3% to 96.8%) and Positive Predictive Value 78.2% (72.1% to 83.6%)

One AMI was felt to be missed of 786 patients ruled out with the one-hour algorithm.

TALK NERDY TO ME

Commentary

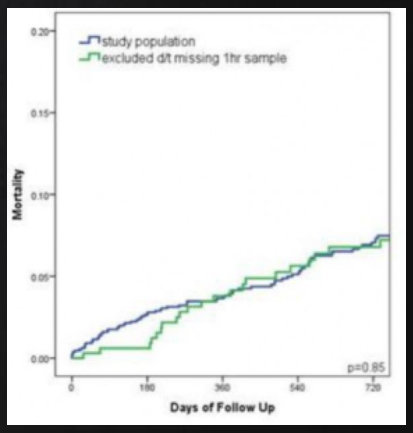
This was an attempt by Reichlin et al to investigate whether 1-hour algorithmto rule-out and rule-in acute myocardial infarction using a high-sensitivity troponin T as a biomarker. There were a number of concerns with this manuscript. Dr. Andrew Worster was invited to help us critically appraise this paper. Dr. Worster does research on high sensitivity troponins and recently published a review of this paper (Ann Int Med 2015).

1. *Bias:* The challenge of conducting high-sensitivity troponin studies is that the diagnosis of NSTEMI is a disease entity based on a test without an independent reference standard. This can lead to a number of biases that can distort the results.

A. *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. The gold standard appears to be two out of three cardiologists agreeing upon the diagnosis of AMI. This seems to have been driven predominantly by defining AMI as a rise in high sensitivity troponin T. While this is a commonly used definition of AMI, it is inappropriate to judge the accuracy of a test to make a diagnosis that requires the results of the test. The results would be much more robust if there was discussion of other tests such as echocardiography showing wall motion abnormalities, abnormal provocative tests, future ECG changes, or abnormalities seen on heart catheterization.

B. *Partial Verification Bias:* This happens when only a certain set of patients who underwent the index test is verified by the reference standard. This would increases sensitivity but decreases specificity. Patients that were deemed to be low risk did not always proceed to 6-hour high sensitivity troponin T. No additional data is given about which patients received additional testing such as coronary angiography or provocative testing. It is implied that those that were low risk did not undergo additional testing.

C. Spectrum Bias: 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 (sicker than who you see in the emergency department). Specificity can look great if you have no sick patients in the cohort (worried well). They included only patients who presented to a cardiac research hospital within 12hrs of pain. These patients could have been potentially more ill. There is also the problem that 20% of eligible patients who failed to complete index testing. We don't know in which direction the loss of 20% favours the bias but the failure of 20% of those enrolled to complete the first phase of the study raises concerns about study protocol adherence. Correspondence with the author revealed a graph showing the outcomes of those that missed the one-hour troponin. This group had significantly lower mortality for the first year after the study before closely following the mortality curve of the study population. This reveals that this population was fairly different than the study population and appears to have been less critically ill than study patients. The author's calculated a Kaplan-Meier Curve p value of 0.85 but it is unclear at what time period this was done on.



- Learn more about how bias can impact the diagnostic test accuracy by reading Kohn, Carpenter and Newman in AEM 2013

TALK NERDY TO ME

Commentary Continued

2. *Risk of Over-Testing:* Another concern with this protocol and others based upon high sensitivity troponin assays is the lack of specificity. The initial high sensitivity troponin T was only 48.4% specific, with more false positives than true positives. If there were inappropriate use of this test in ultra low risk patients, there may be a paradoxical rise in the number of patients being evaluated for chest pain in the emergency department. Similar to the use of d-dimers to evaluate for pulmonary embolism, this tool will need to be carefully applied to avoid over-testing.
3. *Imprecision of the Assay:* The change in high sensitivity troponin T was within the allowable imprecision of the assay. So the change may only be analytical variation and not clinical variation. This is really the keystone because if the change is within the assay's coefficient of variation, all other issues are moot (Kavsak PA. High-five for high-sensitivity cardiac troponin T: depends on the precision and analytical platform. JAMA Intern Med 2013)
4. *Missed AMI:* There was one false negative patient in the study. It is not clear that the single false negative patient was having an AMI from the paper. Her peak high sensitivity troponin T was only 17 and there was no discussion of other factors such, as coronary catheterization results were included.
5. *Conflict of Interest:* Roche supplied the test and several authors had conflicts. This does not invalidate or make the conclusions wrong but should make readers more skeptical of the results. However, greater than 90% of research is funded by industry and it's not necessarily bad. Non-industry sponsors encourage industry-investigator partnerships. In addition, the author was very prompt and generous by sharing data with us.

Author Response to Our Questions:

1. Is there data about what happened to those that were excluded due to not having a one-hour repeat high sensitivity troponin T? What were their outcomes?
    - See the supplemental Table 1 for the baseline characteristics of these patients (seems that this was lost during the publishing process, sorry). Outcomes in terms of mortality during follow-up were equal (see Kaplan Meier below, p=0.85), the initial difference I would attribute due to chance and the different sample size.
2. How complete was follow up by phone or writing? Were any patients lost to follow up?
    - 30 days follow-up was complete in 1316/1320 pts (99.7%).
3. How often did the independent cardiologists require adjudication by a third cardiologist? Is there a kappa value to assess the inter-rater reliability?
    - Adjudication with a third cardiologist was required in 12%. No inter-rater comparisons are available.
4. Is there any information about how the cardiologists decided who was and was not having an MI? What percentage of patients had a heart catheterization or other testing?
    - The adjudication was made by clinical judgment integrating all medical information available up to 90-days including patient history, physical examination, results of laboratory testing (including serial hs-cTnT levels), radiologic testing, Electrocardiogram, echocardiography, cardiac exercise test, lesion severity and morphology in coronary angiography. Troponin levels were interpreted as described in the supplemental methods of the paper. Only the tests that were considered clinically indicated by the medical teams responsible for the patients care were performed, no additional test for

Commentary Cont'd

.... the study only (except for serial blood sampling) were performed. Coronary Angiography was performed in 23%, stress testing in 22%. Given that the adjudication of AMI vs. Non-AMI is based mainly on history, symptoms, ECG and troponin levels, additional testing with coronary angiography and stress testing was particularly helpful to distinguish in the non-AMI group between cardiac and non-cardiac causes of non-AMI chest pain.

Clinical Application

High sensitivity troponin T may/may not have future clinical application to rapidly rule out low risk patients for acute myocardial infarction. It is unclear at this time what effect the low specificity of the test will have.

STUDY QUALITY CHECKLIST

The clinical problem is well-defined	👍
The study population represents the target population (ie no spectrum bias)	👎
The study population included or focused on those in the ED	👍
The study patients were recruited consecutively (ie no selection bias)	👍
The diagnostic evaluation was comprehensive and applied equally to all patients (ie verification bias)	👎
All diagnostic criteria were explicit, valid, reproducible (ie no incorporation bias)	👎
The reference standard was appropriate (ie no imperfect gold-standard bias)	👎
All undiagnosed patients underwent sufficiently long/comprehensive follow-up (ie no double gold-standard bias)	?
The L.R.(s) of the test(s) in presented or can be calculated from the information provided	👍
The precision of the measure of diagnostic performance is satisfactory	👍

CONCLUSION VS COMMENTARY COMPARISON

The author's are much more optimistic of their protocol's current ability to rapidly rule out patient's in the emergency department that we are based on the data presented. Also, our role in the emergency department is not limited to ruling out AMI but as importantly, to determining if the patient has acute coronary syndrome and if not, how soon do they require outpatient follow-up.

WHAT DO I TELL MY PATIENT?

There is a new blood test that checks for very early damage to your heart. If you are having a heart attack, this test often picks up early signs of heart injury. However, the test is so sensitive that it may suggest you are having a heart attack even if you aren't having a heart attack. In order to be as sure as we can be, we will need to get multiple heart tracings and do more than one blood test.

References

Reichlin T, Twerenbold R, Wildi K, Gimenez MR, Bergsma N, Haaf P, Druey S, Puelacher C, Moehring B, Freese M, Stelzig C. Prospective validation of a 1-hour algorithm to rule-out and rule-in acute myocardial infarction using a high-sensitivity cardiac troponin T assay. Canadian Medical Association Journal. 2015 May 19;187(8):E243-52.

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129 That Chest Tube... She's a Beauty

Case Scenario:

A 25-year-old female was allegedly stabbed while standing on the corner minding her own business. She was found unconscious (Glasgow Coma Scale 7) and intubated by EMS. On arrival in the ED, vitals are stable with decreased air entry on the right side. You skillfully insert a right chest tube and get back 100 ml of blood. You review the post insertion chest tube x-ray and are disappointed by the position of the tube. It is hitting the mediastinum and curling back on itself and there is persistent white-out on the right.

Clinical Questions:

1) In a trauma patient, how clinically useful is a CXR after putting in a chest tube?
2) Does chest tube location matter?

Bottom LINE

1. Put the tube on the correct side, within the triangle of safety, and within the pleural space. Continue to obtain a CXR post chest tube knowing it will probably not change management. Be more concerned if the patient is doing poorly or the tube is not draining
2. Safely put the chest tube in the pleural space.

Question 1: In a trauma patient, how clinically useful is a CXR post-chest tube?

What is the yield of routine chest radiography following thoracostomy for trauma? Kong VY et al. Injury. January 2015.

P

Adults presenting or referred to a trauma centre who had a CXR after tube thoracostomy

- Grade A: No CXR prior to tube insertion
- Grade B: CXR prior to tube insertion with clinical outcomes
- Grade C: CXR prior to tube insertion without clinical outcomes
- Grade D: Patients without complete data set

I

CXR following tube thoracostomy

C

None

O

Yield of post CXR tube insertion influencing clinical management

Authors' Conclusion:

Despite the widely accepted practice of routine CXR following tube thoracostomy, the yield is relatively low. In many cases, good clinical examination post tube insertion will provide warnings as to whether problems are likely to result. However, in the more rural setting, and in resource challenged environments, there is a relatively high yield from the CXR, which alters management.

Background

The "B" of the ABCs is really *"Chest Tube"*. Chest tubes didn't become the standard of care for pneumothorax and hemothorax until the 1950s. The idea of draining the chest has been around since Hippocrates (460–370 B.C.) where he used tin tubes, linen, wine, and oil to drain empyemas.

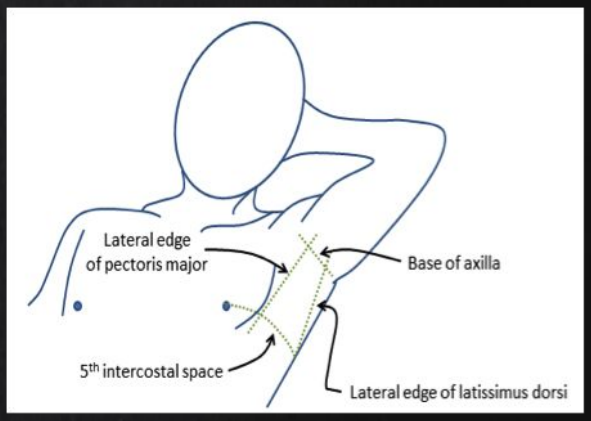
The first mention of chest tubes for trauma was in the 1200s when a knight named Gawan used a tube of bark from a branch of a linden tree to treat a tension hemopneumothorax in another knight who sustained an injury during a joust.

Controversy existed over whether chest wounds should be left open or closed for the next few centuries. In the 17th and 18th century the importance of removing retained blood led to the practice of wound sucking. This was often done by the drummers of the military who sucked the wounds and then applied compresses and bandages.

During the wars of the last century there was debate over drainage systems versus repeated aspirations versus suture closure of open chest wounds. The mortality from chest wounds in World War I was 56%. Repeated chest thoracenteses was the treatment of choice for hemothorax and endorsed by NATO in 1958.

Plastic chest tubes were introduced in 1961 and closed thoracostomy and underwater seal drainage become common during the Vietnam War. The mortality rate dropped to 2.9%.
Current chest tubes are made from clear vinyl or silastic. They have multiple side holes and have centimeter markings to denote depth of insertion. A radiopaque strip allows visualization on chest x-ray. The principle of evacuation of pus, air, blood, and fluid from the pleural cavity that originated in ancient Greece remains the standard to this day.

Triangle of Safety: The triangle of safety is bordered by the anterior axillary line (pectoris major) and posterior axillary line (latissimus dorsi) and the 5th intercostal space (roughly the level of the nipple in a thin male). The only muscles you need to go through are the serratus anterior and intercostals. The only structure of significance is the long thoracic nerve. If injured it will produce a winged scapula. This is rare. This the first choice for chest tube insertion in trauma.



Results

Key Results:

- N=1,004 patients (1,042 tube thoracostomies)
- 91% were male
- Median age 24 years
- 75% penetrating trauma (3/4 from stab wounds)
    - 33% Hemopneumothorax
    - 30% Hemothorax
    - 25% Pneumothorax
    - 8% Tension pneumothorax
    - 5% open pneumothorax

Results

Group A: No initial CXR 103/1004 (10%)

- ¾ thought to be tension pneumothorax clinically and had needle decompression before tube thoracostomy
- ¼ thought to be simple pneumothorax clinically
- Nine had their clinical management changed post CXR
  - Five had kinked tubes that needed adjustment
  - Four tubes were too shallow and needed new tubes

Group B: Initial CXR but clinically not well post tube thoracostomy 191/1004 (19%)

- *Clinical concerns included:*
  - 42% were outside the triangle of safety
  - 39% tubes were not draining or swinging
  - 10% still symptomatic
  - 7% tube dislodged prior to post-CXR
  - 1% blood post simple pneumothorax
  - 1% gastric contents
- *111/191 (58%) post tube CXR had clinical management changed:*
  - 40% New Tube: 17% Subcutaneous, 16% tube was kinked and 7% non re-expansion of lung
  - 14% Tube Adjusted: Tube not inserted far enough
  - 4% Operating Room: 2% violated the diaphragm, 1% hemothorax post tube and 1% gastric cannulation
- Specifically they mention 5 out of the 6 iatrogenic injuries had the tube thoracostomy done in a rural hospital and referred to the trauma centre

Group C: Initial CXR but no clinical concern post tube thoracostomy 710/1004 (71%)

- 32/710 (5%) had clinical management influenced post CXR
  - 27/32 (84%) Tube was too deep
  - 5/32 (16%) Tube on wrong side
  - 4/5 Tube on wrong side were done in a rural hospital and referred to the trauma centre

Commentary

It is always important to question dogma. ATLS has limited data to support its recommendation of routine CXR after tube thoracostomy. This study had a good objective of trying to shed some light on this area of trauma care.

This study had a some limitations

1. *Abstractors:* We do not know much about the abstracting methods from reading the paper. However, Dr. Kong was contacted and he graciously provided more information. The data was collected prospectively and then retrospectively abstracted by one abstractor (Dr. Kong).

Commentary Continued

2. *Exclusion:* The problem of missing data is an interesting one. They just excluded all the patients whose data was not complete or missing a CXR. Dr. Kong reported via personal communication that only a few patients were ultimately excluded from the study due to missing data.
3. *Referral Bias:* They make reference to five out of six iatrogenic injuries who had their tube thoracostomies done in rural centres. Dr. Kong informed us that these were not emergency medicine physicians but rather a variety of physicians placing the chest tubes.
4. *Small Numbers:* The number of complications was low in this data set and was probably even lower than they reported. They reported 152 patients (15%) had their management impacted by the post procedure CXR. However, 59 patients just needed the tube adjusted. This leaves only 93/1,004 (9%) patients that really had their management changed. Group A had four patients who needed a new tube. Group B had 84 patients who needed a new tube (78) or were taken to the operating room (6). Group C had five patients who had the tube inserted on the wrong side.
    a. If the patient was doing well I would be tempted not to make an adjustment to the tube. If the tube is in the pleural space, it is working, i.e. fluctuating with respiration, draining and the lung is up, leave it alone. Repositioning a tube is rarely needed. Treat the patient not the CXR. The small numbers also impacts on their conclusions about rural tube thoracostomy. A retrospective chart review with only a handful of rural complications should be viewed with appropriate caution. However, placing the tube on the wrong side does seem like a significant error that should be avoided.
5. *External Validity:* This was a single trauma center study done in South Africa and the results may or may not be transferable to a North American health care environment. Although ATLS is a world wide training program, how well is it implemented in another country with a different health care system is not known?

STUDY QUALITY CHECKLIST

Were the abstractors trained before the data collection?	?
Were the inclusion and exclusion criteria for case selection defined?	👍
Were the variables defined?	👍
Did the abstractors use data abstraction forms?	?
Was the abstractors' performance monitored?	?
Were the abstractors aware of the hypothesis / study objectives?	?
Was the interobserver reliability discussed?	👎
Was the interobserver reliability tested or measured?	👎
Was the medical record database identified or described?	👍
Was the method of sampling described?	👍
Was the statistical management of missing data described?	👍
Was the study approved by the institutional or ethics review board?	👍

Clinical Application

CXR post tube thoracostomy still seems like a reasonable test to continue to request.

Similar dogma has existed in trauma world about location of chest tube placement based on the injury pattern. The traditional teaching has been:

1. Pneumothorax – superior and anterior
2. Hemothorax – inferior and posterior
3. Avoid the Fissures

CONCLUSION VS COMMENTARY COMPARISON

we agree with the authors that the post tube thoracostomy CXR yield is too low to change management, but it is not zero. If the tube is draining and the patient is doing well the post CXR will probably not alter management.

Question 2: Does Chest Tube Placement Matter?

Does Chest tube location matter? An analysis of chest tube position and the need for secondary interventions.

Benns et al. J Trauma Acute Care Surg 2015.

P All patients presenting to the ED requiring a chest tube with confirmed placement by CT scan
Excluded: No CT scan, died early (< 24hrs), or had thoracotomy (<24hrs)

I Location of chest tube (rib level and position of the tube relative to the lung parenchyma)

C None (observational trial)

O Duration of chest tube (clinical judgment: no air leak, radiographic resolution or < 200mL drainage in 24hrs) and need for secondary intervention

Authors' Conclusion:

Chest tube location does not influence the need for secondary interventions as long as the tube resides in the pleural space. The severity of chest injury is the most important factor influencing outcome in patients undergoing tube thoracostomy fur trauma. Tube thoracostomy technique should focus on safe insertion within the pleural space and not on achieving a specific tube location.

Results

The data set consisted of 291 patients who had chest tubes placed in the emergency department with CT scans confirming position. There were 571 patients excluded because they died, had a thoracostomy or did not have a post tube CT scan. Most of the patients were male (81%) with a mean age of 40 years. Two-thirds of the patients had blunt trauma.

Duration of chest tube did not matter on location. Need for secondary intervention was also not associated with location.

Location did not matter.

A total of 48/291 (17%) of patients required secondary intervention. The most common thing needed was an additional chest tube (59%). Multivariate analysis demonstrated that AIS score, penetrating mechanism and initial chest tube output were significant risk factors.

Commentary

This was another retrospectives study challenging some chest tube dogma about location, location, location. Some limitations include:

1. *Retrospective:* This type of study can only demonstrate association not causation.
2. *Abstractors:* Again we know very little about who these people were, how were they trained, how they performed and did they agree with each other.
3. Missing Data: Always important to know how researchers handle missing data. There is no perfect study and there is always some missing data. This can significantly influence the results of a study.
4. *Selection Bias:* Decision was based on clinical grounds or findings on portable CXRs. Perhaps patients with loculated fluid or air or less severe injuries (small pneuothoraces) would benefit with a chest tube directed to the anterior/superior location.
5. *Exclusion Criteria:* No CT scan, died early (<24hrs) or had thoracotomy (<24hrs). I understand if they do not have a CT scan they will not know exact tube placement. However, what I want to know is does location matter for patients who require a chest tube in the ER due to injury/trauma. It should be consecutive patients. We don't really know if chest tube malposition may have contributed to death or the need for thoracotomy. Perhaps location did matter for those who die early or needed a thoracotomy. It would have been great to get confirm tube placement on all of those patients and compare it to all the patients who survived.

Clinical Application

Focus on getting the chest tube placed in the triangle of safety and try to place it superiorly and posteriorly, but don't worry too much if it is not "perfect" on the post insert CXR. What matters most is if the patient is doing well post procedure.

CONCLUSION VS COMMENTARY COMPARISON

We generally agree that location does not appear to matter as long as you get the tube into the pleural space.

STUDY QUALITY CHECKLIST

Were the abstractors trained before the data collection?	
Were the inclusion and exclusion criteria for case selection defined?	
Were the variables defined?	
Did the abstractors use data abstraction forms?	
Was the abstractors' performance monitored?	
Were the abstractors aware of the hypothesis / study objectives?	
Was the interobserver reliability discussed?	
Was the interobserver reliability tested or measured?	
Was the medical record database identified or described?	
Was the method of sampling described?	
Was the statistical management of missing data described?	
Was the study approved by the institutional or ethics review board?	

WHAT DO I TELL MY PATIENT?

In this case the patient was intubated so I would be speaking to her family. I would let them know she was stabbed in the chest that resulted in some internal bleeding and possibly a collapsed lung. The emergency department physician expertly put in a chest tube that drained out the blood. However, the CXR showed something else was going on. We therefore needed to take her to the operating room to repair an injury to the lung. This was done successfully and she is doing well.

References

Kong VY, Oosthuizen GV, Clarke DL. What is the yield of routine chest radiography following tube thoracostomy for trauma?. Injury. 2015 Jan 1;46(1):45-8.

Benns MV, Egger ME, Harbrecht BG, Franklin GA, Smith JW, Miller KR, Nash NA, Richardson JD. Does chest tube location matter? An analysis of chest tube position and the need for secondary interventions. Journal of Trauma and Acute Care Surgery. 2015 Feb 1;78(2):386-90.

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130 Low Dose Ketamine for Acute Pain Control in the Emergency Department

Case Scenario:
A 48-year-old man presents to the emergency department with acute lumbar pain after trying to lift a heavy garbage can. He says his pain is ten out of ten despite taking ibuprofen. He does not have any "red flags" and you are considering how to safely and effectively address his pain.

Clinical Question:
1) Is a sub dissociative dose of ketamine equivalent to a standard dose of morphine for control of moderate to severe pain in the emergency department?
2) Is the addition of low-dose ketamine to morphine superior to morphine alone in the emergency department pain patients?

Bottom LINE

1. For patients who have a contraindication to opioids such as allergy or hypotension, sub dissociative ketamine would be a reasonable option to consider for treating acute pain.
2. While further validation in other settings is needed, this study suggests ketamine as a relatively safe option for patients who do not achieve analgesia with high doses of morphine or are unable to tolerate them.

Question 1: Is a sub dissociative dose of ketamine equivalent to a standard dose of morphine for control of moderate to severe pain in the ED?

Intravenous Subdissociative-Dose Ketamine Versus Morphine for Analgesia in the Emergency Department: A Randomized Controlled Trial. Motov et al. Ann Emerg Med 2015

P

Patients aged 18 to 55 years who presented to emergency department of a single-center teaching hospital with acute abdominal, flank, back, or musculoskeletal pain score of five or more on a standard 11-point (0 to 10) numeric rating scale and required opioid analgesia, as determined by the treating attending physician.

✘ Exclusions: Pregnancy, breast-feeding, altered mental status, allergy to morphine or ketamine, weight ≤46 kg or ≥115 kg, unstable vital signs (systolic blood pressure <90 or >180 mm Hg, pulse rate <50 or >150 beats/minute, and respiration rate <10 or >30 breaths/minute), and medical history of acute head or eye injury, seizure, intracranial hypertension, chronic pain, renal or hepatic insufficiency, alcohol or drug abuse, psychiatric illness, or recent (within 4 hours) opioid use.

I

Ketamine at 0.3 mg/kg intravenously.

C

Morphine at 0.1 mg/kg intravenously.

O

Primary: Comparative reduction of numeric rating scale pain scores at 30 minutes.
Secondary: Incidence of rescue analgesia at 30 and 60 minutes.

Authors' Conclusion:

"Subdissociative intravenous ketamine administered at 0.3 mg/kg provides analgesic effectiveness and apparent safety comparable to that of intravenous morphine for short-term treatment of acute pain in the ED."

Background

Oligoanalgesia is defined as the lack of or inadequate pain control. There are many studies showing this is a big problem in the emergency department (Wilson and Pendleton, Motov and Khan) with some groups of patients being at greater risk for oligoanalgesia (elderly, women, mentally ill, certain ethnic groups, insurance status and children).

To raise awareness about oligoanalgeisa, the Joint Commission made pain the "*fifth vital sign*" in 2001. American physicians started being evaluated and compensated by means of patient satisfaction with emergency department pain control on factor. This provided misguided incentives for giving out opioids.

There are some disturbing trends reported by the Center for Disease Control(CDC) over the last few years. Between 1991 and 2010, prescriptions for opioid analgesics increased from about 75 million to 210 million according to the National Institute of Drug Abuse (NIDA). This was followed by an increase in abuse and overdose. The CDC estimates that narcotic pain relievers now cause or contribute to nearly three out of four prescription drug overdoses and about 15,000 deaths per year

In October 2012, American College of Emergency Physicians (ACEP) published practice guidelines regarding opioid including these Level C recommendations:

- Physicians should avoid the routine prescribing of outpatient opioids for a patient with an acute exacerbation of chronic non-cancer pain seen in the emergency department.
- The Prescriber should consider the patient's risk for opioid misuse, abuse or diversion.
- If opioids are prescribed on discharge, the prescription should be for the lowest practical dose for a limited duration.

If you want to watch a YouTube video that combines ACEP recommendations with a Taylor Swift song then check out Michael Barton's parody video called We are Never (Giving you Drugs in the ER).

Besides abuse, there are other well know limitations to using opioids including: allergy, respiratory depression, hypotension, nausea and vomiting.

Other options to manage acute pain in the emergency department are being explored. Ketamine is one of those options being actively studied. Ketamine is a NMDA receptor antagonist that exerts sedative, amnestic, and analgesic effects as a dissociative anesthetic. It has been used for rapid sequence and delayed sequence intubation.

However, ketamine has a historic bad reputation for raising intracranial pressure. We now know ketamine does not deserve this bad reputation (SGEM#93).

The use of Ketamine in the emergency department has been expanding lately. One area has been for procedural sedation. This was covered on SGEM#114: Ketofol – Does It Take Two to Make a Procedure Go Right?

A recent SGEMHOP covered a systematic review on sub dissociative-dose ketamine as an adjunct for pain control. There were only 4 studies included with just over 400 patients. The bottom line from SGEM#111 was that high-quality published evidence to support the use of sub dissociative-dose ketamine to quickly reduce acute pain in emergency department settings is lacking, but lower quality studies inconsistently demonstrate effectiveness with uniformly low risk of adverse effects.

Results

Ninety patients (45 ketamine and 45 morphine) were enrolled in this study. The patients' mean age was around 35 years of age and about two-thirds of patients were women. There were no differences between the groups in terms of demographic characteristics or baseline vital signs, pain scores, or chief complaint.

Primary Outcome: Change in mean pain scores was not significantly different in the ketamine and morphine groups: 8.6 versus 8.5 at baseline (mean difference 0.1; 95% CI: 0.46, 0.77) and 4.1 versus 3.9 at 30 minutes (mean difference 0.2; 95% CI: 1.19, 1.46; P=0.97). The 95% CI for the mean difference at 30 minutes according to the mixed-model regression SD was −0.77 to 1.05.

Secondary Outcomes: No difference in the incidence of rescue fentanyl analgesia at 30 or 60 minutes. No statistically significant or clinically concerning changes in vital signs were observed. No serious adverse events occurred in either group. However, patients in the ketamine group reported increased minor adverse effects (dizziness, disorientation) at 15 minutes post-drug administration.

Commentary

Not all emergency department patients with moderate to severe pain respond to or even tolerate opioids at standard doses. While some patients with high opioid tolerance prefer higher than standard doses, emergency staff do not.

There are few analgesics we can offer our patients and this trial adds more to the accumulating evidence that ketamine at a sub dissociative dose is a safe and effective alternative. Here are some limitations with this article:

1. ***Single Centre*:** This was a single center study done in New York so the results may not reflect your patient population.
2. ***Consecutive Patients:*** This was a convenience sample with patients being enrolled at various times of the day when both a study investigator and an emergency department pharmacist were available for medication preparation. This has the potential to introduce selection bias that would move us away from the truth.
3. ***Superior, Equivalence or Inferior?*** The author says it was an equivalence study. Equivalence trials are designed to confirm the absence of a significant clinical difference between treatments (Lesaffre E). To conclude that the two treatments are equivalent, then the two-sided 95% confidence interval should lie entirely within the interval −Δ to + Δ. They set the minimal clinically meaningful difference at 1.3 on the numeric rating scale. This was an equivalence study.

Commentary con't

4. ***Adverse Events:*** We cannot just consider potential benefit but we must also consider potential harm. There were statistically significant more adverse events in the ketamine group. This mainly consisted of dizziness, disorientation and mood changes. Remember that the study was powered to find a 1.3 difference on the numeric rating scale not for adverse events.
5. ***Blinding:*** The study was possibly un-blinded due to some patients in the ketamine group exhibiting nystagmus, a ketamine-specific reaction.

Clinical Application

I will consider sub dissociative dose ketamine as a second line agent for patients who cannot be treated with an opioid.

CONCLUSION VS COMMENTARY COMPARISON

We agree that a sub dissociative dose of ketamine (0.3mg/kg) appears effective for treatment of acute pain in the emergency department and has a similar reduction in a numeric rating scale to morphine. However, we are not as confident in commenting on safety as the study was not powered for this result and there were more adverse reactions with ketamine.

Study Quality Checklist

The study population included or focused on those in the ED	
The patients were adequately randomized	
The randomization process was concealed	
The patients were analyzed in the group to which they were randomized	
The study patients were recruited consecutively (ie., no selection bias)	
The patients in both groups were similar with respect to prognostic factors	
All participants (patients, clinicians, outcome assessors) were unaware of group allocation	
All groups were treated equally except for the intervention	
Follow-up was complete (i.e., at least 80% for both groups)	
All patient-important outcomes were considered	
The treatment effect was large enough and precise enough to be clinically significant	

Question 2: Is the addition of low-dose ketamine to morphine superior to morphine alone in the emergency department pain patients?

Low-dose ketamine improves pain relief in patients' receving intravenous opiods for acute pain in the emergency department: results of a randomized, double-blind, clinical trial.

Beaudoin et al. Acad Emerg Med Nov 2014

P

English-speaking adults (18 to 65 years old), moderate to severe pain (NRS>5/10) for < seven days, deemed appropriate for IV opioid analgesia by ED physician.

- ✘ Exclusions: Neurologic, respiratory or hemodynamic compromise; known or suspected allergy to ketamine or morphine; acute psych illness; history of stroke; renal insufficiency; liver failure; coronary artery disease; pregnant; breastfeeding; pain not moderate; severe with just IV opioids/other adjuncts; or unable to provide consent.

I

Group 1: Morphine 0.1mg/kg IV (max 10 mg) + ketamine 0.15mg/kg IV
Group 2: Morphine 0.1mg/kg IV (max 10mg) + ketamine 0.3mg/kg IV

C

Morphine 0.1mg/kg IV (max 10mg) + normal saline

O

Primary: Summed pain-intensity difference (SPID) at two hours (measured q30min) of >33%. This is different from the numeric rating scale from 0-10 that most of us are familiar with and was used in the last study. The clinically important change on the NRS is 1.3. The SPID is another recognized method to quantify clinically important difference in pain (Farrar et al 2000). It has been previously established that a 33%SPID represent a clinically important measurement in pain outcomes (Farrar et 2003).

Secondary: Numeric rating scale (NRS) score at each time point (0-10), total pain relief (5-point scale), adverse events, amount of rescue analgesia needed, time to rescue analgesia and global analgesia effectiveness (Silverman integrated analgesic [SIA] assessment score = SPID + rescue analgesia usage).

Authors' Conclusion:

"Low-dose ketamine is a viable analgesic adjunct to morphine for the treatment of moderate to severe acute pain. Dosing of 0.3 mg/kg is possibly more effective than 0.15 mg/kg, but may be associated with minor adverse events. Future studies should evaluate additional outcomes, optimum dosing, and use in specific populations."

Results

78 patients enrolled, 69 were randomized and 60 completed the study (20 per group).

Primary Outcomes: Combo treatment with morphine plus ketamine was superior to morphine alone. There was no difference observed between the higher vs. lower dose ketamine groups.

Pain Intensity	Control	Group 1	Group 2
SPID	4.0 (1.8-6.5)	7.0 (4.3-10.8)	7.8 (4.8-12.8)
%SPID	21% (10-37)	39% (22-86)	42% (29-80)
Achieve 33% SPID	25% (5/20)	50% (10/20)	70% (14/20)

Secondary Outcomes: Similar numbers of patients received rescue analgesia: There were more adverse events in the ketamine groups.

Commentary

1. *Small/Single Centre/Many Exclusions:* This was a small (20 in each group) single center study done in Rhode Island and therefore the results may not reflect your patient population. In addition, there were so many exclusion criteria it would be hard to find many patients that fit the strict study protocol
2. *Side Effects:* There were more adverse events in the ketamine+morphine group than the morphine group alone. These small studies are not powered for safety; however, ketamine has a fairly long history of being a safe drug.
3. *Multiple Drugs:* Going from monotherapy to combination therapy increases the risk of drug error. We need to be very careful when making systems more and more complex. Ketamine also comes in different concentrations that could compound the chance of error.

Commentary con't

4. *What are we Trying to Treat?* The right dose of morphine for the patient in pain is when they no longer request pain medication. We get fixated on the mg/kg rather than the looking at the patient.
5. *Now What?* So after we have successfully treated the acute pain in the emergency department what do we use when discharging them home for pain control? How long will their treatment last? Will the combination treatment result in less pain medication needed in the near term. All of these questions and more remain unanswered.

Clinical Application

I am going to use morphine as my first line agent unless there is a contraindication to using an opioid.

CONCLUSION VS COMMENTARY

COMPARISON

We generally agree with the author's conclusions.

Study Quality Checklist

The study population included or focused on those in the ED	👍
The patients were adequately randomized	👍
The randomization process was concealed	👍
The patients were analyzed in the group to which they were randomized	👎
The study patients were recruited consecutively (ie., no selection bias)	👎
The patients in both groups were similar with respect to prognostic factors	?
All participants (patients, clinicians, outcome assessors) were unaware of group allocation	👍
All groups were treated equally except for the intervention	?
Follow-up was complete (i.e., at least 80% for both groups)	👍
All patient-important outcomes were considered	👎
The treatment effect was large enough and precise enough to be clinically significant	👍

WHAT DO I TELL MY PATIENT?

We are going to give you some morphine to see if it improves your back pain?

If your back pain does not improve with morphine we can always try an additional medication called ketamine.

References

Motov S, Rockoff B, Cohen V, Pushkar I, Likourezos A, McKay C, Soleyman-Zomalan E, Homel P, Terentiev V, Fromm C. Intravenous subdissociative-dose ketamine versus morphine for analgesia in the emergency department: a randomized controlled trial. Annals of emergency medicine. 2015 Sep 1;66(3):222-9.

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GUEST SKEPTIC: Dr. Marcel Emond
Associate professor, Laval University, Quebec City, Canada

131 Gimme Some Antibiotics for Uncomplicated Skin Infections

Case Scenario:

A 26-year old male presents to the ED with a painful, reddened area on his right arm. No significant PMH, PSH, or social history, but reports allergy to Penicillin and cephalosporins.

He has an abscess 6cm in diameter with surrounding cellulitis. After I&D, you contemplate sending the patient home with antibiotic therapy.

The patient saw a news report on MRSA (methicillin-resistant Staphylococcus auereus) and is worried this may be involved in his infection.

Clinical Question:

For patients with uncomplicated skin infections, is clindamycin superior to trimethoprim – sulfamethoxazole?

Bottom LINE

For patients with uncomplicated cellulitis, TMP-SMX may represent an alternative to clindamycin in patients with no major comorbidities

Clindamycin versus Trimethoprim – Sulfamethoxazole for Uncomplicated Skin Infections.

Miller et al. NEJM. March 2015.

P

All patients between the ages of six months to 85 years with at least two of the following for 24 hours or more: erythema, swelling / induration, local warmth, purulent drainage, tenderness to pain / palpation.

Exclusion: Body site involvement requiring special management (e.g., perirectal, genital, hand), human or animal bites, high fever, immunosuppression, diabetes, chronic renal failure, morbid obesity, surgical site infection, or received antibiotics w/in 14 days that included anti-staph activity, residence in long term care facility, or majory surgery in previous 12 months

I

Clindamycin 300 mg PO TID x 10 days (or weight-based pediatric dose)

C

TMP-SMX 160-800 mg x 10 days BID (or weight-based pediatric dose)

O

Primary: Clinic cure at the test of cure (TOC) visit (7-10 days after completion of antibiotic course)

Secondary: Patients evaluated at the end of treatment at 30 days post 10 day antibiotic course (day 40) for symptoms resolution and medication-related adverse effects

Authors' Conclusion:

We found no significant differences between the efficacy of clindamycin and that of TMP-SMX for the treatment of uncomplicated skin infections in children and adults with no major coexisting conditions

Background

Skin and soft tissue infections (SSTIs) are a common reason for visits to the emergency department, hospital admissions, and may result in considerable morbidity and mortality.

Classically, it has been thought that beta-hemolytic Streptococci are the causative organisms for cellulitis and Staph species are commonly implicated in cases of skin abscesses.

More recently, MRSA has been recognized as a common cause of SSTIs.

Results

524 patients were enrolled in the study.

- 30% (155/524) were children.
- 53% had cellulitis, 31% had an abscess and 16% had both
- 40% of those cultured had S. aureus
- 77% (167/217) of the S. aureus were MRSA

In the intention to treat population, 80% of clindamycin patients and 78% of TMP-SMX patients had clinical cure at the test of cure (TOC) visit (p=NS).

No significant differences were found in subgroup analysis based on cellulitis, abscess, or mixed cellulitis/abscess, or causative organism.

One-month cure rates were similar between groups, and rates of adverse events were similar between groups. The adverse event rate was about 20% for both groups with the most common adverse event being diarrhoea (easy to smell but hard to spell) in 10% of patients. The discontinuation rate was similar between both groups also at 8%

Commentary

This was a high-quality randomized, controlled trial of two generically available antibiotics that have been around for a while. However, there are some major points of the study that limit its clinical applicability.

The Infectious Disease Society of America released its latest guideline for the management of skin and soft tissue infections in 2014. In this document, clindamycin is mentioned as an alternative treatment for mild cellulitis, but TMP-SMX is not mentioned at all as a recommended agent.

For patients with mild abscess, no antibiotic treatment is recommended. That is because the treatment of an abscess is typically cold hard steel. However, the IDSA does recommend clindamycin or TMP-SMX as treatment options for moderate abscess. It is likely that these patients with "moderate" abscesses would have been excluded from the present trial due to the severity of infection. Thus, for both cellulitis and abscess, the present study does not reflect the most current recommendations for management of skin and soft tissue infections.

TALK NERDY  TO ME

Commentary

There could also have been a problem with patient selection. Patients in this study were recruited from emergency departments, but also from urgent care clinics and clinics affiliated with the participating institutions. Therefore, some patients represented may not best reflect patients that we see in the emergency department.

They also did not explicitly state that the patients were recruited consecutively. This could have introduced some selection bias by the provider as to who was enrolled in the study. Furthermore, the exclusion criteria outlined in the paper's supplementary index were extensive, and resulted in a study population that was otherwise pretty healthy. This may be why the cure rates for a less-than-ideal cellulitis agent like TMP-SMX were surprisingly high.

Additionally, the IDSA guidelines recommend a five day treatment duration for cases of uncomplicated cellulitis. The 10-day treatment course used in this study is not congruent with that recommendation, and may not be translatable into everyday practice even if many clinicians use a seven day treatment course rather than five.

While the investigators accounted for comorbidities that may have influenced the results of the study, they did not describe skin and soft tissue infections that may have been secondary to trauma. This particular aspect is addressed in multiple sections of the IDSA treatment guidelines as influencing management. Additionally, patients with trauma-associated SSTI may benefit from a higher dose of TMP-SMX (2 double strength tablets BID) (Cadena J, et al).

The necessity of covering for MRSA in patients with skin abscesses is unclear. In a study by Pallin and colleagues, the addition of TMP-SMX to cephalexin for MRSA coverage in patients with cellulitis without abscess did not improve cure rates (Pallin DJ, et al). Additionally, in patients with abscess, for which MRSA coverage is recommended in the IDSA guidelines, several studies have demonstrated efficacy of antibiotic therapy that lacked MRSA coverage even in patients where MRSA was isolated when cultured (Moran GJ, et al).

However, the authors included culture information in the supplementary index for patients with cellulitis (without abscess) and non-purulent drainage, strangely. This leads me to question first of all the utility of cultures in these patients to begin with, as the skin is not a sterile site. But also wondering what to do with the information obtained from cultures, as it doesn't necessarily seem like it should be used to change management.

Finally, the authors comment that TMP-SMX has previously thought to be a poor choice for cellulitis, suggesting that their findings would support its use as comparable to clindamycin. This suggestion should be scrutinized, as the results apply to a pretty narrow patient population (that being a patient with nearly zero comorbid conditions, not with an SSTI secondary to trauma).

While this may be an attractive option for patients with multiple drug allergies not able to tolerate first line therapies, it's important to remember that needlessly starting anti-MRSA antibiotics is not without consequences.

Clinical Application

TMP-SMX may represent an alternative to clindamycin in patients with uncomplicated SSTIs, but this should be considered only in select patients.

CONCLUSION VS COMMENTARY

COMPARISON

While TMP-SMX appears to have similar efficacy to clindamycin for uncomplicated SSTIs in this trial, these results are applicable to only a select patient population. Additionally, TMP-SMX does not represent a first line option for uncomplicated cellulitis, and should only be considered after other options have been exhausted.

STUDY QUALITY CHECKLIST

The study population included or focused on those in the ED	
The patients were adequately randomized	
The randomization process was concealed	
The patients were analyzed in the group to which they were randomized	
The study patients were recruited consecutively (ie., no selection bias)	
The patients in both groups were similar with respect to prognostic factors	
All participants (patients, clinicians, outcome assessors) were unaware of group allocation	
All groups were treated equally except for the intervention	
Follow-up was complete (i.e., at least 80% for both groups)	
All patient-important outcomes were considered	
The treatment effect was large enough and precise enough to be clinically significant	

WHAT DO I TELL MY PATIENT?

It appears you have an uncomplicated skin infection. We are going to cut it open to release the infection and then send you home on an antibiotic. You should see your primary care provider for follow-up in the next 24-48hrs. It can take a few days to get better but if you are getting worse (more pain, fever, red line up your arm) or you are worried then come back the emergency department to be reassessed. Sometimes a different antibiotic is needed.

References

Miller LG, Daum RS, Creech CB, Young D, Downing MD, Eells SJ, Pettibone S, Hoagland RJ, Chambers HF. Clindamycin versus trimethoprim-sulfamethoxazole for uncomplicated skin infections. New England Journal of Medicine. 2015 Mar 19;372(12):1093-103.

GUEST SKEPTIC: Meghan Groth, PharmD, BCPS
Emergency Medicine Clinical Pharmacist, UMass Memorial Medical Center, Worcester, MA

132 One Balloon for Otitis Media with Effusion

Case Scenario:
A four-year old boy presents to the ED with his mother. The mother is worried he has another ear infection because the teacher thought he was having trouble hearing in class. The boy completed a course of antibiotics two months ago for acute otitis media. On exam, the child looks well and has no fever. Otoscopic examination demonstrate some fluid behind the tympanic membrane.

Clinical Question:
Can a nasal balloon autoinflation device be a safe and effective treatment for children with otitis media with effusion?

Bottom LINE

Autoinflation devices to treat otitis media with effusion do not have enough good evidence to recommend their use at this time.

Effect of nasal balloon autoinflation in children with otitis media with effusion in primary care: an open randomized controlled trial.

Williamson et al. CMAJ. Sept 2015.

P

Children aged 4 to 11 years with recent history of ear symptoms and otitis media with effusion in one or both ears confirmed by tympanometry

✘ Exclusion: Acute otitis media; clinical judgment to have high risk of risk of recurrence (Down's syndrome, Kartagener's (Primary Ciliary Dyskinesia), immunodeficiency state, etc; 4yo children not attending school or unable to comply with auto inflation device; recent or planned venting tube surgery; latex allergy; recent nose bleed

I

Autoinflation three times a day for one to three months

C

Usual Care

O

Primary: Tympanometric resolution of effusion at one month

Secondary: Tympanometric resolution of effusion at 3 months

- Study questionnaire at 1 and 3 months
- Weekly diaries up to 3 months (record days with hearing loss, earache, remission, recurrence)
- Tympanometric resolution in at least one affected ear per child per 3 months
- QOL measured at three months using OMQ-14, parents complete weekly diaries (hearing loss, earache, days off schools, days requiring pain relief, sleep disturbance)
- Hearing as determined by Two Alternative Auditory Disability and Speech Reception Test (TADAST) speech recognition

Authors' Conclusion:

Autoinflation in children aged 4 – 11 years with otitis media with effusion is feasible in primary care and effective both in clearing effusions and improving symptoms and ear-related child and parent quality of life.

Background

Otitis media with effusion or glue ear can be defined as a condition that that persists for more than six weeks. There were over two million cases diagnosed in the USA in 2004 with a cost of approximately four billion dollars.

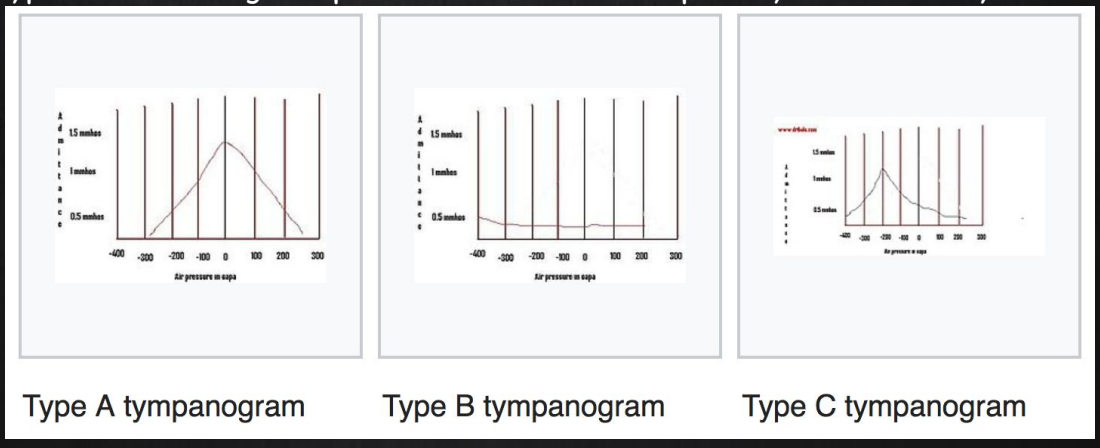
Otitis media with effusion has been reported as the most common chronic condition of childhood and the most common reason for surgery in this age group. The reason we are so concerned about these effusion is hearing loss. Fluid in the middle early can cause a conductive hearing loss that if unrecognized and untreated can translate to broader developmental difficulties.

There are a number of ways to check for middle ear effusions all with various strengths and weaknesses:

- *Otoscopy:* This allows you to look at the tympanic membrane and see if there is fluid but this does not tell you if the eardrum actually moves.
- *Pneumatic Otoscopy:* This gives you a more dynamic assessment of the tympanic membrane (does it move in response to pressure changes).
- *Tympanometry:* This give you objective/quantitative measure of the compliance of the tympanic membrane.
- *Pure Tone Audiometry:* This can determine the degree and type of hearing loss. Depending on the results it can suggest a conductive hearing loss due to fluid in the middle ear.

Tympanometric evaluation to diagnose otitis media with effusion can give three main results:

- Type A normal
- Type B (flat) abnormal
- Type C indicates negative pressure in middle ear and possibly an abnormality



Type A tympanogram | Type B tympanogram | Type C tympanogram

Various treatments have been tried for treating otitis media with effusion:

1. *Antibiotics – "our review do not support the routine use of antibiotics for children up to 18 years with otitis media with effusion".* Van Zon et al CDSR 2012
2. *Antihistamines/Decongestants – "No statistical or clinical benefit was found for any of the interventions or outcomes studied. However, treated study subjects experienced 11% more side effects than untreated subjects (number needed to treat to harm = 9).* Griffin and Flynn CDSR 2011

Background Continued

3. *Oral or Topical Nasal Steroids*: *"there is no evidence of longer-term benefit and no evidence that they relieve symptoms of hearing loss. We found no evidence of benefit from treatment of OME with topical intranasal steroids, alone or in combination with an antibiotic, either at short or longer-term follow up."* Simpson et al CDSR 2011

4. *Grommets (venting tubes)*: *"effect of grommets on hearing, as measured by standard tests, appears small and diminishes after six to nine months by which time natural resolution also leads to improved hearing in the non-surgically treated children"* Browning et al CDSR 2010

5. *Nasal Balloon Devices*: *"All of the studies were small, of limited treatment duration and had short follow-up. However, because of the low cost and absence of adverse effects it is reasonable to consider autoinflation whilst awaiting natural resolution of otitis media with effusion".* Perera et al CDSR 2013 This Cochrane review finished with a call for further research.

Results

Primary Outcome: Resolution at One Month:

- 36% (standard) vs. 47% (intervention)
- Adjusted Relative Risk (RR)=1.39 (95% CI 0.99–1.88)
- **RR=1.27 (95% CI 0.95–1.71)

Secondary Outcome: Resolution at Three Months:

- 38% (standard) vs. 50% (intervention)
- RR= 1.37 (95% CI 1.03–1.83)
- ** RR=1.22 (95% CI 0.92–1.63)

** Sensitivity Analysis: multiple imputation of all missing data using baseline variables

Harm to Autoinflation:

- Table #4 of the manuscript lists the adverse events by study group. They were fairly similar between standard care and autoinflation. However, there were more respiratory infections in the treatment group 15% vs. 10%. Most of these were mild afebrile rhinorrhea.
- There were also two children removed from the treatment group after randomization. One child was removed because of mild/early mastoiditis and the other due to otalgia. These two children had their data excluded from analysis as part of their "modified" intention to treat analysis.

Commentary

1. *Not Emergency Department Patients* – This was a pragmatic primary care study. It is not known if the child recruited from the office setting would be different than the child brought into the emergency department.
2. *Not Consecutive Patients* –There could be selection bias. These were not patients consecutively recruited presenting to the office. Despite otitis media with effusion being the most common chronic condition of childhood, it would have taken many more sites or more time to recruit enough children with this condition.
3. *Not Blinded* – Lack of blinding is one of the big limitation of this study, especially when it comes to the subjective secondary outcome measures. They say that a placebo was not possible. Why not just have balloons that can be inflated with much less pressure? Why not have a sham device that would not impact the eustachian tube. This could have minimized the placebo effect and made the secondary results much stronger.

Commentary cont'd

4. *Modified Intention to Treat Analysis (ITT)* – They performed a modified ITT (excluded children for whom no outcome measurements could be made). When they did the sensitivity analysis for missing data they got *"similar"* but smaller relative risk that were not statistically significant (crossed the line of no difference). They removed two children who had difficulty performing the technique. This should have been included in their analysis. They also removed two children in the treatment arm with adverse events (mastoiditis and otalgia)
5. *Surrogate Marker* – They used a surrogate marker of tympanometry rather than pure tone testing for hearing loss. This was because pure tone audiometry could not be done with adequate precision in a non-specialized setting. But hearing loss is a more patient oriented outcome than just having fluid in the middle ear. They had subjective hearing loss reported in their secondary analysis by parents/guardians. However, hearing loss was also to by determined by TADAST speech recognition but the results of these tests could be found in the published material.

Clinical Application

Will not change current management

CONCLUSION VS COMMENTARY COMPARISON

The conclusion at the end of the discussion state: "We have found use of autoinflation in young, school-aged children with otitis media with effusion to be feasible, safe and effective in clearing effusions, and in improving important ear symptoms, concerns and related quality of life over a 3-month watch-and-wait period. We do not think it was shown to be effective for the primary outcome, there were some concerning adverse events in the treatment group and it was underpowered to claim safety.

Study Quality Checklist

The study population included or focused on those in the ED	👎
The patients were adequately randomized	👍
The randomization process was concealed	👍
The patients were analyzed in the group to which they were randomized	👎
The study patients were recruited consecutively (ie., no selection bias)	👎
The patients in both groups were similar with respect to prognostic factors	?
All participants (patients, clinicians, outcome assessors) were unaware of group allocation	👎
All groups were treated equally except for the intervention	?
Follow-up was complete (i.e., at least 80% for both groups)	👍
All patient-important outcomes were considered	?
The treatment effect was large enough and precise enough to be clinically significant	👎

WHAT DO I TELL MY PATIENT?

YOUR CHILD HAS FLUID IN THE MIDDLE EAR. UNFORTUNATELY ANTIBIOTICS, ANTIHISTAMINES, DECONGESTANTS, AND NASAL STEROIDS DO NOT HELP CLEAR THIS UP QUICKER. MOST CHILDREN WILL GET BETTER WITHOUT TREATMENT AND IT CAN TAKE A FEW MONTHS. IF THEY GET A FEVER, EAR PAIN, OR YOU ARE WORRIED BRING THEM BACK IN AND I WILL TAKE A LOOK. IF THE PROBLEM PERSISTS PAST A FEW MONTHS WE WILL ARRANGE PURE TONE AUDIOMETRY TESTING TO CHECK ON YOUR SON'S HEARING.

REFERENCES

Williamson I, Vennik J, Harnden A, Voysey M, Perera R, Kelly S, Yao G, Raftery J, Mant D, Little P. Effect of nasal balloon autoinflation in children with otitis media with effusion in primary care: an open randomized controlled trial. Canadian Medical Association Journal. 2015 Sep 22;187(13):961–9.

GUEST SKEPTIC: Dr. Richard Lubell
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133 Just Beat It (Atrial Fibrillation) with Diltiazem or Metoprolol?

Case Scenario:
A 53-year old women with no PMH presents to the ED with palpitations for 4 days. She feels fatigued and short of breath. Her BP is 153/72 with a heart rate of 137 bpm. On physical exam, her heart rate is irregularly irregular and a 12-lead EKG confirms that the patient is in atrial fibrillation (Afib) with rapid ventricular response (RVR)

Clinical Question:
In patients with Afib and RVR, what agent, beta blocker or calcium channel blocker, will obtain rate control the fastest?

Bottom LINE

The best available evidence shows that diltiazem will achieve more rapid rate control in patients with atrial fibrillation than metoprolol

Diltiazem vs. metoprolol in the management of atrial fibrillation or flutter with rapid ventricular rate in the emergency department.

Fromm C et al. J Emerg Med. Aug 2015.

P Adult patients 18 years and older presenting with Afib or atrial flutter
Exclusion: SBP < 90 mmHg, ventricular rate greater than or equal to 220 bpm, QRS > 0.100 s, 2nd or 3rd degree AV block, T > 38.0 C, acute STEMI, known history of NYHA Class IV HF, active wheezing with a history of bronchial asthma or COPD

I Diltiazem 0.25 mg/kg (max dose 30mg) or metoprolol 0.15 mg/kg (max dose of 10mg) IV

C As above

O Primary: HR < 100 bpm within 30 minutes of drug administration
Safety: HR < 60 and SBP < 90 mmHg

Authors' Conclusion:

"Diltiazem was more effective in achieving rate control in ED patients with AFF and did so with no increased incidence of adverse effects."

Background

Atrial fibrillation is a commonly encountered dysrhythmia in the Emergency Department. Atrial flutter is less common but its management is very similar to that of atrial fibrillation.

There is quite a bit of debate on the management of patients with recent onset atrial fibrillation as to whether it is optimal to cardiovert patients or to leave them in atrial fibrillation.

We did a podcast looking at the Ottawa Aggressive Atrial Fibrillation Protocol on SGEM#88. It is a very effective approach to new onset atrial fibrillation but would not apply to this patient who has had four days of symptoms.

In patients with chronic atrial fibrillation or unknown time of onset and a rapid ventricular response, rate control and consideration and initiation of anticoagulation therapy are the standard emergency department approach.

Both beta-blockers and calcium channel blockers are commonly used for rate control in the emergency department, but it is unclear whether one of these agents is superior to the other as there is scant high-quality data on the topic (Demircan 2005).

Results

They had 52 patients enrolled in the study (28 in the metoprolol group, 24 in the diltiazem group). The mean age was 66 years and 53% were women.

The mean SBP was 132mmHg and DBP 89 mmHg. About 2/3 of the patients were new onset atrial fibrillation.

- Primary Outcome: Heart Rate < 100 beats per minute at 30 minutes

96% Diltiazem vs. 46% Metoprolol (NNT=2)

At every 5-minute interval, the diltiazem group was more likely to be rate controlled to a HR<100bpm than the metoprolol group. No difference was noted between groups in terms of hypotension or bradycardia.

Commentary

Using an informal poll of emergency physicians, diltiazem seems to be the preferred agent for rate control in atrial fibrillation with rapid ventricular response. Cardiologists, on the other hand, seem to prefer beta-blockers like metoprolol. This study appears to support the preference of emergency physicians. However, there are some issues with this paper that need to be discussed.

1. *Convenient Sample* – These were not consecutive patients presenting to the emergency department with rapid atrial fibrillation but rather a convenience sample. This can introduce selection bias into the study. We aren't given information on how many patients presented in atrial fibrillation with rapid ventricular response that would allow us to know how many were not approached for the study. This adds in the possibility that some patients were felt to not be good candidates and were thus not even considered for the study or there were patient characteristics that caused physicians to not approach them.

Commentary

2. *Stopped Trial Early* – The authors performed a sample size calculation and determined that 200 patients would have to be recruited to have 80% power to detect non-inferiority. However, only 54 patients were recruited and only 52 included for analysis. They explain that a blinded, independent biostatistician recommended stopping the study because more patients in the diltiazem group were reaching the desired endpoint.

- The researchers observed a large effect size during an interim analysis. This probably over inflates the effect size and it would probably have regressed to the mean if the study had continued.
- There are differences between superiority, non-inferiority and equivalence trials. I have asked my friend and Pediatric Emergency Medicine EM Super Hero Anthony Crocco at SketchyEBM to create a video to explain these concepts in more detail.
    a. Mulla et al. How to Use a Noninferiority Trial. JAMA 2012
    b. Montori et al Randomized Trials Stopped Early for Benefit: A Systematic Review. JAMA 2005
    c. Mueller et al. Ethical Issues in Stopping Randomized Trials Early Because of Apparent Benefit. Annals of Int Med 2007

3. *Drug Dosing* – A third critique is about the dosing of the different medications. The diltiazem was dosed at 0.25 mg/kg (with a max dose of 30 mg) and the metoprolol was given at 0.15 mg/kg (with a max dose of 10 mg). This may not be an equivalent comparison. I've talked with some of doctors I work with on this and they use a bit higher doses of metoprolol. However, the study authors did allow for additional doses to be given if rate control was not achieved at 15 minutes.

4. *Patient Oriented Outcome* – We question whether or not achieving a heart rate < 100 bpm in 30-minutes is an important patient oriented outcome. It's definitely not a hard patient centered outcome like death but you're not going to see much, if any, death when it comes to rate control. It would have been nice to have additional longer term outcomes aside from simply 30 minutes after drug administration. Did the patients stay rate controlled? Did either of the groups (once rate controlled) require additional medications to stay rate controlled and if so how much? I think these are important questions to answer.

5. *External Validity* – There were some other issues including external validity, as this was a single center study. This isn't an issue for Swami because this study was done up the street from his hospital in the Bronx and they've got an inner-city population similar to his. In contrast, this may not apply to smaller community or rural hospitals.

Despite these limitations, this study represents some of the best evidence on this particular topic. There is limited research looking at the optimal agent for rate control. Bryan Hayes did an excellent review of all the literature on this topic for ALiEM some time ago and recently updated that post with this study.

Clinical Application

Although the evidence is sub-optimal and this study has some flaws, this set of data defends emergency physicians use of diltiazem for rate control in atrial fibrillation with rapid ventricular response.

CONCLUSION VS COMMENTARY COMPARISON

I agree with the authors' conclusions. Despite the above limitations, they did demonstrate non-inferiority of diltiazem to metoprolol for rapid rate control in patients with AF with RVR and this goes along with my clinical experience.

Study Quality Checklist

The study population included or focused on those in the ED	👎
The patients were adequately randomized	👍
The randomization process was concealed	👍
The patients were analyzed in the group to which they were randomized	👍
The study patients were recruited consecutively (ie., no selection bias)	👎
The patients in both groups were similar with respect to prognostic factors	👍
All participants (patients, clinicians, outcome assessors) were unaware of group allocation	👍
All groups were treated equally except for the intervention	👍
Follow-up was complete (i.e., at least 80% for both groups)	👍
All patient-important outcomes were considered	👎
The treatment effect was large enough and precise enough to be clinically significant	👍

WHAT DO I TELL MY PATIENT?

It appears that the cause of your symptoms is that your heart is in an irregular rhythm called atrial fibrillation. Your heart rate is very high and so we need to give you medicine to reduce it. This will also make you feel more comfortable. We have two major medication choices but the best available evidence indicates that a medication called diltiazem will get you rate controlled the fastest.

References

Fromm C, Suau SJ, Cohen V, Likourezos A, Jellinek-Cohen S, Rose J, Marshall J. Diltiazem vs. metoprolol in the management of atrial fibrillation or flutter with rapid ventricular rate in the emergency department. Journal of Emergency Medicine. 2015 Aug 1;49(2):175-82.

GUEST SKEPTIC: Dr. Anand Swaminathan
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134 Listen, to what the British doctors say about LPs post CT for SAH

Case Scenario:
A 34-year old woman presents with acute onset of headache peaking in 30 minutes with no recent trauma, focal deficits, and a normal neurological examination.

Clinical Question:
In emergency department acute headache patients, how frequently does LP diagnose subarachnoid hemorrhage (SAH) after an unremarkable CT scan?

Bottom LINE

In this study, one patient would be diagnosed with SAH out of every 250 patients receiving a LP who presented to the ED with a headache that did not have their bleed identified on CT scan.

An observational study of 2248 patients presenting with headache, suggestive of Subarachnoid Hemorrhage, that received a lumbar puncture following a normal CT head

Sayer et al. Acad Emerg Med. Nov 2015.

P Adult patients (2248 total, > 17 years old) presenting to one of six urban EDs in the United Kingdom with acute headache suspicious for subarachnoid hemorrhage, who had both a negative CT and a lumbar puncture performed.

I LP to achieve identification of CT-negative SAH patients

C None

O Incidence of positive LP (defined only by spectrophometric detection of bilirubin, not by any CSF RBC count) and proportion with cerebral aneurysm identified.

Authors' Conclusion:

In patients presenting to the ED with acute, non-traumatic severe headache, LP to diagnose or exclude SAH after negative head CT has a very low diagnostic yield, due to low prevalence of the disease and uninterpretable or inconclusive samples. A clinical decision rule may improve diagnostic yield by selecting patients requiring further evaluation with LP following non-diagnostic or normal non-contrast CT brain imaging

Background

Headaches represent around 2% of all emergency department visits. Of these presentations 1–3% turn out to be a subarachnoid hemorrhage (SAH) (Edlow, Vermeulen, Perry, Morgenstern).

About 5% of SAH are misdiagnosed on the first emergency department assessment (Vermeulen). This is partly because 50% of SAH present with no neurologic deficit (Weir).

Dr. Jeff Perry and his team have tried to create a clinical decision tool to rule out SAH for acute headaches (SGEM#48). The Ottawa SAH Tool contains six variables to decide if a CT scan is necessary.

Applying the tool could decrease the miss rate of SAH from about five percent down to almost zero with a slight increase in utilization. However, the tool needs further evaluation in implementation studies before it is ready for "*prime time*".

Traditional methods of working up a SAH has been non-contrast CT followed by a lumbar puncture (LP). Dr. David Newman has questioned this dogma on his SMART-EM podcast. He suggested LPs are not always needed after a negative CT scan.

Dr. Newman calculated the number needed to LP to identify one SAH for which an intervention was indicated to be 700, prompting the question "are you part of the '700 Club'?" Should any of us be part of the 700 Club?

Results

The population was 45% male with a mean age of 41 years. Using the authors' spectrophotometric criteria for the total population evaluated (2,248 patients), the LP results broke down as follows:

- 4% positive
- 13% inconclusive
- 16% un-interpretable
- 67% negative

Of the *92 "positive"* LP results, 9 were identified with an aneurysm (9/2248 = 0.4%), which equates to 250 LPs to identify one aneurysm.

Number Needed to Tap (NN_{Tap}) of 250 to diagnose one aneurysm not picked up on CT

Commentary

This was a retrospective study including acute, non-traumatic adult headache patients with suspected SAH presenting to one of six urban training EDs in the UK between 2006 and 2011. Eligible subjects had a non-diagnostic head CT and had a lumbar puncture performed.

Commentary Continued

1. *Spectrophotometry to Evaluate CSF*: The authors' note using appropriate chart review methods and evaluated only spectrophotometric CSF analysis, not CSF RBC counts or visual xanthochromia. This outcome may be problematic since 99% of North American hospitals use visible xanthrochromia rather than spectrophotometry to evaluate for CSF bilirubin. Emergency department providers at centers that lack spectrophotometry would benefit from understanding the sensitivity, specificity, and likelihood ratios and interval likelihood ratios for CSF RBCs, although that becomes problematic with traumatic taps. However, traumatic LPs are a real-world problem and these authors had access to LP results that could have been analyzed as a secondary outcome.

2. *Differential Verification Bias (Double Gold Standard)*: This occurs when the test results influence the choice of the reference standard. So a positive index test get 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. Since only LP-positive patients routinely underwent additional neuroimaging (CTA or MRA), this study is at risk for differential verification bias that lowers estimates of sensitivity and specificity for disease processes that only become apparent during periods of follow-up (Understanding the Direction of Bias). Un-interpretable LPs were only evaluated at two (out of six) sites and only 5/28 (18%) and 17/56 (30%) had further imaging at those sites so unrecognized cerebral aneurysms probably occurred. Prospective studies would have the benefit of routine criterion standard testing for all patients or alternatively a period of follow-up to ensure that *"negative"* LP patients were not false-negatives with subsequent symptomatic SAH at a later date.

3. *Chart Review Methods*: The authors' reference chart review methods (Gilbert et al), but they do not describe them explicitly in their methods. Who abstracted the data from the medical records? How were these individuals trained and monitored? Were they blinded to the study hypothesis? Was a standardized abstraction form used? Was inter-rater reliability of chart abstraction assessed for key variables? Without understanding the authors' specific chart abstraction methods, it is not possible to meaningfully evaluate the possibility of bias in this study.

4. *More Details on Time to CT and Time to LP*: Since CT is less accurate for SAH beyond 12-hours after the onset of headaches, additional details about the average delay between headache and imaging is important to understand. Also, theoretically at least 12-hours must elapse between headache onset (sentinel bleed) and formation of CSF bilirubin, so the timing of headache onset and LP should also be reported.

5. *Temporal Bias*: Diagnostic tests that rely upon evolving imaging technology are sometimes at risk for temporal bias in which improved ability to obtain high-quality images or finer anatomical cross-sections yield more accurate results (Evidence-Based Emergency Care: Diagnostic Testing and Clinical Decision Rules, 2nd Edition, 2013, pages 54- 64). Since CT technology was evolving between 2006 and 2011, readers should interpret these results conservatively in 2015 and beyond. In other words, when multi-slice CTs (64-slice, 128-slice) are used in your ED today they probably detect CSF blood with even higher resolution than in 2006, resulting in higher sensitivity of the initial CNS imaging, and an even higher number needed to LP than this study suggests.

Clinical Application

Contrary to classic teaching, LP in the setting of acute, non-traumatic headache of <12 hours duration concerning for SAH rarely yields the elusive cerebral aneurysm diagnosis and is often falsely positive or inconclusive.

CONCLUSION VS COMMENTARY COMPARISON

In the setting of acute, non-traumatic headache presenting to the ED, a multi-slice CT (16-64 slice) that does not demonstrate radiographic evidence of SAH is likely sufficient to rule-out a SAH in most patients.

STUDY QUALITY CHECKLIST

The clinical problem is well-defined	👍
The study population represents the target population (ie no spectrum bias)	👍
The study population included or focused on those in the ED	👍
The study patients were recruited consecutively (ie no selection bias)	👎
The diagnostic evaluation was comprehensive and applied equally to all patients (ie verification bias)	👎
All diagnostic criteria were explicit, valid, reproducible (ie no incorporation bias)	👎
The reference standard was appropriate (ie no imperfect gold-standard bias)	👍
All undiagnosed patients underwent sufficiently long/comprehensive follow-up (ie no double gold-standard bias)	👎
The L.R.(s) of the test(s) in presented or can be calculated from the information provided	👎
The precision of the measure of diagnostic performance is satisfactory	👎

WHAT DO I TELL MY PATIENT?

Sudden onset headaches are clinically concerning for SAH, which can have devastating long-term consequences if misdiagnosed. Unfortunately, migraine headaches outnumber SAH headaches 50:1 in ED settings and do not benefit from CT-imaging of your brain, evaluation of your cerebrospinal fluid, or surgery. Modern CT scanners are very good at identifying blood in your brain from a SAH, if the CT is obtained within 12-hours of when the headache began. Older research indicated that only 9/10 SAH were detected by a CT so evaluation of fluid around your brain (CSF) was recommended to be completely certain that SAH was not the cause of the headache. Newer research indicates that CT scans almost never miss the diagnosis of SAH and that 250 lumbar punctures (LP) are needed to identify one cerebral aneurysm that CT missed. LPs are not benign procedures and can cause post-LP headaches, infections, nerve damage, and bleeding around your spinal cord.

References

Sayer D, Bloom B, Fernando K, Jones S, Benton S, Dev S, Deverapalli S, Harris T. An observational study of 2,248 patients presenting with headache, suggestive of subarachnoid hemorrhage, who received lumbar punctures following normal computed tomography of the head. Academic Emergency Medicine. 2015 Nov 1;22(11):1267-73.

GUEST SKEPTIC: Dr. David Sayer
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135 The answer my friend is blowin' in your nose – High flow nasal oxygen

Case Scenario:
A 60-year-old male with no PMH presents to the ED with a 3 day history of cough, fever, and increasing shortness of breath. He is tachypneic with a respiratory rate of 28 and an oxygen saturation of 89% despite facemask oxygen, but he mentating normally. Your respiratory therapist asks you whether you want her to try the new high flow nasal oxygen machine in the ED?

Clinical Question:
In adult ICU patients with hypoxic respiratory distress not due to COPD, asthma, or CHF, who do not require immediate intubation, does high-flow oxygen therapy or non-invasive ventilation therapy compared to standard therapy alone, reduce the rate of endotracheal intubation and improve outcomes?

Bottom LINE

High flow nasal oxygen can be another tool in the toolbox to address patients in acute respiratory distress, but does not appear to be superior to standard of care or non-invasive positive pressure ventilation (NIV)

High-flow oxygen through nasal cannula in acute hypoxemic respiratory failure. Frat JP et al. NEJM. June 2015.

P

Adult ICU patients with acute hypoxic respiratory failure

Inclusion: All 4 of the following: RR > 25/min, PO2/FiO2 </= 300, pCO2 </= 45 mmHg, no clinical underlying chronic respiratory failure

Exclusion: PaCO2 > 45 mmHg, exacerbation of asthma or COPD, cardiogenic pulmonary edema, hemodynamic instability, use of vasopresors, GCS of 12 or less, contraindications to NIV, urgent need to intubate, DNR ORder

I

High flow nasal oxygen (HFNO)

Non-invasive positive pressure ventilation

C

Standard face mask oxygen

O

Primary: Rate of intubation at 28 days

Secondary: mortality in ICU, mortality at 90 days, duration of ICU stay, number of ventilator free days. (Although at clinicaltrials.gov the secondary outcome was originally ventilator free days at 28 days and ICU morbidity at 28 days)

Authors' Conclusion:

In patients with nonhypercapnic acute hypoxemic respiratory failure, treatment with high-flow oxygen, standard oxygen, or NIV did not result in significantly different intubation rates. There was a significant difference in favor of high-flow oxygen in 90-day mortality

Background

High flow nasal oxygen is a novel device that actively humidifies and heats air to make flows of up to 60 liters a minutes tolerable. These incredibly high flows are important, because in order to provide 100% fiO_2 to patients in respiratory distress, we must be able to match their minute ventilation.

High flow nasal oxygen also offers the theoretical benefits of low levels of PEEP and allows for much easier communication with our patients.

It has gained popularity in pediatrics for the treatment of severe bronchiolitis and it is seeing wider adoption among adult patients.

Results

A total of 310 patients were included in the analysis, 106 in the high flow oxygen group, 94 in the standard oxygen group, and 110 in the noninvasive ventilation group.

Primary Outcome: Rate of intubation at 28 days

– No statistical difference.

- Standard O2: 47% (95% CI 37–57%)
- High Flow Nasal O2: 38% (95% CI 29–47%)
- Non–Invasive Ventilation: 50% (95% CI 41–59%)
- Not statistically significant (p=0.18)

Secondary Outcome – ICU Mortality at 90d: Standard 23% vs. High flow 12% vs. NIV 28% (statistically different)

- Standard O_2: 23% (95% CI 16–33%)
- High Flow Nasal O_2: 12% (95% CI 7–20%)
- Non–Invasive Ventilation: 28% (95% CI 21–37%)
- HR 2.01 Standard vs. HFNO (95% CI 1.01–3.99 p=0.046)
- HR 2.50 NIV vs. HFNO (95% CI 1.31–4.78 p=0.006)

Commentary

This was a multicenter trial attempting to ask an important question in critical care medicine. However there were a number of concerns/limitations in this study that threaten the validity of the conclusions.

TALK NERDY TO ME

Commentary Cont'd

1. *Exclusion/Inclusion* – We see a lot of patients that require respiratory support. They had close to 5,000 patients with acute respiratory failure. Over 2,000 patients were excluded with almost 1,400 for chronic lung disease and close to 700 because of cardiogenic pulmonary edema. We know from many studies that patients with COPD and cardiogenic pulmonary edema have a mortality benefit from NIV (Ram et al and Vital et al).Of the 525 eligible for inclusion, 160 had *"logistic"* reasons. It is not clear what that means but it could have introduced some selection bias and negated the recruitment of consecutive patients.The vast majority of these patients (>80%) had a diagnosis of pneumonia. This makes it difficult to extrapolate to all patients with acute hypoxic respiratory distress.
2. *Not Blinded* – This could have introduced some bias into the results by influencing the treating staff not to intubate the intervention group compared to the control. However, they did have pre-specified criteria for endotracheal intubation, some of which was objective while other criteria was subjective (copious tracheal secretions).
3. *Contamination* – There was a fair amount of contamination between the groups. This was because it was left up to the treating physicians to try NIV for the standard group or HFNO group if the patient was looking worse. For example, 50% of the non-invasive group was on positive pressure for 8 hours or less each day, and the remainder of the time they were wearing a standard facemask. Similarly, the high flow oxygen group may have been put on non-invasive ventilation before intubation, although they don't tell us how many actually were. This amount of cross-over/contamination between groups could have impacted the ITT analysis.
4. *Power* – This was a negative trail. They powered the study to detect a 20% difference in intubation rate and failed to achieve this result. That does not mean there is no difference or that the treatments are equivalent. This was a superiority trial and we can only conclude that the treatments were not show to have 20% superiority to the control.
5. *Secondary Outcome* – They highlight in their conclusion the significant difference in mortality at 90 days. The study was not powered for mortality but rather to demonstrate an absolute difference of 20% in intubation rates assuming an intubation rate of 60%. In addition, if you search ClinicalTrial.gov for their protocol it states the secondary outcome was ICU *morbidity* at 28 days, not mortality and mechanical ventilation-free to day 28. This is in contrast to the listed secondary outcomes of mortality in the ICU, mortality at 90 days, the number of ventilatory-free days between day 1 and day 28, and the duration of ICU stay. The lack of power and differences between published paper and original protocol should make us more skeptical of the secondary results.

Clinical Application

I am comfortable using NIV and will probably continue doing this given the good evidence to support this practice. However, for those patients not able to tolerate NIV, high flow nasal oxygen would be a reasonable option to try.

CONCLUSION VS COMMENTARY COMPARISON

We agree that the three different oxygenation strategies did not result in significantly different intubation rates.

We are less enthusiastic about the secondary endpoint that showed decreased mortality with high flow nasal oxygen, but think this is an interesting finding that should generate a hypothesis for future research.

STUDY QUALITY CHECKLIST

The study population included or focused on those in the ED	👎
The patients were adequately randomized	👍
The randomization process was concealed	👍
The patients were analyzed in the group to which they were randomized	👍
The study patients were recruited consecutively (ie., no selection bias)	👍
The patients in both groups were similar with respect to prognostic factors	👍
All participants (patients, clinicians, outcome assessors) were unaware of group allocation	👎
All groups were treated equally except for the intervention	👎
Follow-up was complete (i.e., at least 80% for both groups)	👍
All patient-important outcomes were considered	👍
The treatment effect was large enough and precise enough to be clinically significant	👎

WHAT DO I TELL MY PATIENT?

Your current oxygen level is low and I think you require supplemental oxygen. We have three different types of oxygen mask: the usual one you are wearing, a tight fitting high-pressure mask, and a mask that only goes in the nose. The current evidence indicates they will probably all work for you, so you should tell us which seems the most comfortable.

References

Frat JP, Thille AW, Mercat A, Girault C, Ragot S, Perbet S, Prat G, Boulain T, Morawiec E, Cottereau A, Devaquet J. High-flow oxygen through nasal cannula in acute hypoxemic respiratory failure. New England Journal of Medicine. 2015 Jun 4;372(23):2185-96.

GUEST SKEPTIC: Dr. Justin Morgenstern
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136 CPR – Man or Machine?

Case Scenario:

65-year old male has a witnessed cardiac arrest. He receives immediate CPR, early defibrillation, one round of ACLS medications. He arrives via EMS to your ED, where they tell you that he has had a total of 10 – 15 minutes of CPR with no return of spontaneous circulation. You are working in a small community ER with limited staffing.

The patient was already intubated by EMS, but the patient is still requiring CPR. There is a mechanical CPR device in your department and you are considering using it. You cannot recall any trials that have ever shown benefit in clinically important outcomes for adult patients with out-of-hospital cardiac arrest (OHCA), but you also don't have the staffing to continue prolonged CPR.

Clinical Question:

Are mechanical chest compression devices superior to manual chest compression when used during resuscitation from OHCA?

Bottom LINE

Mechanical chest compression devices do not appear superior to manual chest compression for out of hospital cardiac arrest.

Mechanical Chest Compression for Out of Hospital Cardiac Arrest: Systematic Review and Meta-Analysis.
Gates et al. Resuscitation Sept. 2015.

- **P** Adult patients following out of hospital cardiac arrest
- **I** Mechanical compression devices
- **C** Manual compression
- **O** Return of spontaneous circulation (ROSC), survival of event, overall survival and survival with good neurologic outcome.

Authors' Conclusion:

Existing studies do not suggest that mechanical chest compression devices are superior to manual chest compression, when used during resuscitation after out of hospital cardiac arrest."

Background

In cardiac arrest, high quality, uninterrupted CPR has been promoted as being essential to help improve survival rates. This was emphasized again in the American Heart Association (AHA) 2015 guidelines. Besides encouraging providers to have adequate compression rate and depth, they also want providers to minimizing interruptions in compressions. Great summaries of these new AHA guidelines can be found at BoringEM.

In theory, mechanical CPR should provide CPR at a standard depth and rate for prolonged periods without a decline in quality and without interruptions, which should help improve survival and survival with good neurologic outcomes.

There are many types of mechanical chest compression devices but the two main technologies can be generalized as piston devices and load-distributing bands. The piston driven devices work by compressing on the chest in an up and down type of motion, similar to how we do manual CPR. The load distributing bands wrap all the way around the chest and shorten and lengthen which provides more of a rhythmic type of chest compression.

To date, we are not aware of any individual trials have ever shown superiority on clinically important outcomes for adult patients with OHCA, regardless of device.

A new study was published in NEJM last week that questioned the importance of continuous chest compressions. Their results showed no superiority to continuous chest compressions by EMS. If you want the SGEM to put our skeptical eye upon this study and do a structured critical review, then vote for this paper using Hot or Not function on the SGEM.

Results

Five randomized trials were included in the analysis with over 10,000 patients.

No superiority with mechanical chest compression devices

- ROSC: OR 0.96 (CI 0.85 – 1.10)
- Survival of Event: OR 0.95 (CI 0.85 – 1.07)
- Survival to Discharge or at 30 days: OR 0.89 (CI 0.77 – 1.02)
- Survival with Good Neurological Outcomes: OR 0.76 (CI 0.53 – 1.11)

TALK NERDY TO ME

Commentary

Despite having over 10,000 patients with OHCA, this study found no statistically significant evidence of benefit with the use of mechanical chest compression devices. It also found no evidence of harm. There were a number of concerns/limitations with this meta-analysis:

1. *Confidence Intervals*: There were relatively wide confidence intervals (CI) around their point estimates despite the large number of patients in the study. This was most likely due to the low survival rate from OHCA. Confidence intervals describe the range around a point estimate. The wider the CI the less certain the point estimate is the "truth". The smaller or narrower the CI the more certain the point estimate is the "truth".

2. *Quality of CPR*: The quality of CPR provided in the manual group was not documented in studies. This is an important point that cannot be emphasized enough. If manual CPR was high quality, then maybe mechanical devices may not seem as good, but if the CPR is low quality, then mechanical devices may be better.

3. *Blinding*: Blinding of patients and EMS providers to the type of CPR used was not possible. However, outcome assessors to group allocation should also be blinded to avoid introducing bias. This may not be important to things like ROSC, survival to hospital and survival to discharge, but could be important when assessing neurological outcomes. Only one of the five studies explicitly stated the people assessing neurological status were blinded to the treatment group. The bias should have been in favor of the intervention (mechanical CPR) and given the lack of superiority found would strengthen confidence in the findings of no superiority.

4. *Cognitive Offloading*: CPR is a means to an end. In other words doing high quality, CPR is important, but this is not the end point. Instead this is a way to continue to perfuse the brain while we figure out what caused the OHCA. Therefore, mechanical CPR is a way to cognitively offload our minds about depth of compressions, rate of compressions, while we try and figure out why our patient arrested. Certainly, none of the studies showed inferiority of mechanical CPR, just no superiority to manual CPR.

5. *Missing Data*: An important part of any study is to know how much data was missing for analysis. We like to see at least 80% follow-up. While the overall missing data was low, there were some important areas where the missing data was high. Some trials were missing information on assessment of neurologically intact survival. This missing data was concentrated among survivors. In one study, about 3% of participants had missing data for modified Rankin Scale (mRS). They represented 28% of survivors. In other words, 28% of survivors in this one study lacked data for this important outcome. This could have introduced bias that systematically moves us away from the "truth".

Clinical Application

Mechanical CPR still has a role in cardiac arrest. Imagine working in an ED where you are the lone doctor with minimal staff. You only have so many people that can perform CPR before they get tired and the quality of the CPR decreases. Imagine another scenario like being on the back of an ambulance or a helicopter as a patient is being transported. Mechanical CPR may be higher quality and safer for the crew than manual CPR.

STUDY QUALITY CHECKLIST

The clinical question is sensible and answerable	
The search for studies was detailed and exhaustive	
The primary studies were of high methodological quality	
The assessment of studies were reproducible	
The outcomes were clinically relevant	
There was low statistical heterogeneity for the primary outcomes	***
The treatment effect was large enough and precise enough to be clinically significant.	

*** Yes and no. There was low heterogeneity for survival of event and survival to discharge. The heterogeneity was high ROSC and survival with good neurological outcome

CONCLUSION VS COMMENTARY

COMPARISON

We generally agree with the author's conclusions.

WHAT DO I TELL MY PATIENT?

You inform his wife that you are going to apply a mechanical device to help continue high quality CPR long enough to get her husband to the cath lab.

References

Gates S, Quinn T, Deakin CD, Blair L, Couper K, Perkins GD. Mechanical chest compression for out of hospital cardiac arrest: systematic review and meta-analysis. Resuscitation. 2015 Sep 1;94:91–7.

GUEST SKEPTIC: Salim Rezaie, MD
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137 A foggy day – Endovascular treatment for acute ischemic stroke

Case Scenario:
An 78-year-old woman presents to your emergency department with right arm weakness and slurred speech for the last two hours. She has a history of hypertension and diabetes. A CTA is performed that shows an Intracranial arterial occlusion of the right M1 middle cerebral artery segment.

Clinical Question:
Do endovascular therapies for acute ischemic stroke lead to improved neurological outcomes when compared to medical therapies alone and what is the effect size?

Bottom LINE

Despite its methodological rigor, Badhiwala et al's meta-analysis brings us no closer to certitude. It serves to place an objective number on the current ambiguous state of the data concerning endovascular therapy for acute ischemic stroke. The inherent value of the statistical manipulations in this pooled data set is unclear. This analysis provides little utility over our unstructured judgment of each respective trial's importance, while validating our suspicion that these trials are examining very different populations.

Endovascular Thrombectomy for Acute Ischemic Stroke A Meta-analysis Badhiwala et al. JAMA 2015.

P Varied depending on primary trial's inclusion and exclusion criteria. Essentially, patients presenting with signs and symptoms of acute ischemic stroke with either clinical or radiographic evidence of large vessel occlusion conducive to endovascular intervention.

I Various endovascular therapies including intra-arterial tPA and clot retrieval devices.

C Optimal medical therapy which included the use of IV tPA in the majority of the patients.

O Functional neurological status at 3-months, as assessed by an ordinal analysis of the modified Rankin Scale (mRS).

Authors' Conclusion:

"Among patients with acute ischemic stroke, endovascular therapy with mechanical thrombectomy vs. standard medical care with tPA was associated with improved functional outcomes and higher rates of angiographic revascularization, but no significant difference in symptomatic intracranial hemorrhage or all-cause mortality at 90 days."

Background

Prior to the publication of MR CLEAN and the four trials published in its wake, the data regarding endovascular therapy has been consistently negative. Over the past year five RCTs examining endovascular therapy for acute ischemic stroke have been published. In direct contrast to the three trials published in 2013, all of the recent trials were impressively positive.

Because of methodological flaws, the true size of benefit these interventions provide is still unclear. Without an understanding of this effect size, it is difficult to assess whether this benefit justifies the resources required to support its implementation on a national level.

Results

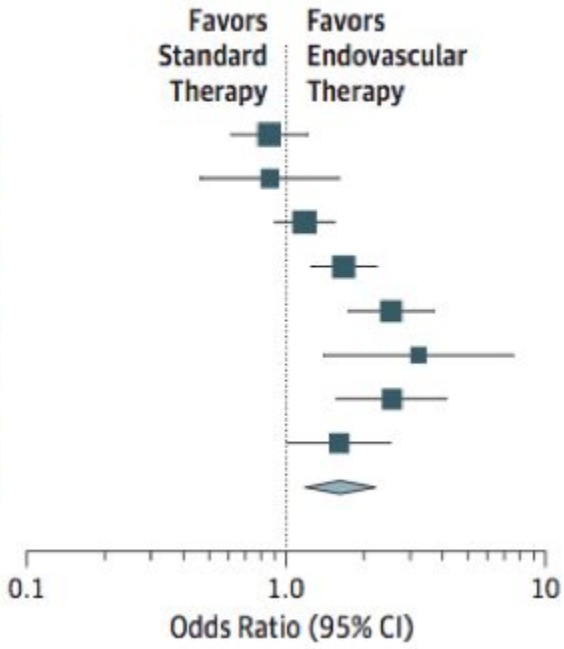
In their pooled analysis, the authors found a shift towards improved functional outcomes at 90-days in the patients randomized to receive endovascular therapy when compared to standard care.

Odds Ratio 1.56 (95% CI, 1.14–2.13 p=0.005)

B Reduced disability at 90 d

Source	Odds Ratio (95% CI)	P Value	Weight, %
SYNTHESIS,[26] 2013	0.86 (0.60-1.23)	.40	14.2
MR RESCUE,[27] 2013	0.86 (0.45-1.63)	.65	10.1
IMS III,[28] 2013	1.17 (0.88-1.57)	.28	15.3
MR CLEAN,[29] 2015	1.66 (1.22-2.28)	.001	14.9
ESCAPE,[30] 2015	2.53 (1.70-3.79)	<.001	13.6
EXTEND-IA,[31] 2015	3.22 (1.36-7.61)	.008	7.5
SWIFT-PRIME,[32] 2015	2.55 (1.53-4.26)	<.001	11.9
REVASCAT,[33] 2015	1.57 (0.97-2.55)	.07	12.4
Overall	1.56 (1.14-2.13)	.005	100.0

$I^2 = 75.9\%$, $P<.01$



Functional independence at 90 days (mRS 0–2) was seen in 44.6% (95% CI, 36.6%–52.8%) in the treatment group compared to 31.8% (95% CI, 24.6%–40.0%) in the standard care grow. This translates into a 12% risk difference (3.8%–20.3%; p = 0.005).

- The authors also found no difference in the following secondary outcomes:
- Symptomatic intracranial hemorrhage 5.7% vs. 5.1% (OR, 1.12; 95% CI, 0.77–1.63; P=0.56)
- 90-day all-cause mortality 15.8% vs.17.8% (OR, 0.87; 95% CI, 0.68–1.12; P=0.27).

Commentary

Though the question of whether endovascular therapy for acute ischemic stroke is an important one, whether it was answerable through a meta-analysis of the current literature is far less clear.

The assumed benefit to performing a meta-analysis is that the summation of these data sets provides a more accurate description of the true effect size than each individual data set can provide.

These trials examined different populations, using different inclusion criteria and different endovascular treatment strategies; essentially they examined different populations.

TALK NERDY TO ME

Commentary cont'd

1. *Heterogeneity*: A way to quantify heterogeneity is by using the I2 test. This study had high heterogeneity (I2=75.9) for its primary outcome. This questions whether the data should have been combined in a meta-analysis.

a) The assumed benefit to performing a meta-analysis is that the summation of these data sets provides a more accurate description of the true effect size than each individual data set can provide. This supposition rests on the notion that all the studies included in the meta-analysis are examining the same study population, and that the variance of results is due to random errors in sampling.

b) This is what is known as a "fixed effect" model. Unfortunately most data is not so homogeneous. It is common for the variations observed between trials to be due to more than just random error, but to considerable differences in the populations being compared. In such cases, the results of a direct-pooled analysis will likely deviate from reality. Statistical models that attempt to account for these random deviations should be utilized. These are known as "random-effect" models (Cornell et al 2014).

c) The authors used the I2 index to assess the degree of variation between studies. I2 describes the extent of variation across trials that cannot be explained by random chance. An I2 score of 0.0 implies all of the variation observed between trials can be accounted for by random errors in sampling. Conversely, if the I2 is 75, only 25% of the variation can be accounted for by sampling error with the remaining variation (75%) due to heterogeneity between trials (Higgins et al BMJ 2003). In the Badhiwala et al meta-analysis the I2 = 75.9, so they correctly did a random effect model.

2. *Included Studies*: Though the authors search for studies was exhaustive, they were very particular in which trials they selected. In fact, it seems the authors knew which trials would be included in the analysis before conducting it, and the systematic review was merely perfunctory.

3. *Stopping Early:* A number of the more recent studies included in this analysis were stopped early. This was after the positive results seen in the MR CLEAN trial. Due to this premature stoppage of these trials, the data is likely to be a distortion of reality. This makes it even harder to interpret the point estimate of effect size.

4. *Time is Brain*: One of the subgroups the authors examined in their secondary analysis was whether time to randomization had any effect on the efficacy of endovascular therapy. Specifically they looked at time from symptom onset to randomization. They examined the effect size of endovascular therapy as compared to standard care depending on whether patients were randomized before or after three hours from symptom onset. Temporality did not seem to affect outcomes. Once again calling into question the time is brain mantra so frequently proclaimed.

5. *Ordinal Analysis*: The authors utilized an ordinal analysis of the modified rankin Scale (mRS) for their primary outcome. An ordinal analysis is a statistical attempt to assess the shift of outcomes across the entire mRS. This statistical manipulation assumes the reliability of the scale used to measure functional status. It has been shown that when two neurologists assess the same patient, their mRS assessment may vary wildly. This scale is hardly granular enough to apply an ordinal analysis with any accuracy. We have a classic example in the stroke literature where a dichotomous outcome (alive/independent vs. dependent/dead) showed no statistical difference, but a secondary ordinal analysis showed a difference (SGEM#29).

Clinical Application

The recent trials on endovascular therapy for acute ischemic stroke have demonstrated that there is likely a subset of stroke patients who will benefit from reperfusion therapy. This is a small portion of patients that present to the emergency department with acute ischemic stroke. They also demonstrate that this subset of patients is more accurately identified with the use of advanced perfusion imaging rather than an empiric time since symptom onset that we have more traditionally used. The true extent of this benefit is still unclear.

CONCLUSION VS COMMENTARY COMPARISON

The authors are likely correct in their assertion that endovascular therapy for acute ischemic stroke leads to improved functional outcomes when compared to medical therapy alone, and yet the true effect size is unknown.

STUDY QUALITY CHECKLIST

The clinical question is sensible and answerable	*
The search for studies was detailed and exhaustive	
The primary studies were of high methodological quality	**
The assessment of studies were reproducible	
The outcomes were clinically relevant	
There was low statistical heterogeneity for the primary outcomes	
The treatment effect was large enough and precise enough to be clinically significant.	***

* Sensible, yes. Answerable with current data, no.

** Variable

*** Large enough, yes. Precise enough, no.

WHAT DO I TELL MY PATIENT?

This is difficult. I might say…It appears you are having a stroke. There is a blockage of blood flow to part of your brain. You do have some treatment options. Each option carries potential benefit and potential harm. One involves a clot-busting drug to try and dissolve the clot. Another option is a special type of surgery called endovascsular surgery. It can potentially remove the blockage and restore the blood flow. Both have the risk of bleeding and in some cases even death. But they each also have the potential to improve your weakness and speech. Another option is to do nothing and see if you get better. This too is not without risk. However, the stroke team will be here soon. They can talk with you about your various options in more detail. I am around and happy to answer any question you may have to the best of my ability.

References

Badhiwala JH, Nassiri F, Alhazzani W, Selim MH, Farrokhyar F, Spears J, Kulkarni AV, Singh S, Alqahtani A, Rochwerg B, Alshahrani M. Endovascular thrombectomy for acute ischemic stroke: a meta-analysis. Jama. 2015 Nov 3;314(17):1832-43.

GUEST SKEPTIC: Dr. Rory Spiegel
Clinical Instructor and Advanced Resuscitation trainee, Stony Brook University School of Medicine, Stony Brook, NY

138 Hip to be blocked – regional nerve blocks for hip and femoral fractures

Case Scenario:
A 75-year-old woman has a ground level fall in her apartment. She is brought to the emergency department with an isolated hip injury. She has a past medical history of high blood pressure and gastroesophageal reflex disease. Her only complaint is hip pain. On exam her vital signs are normal. The only abnormality found is a shortened and externally rotated left leg. An x-ray demonstrates a femoral neck fracture. The nurse wants to know what you want to give her for pain.

Clinical Question:
Do regional nerve blocks effectively reduce pain, decrease opiate use and are they safe compared to standard pain management in patients with hip or femoral neck fractures?

Bottom LINE

While the evidence comes from small studies with a moderate to high risk of bias, femoral nerve blocks appear to be an effective alternative to standard treatment of pain associated with femoral neck or hip fracture in the emergency department. More high-quality studies are needed to comment strongly about safety.

Regional Nerve Blocks for Hip and Femoral Neck Fractures in the Emergency Department: A Systematic Review

Ritcey et al. CJEM. Nov 2015.

P Adults over 16 years old with femoral neck or hip fracture

I Femoral nerve block (FNB), 3-in-1 FNB or fascia iliaca compartment block (FICB)

C Standard pain management with opiates, acetaminophen or NSAIDs

O Primary: Reduction in visual analogue scale (VAS) pain scores.
Secondary: Parenteral opioid use and complication rates.

Authors' Conclusion:

"Regional nerve blocks for hip and femoral neck fractures have a benefit in reducing pain and decreasing the need for IV opiates. The use of these blocks can be recommended for these patients. Further high-quality randomized controlled trials are required".

Background

Oligoanalgesia is a well-recognized problem in the emergency department (Wilson JE and Pendleton JM). It can be defined as inadequate pain control (Motov SM and Khan A). There are various groups at risk for oligoanalgesia and the elderly is one of those groups (Cavalieri TA).

Hip fractures are common in the elderly population. They are often very painful and are a significant cause of morbidity and mortality. Pain management can be challenging in these cases, particularly because of increased complications of opiate medications in this population.

Background Continued

- Traditional Femoral Nerve Block (FNB) – This involves injecting local anaesthetic directly around the femoral nerve and neurovascular bundle in the groin
- 3-in-1 Femoral Nerve Block – In this technique, you just put pressure distal to the needle while doing a traditional FNB. This allows the anaesthetic to track superiorly and also anaesthetize the obturator and lateral femoral cutaneous nerves.
- Fascia Iliaca Compartment Block (FICB) – The fascia iliaca block indirectly anaesthetizes the same three nerves as the 3 in 1 block by injecting a large volume of dilute anaesthetic lateral to the nerve in the fascia iliaca compartment.

Results

Nine articles were included in the systematic review for a total of 547 patients. The data could not be combined into a meta-analysis.

Primary Outcome: Regional nerve blocks were equal or superior in reducing pain scores compared to standard therapy.

Secondary Outcomes

- Five out of six studies demonstrated significant reduction of parenteral opiate use
- No life threatening complications
- Some increase in minor complications

Commentary

This was a well-done systematic review looking at an important topic. Listen to the podcast to hear Dr. Ritcey's respond to our questions about the strengths and weaknesses of the study.

1. *Search*: It was a good search strategy of a number of databases, a hand search of references of the articles selected with no language restrictions. Awareness is one of the barriers to knowledge translation according to the Leaky Pipe Model by Pathman. We were pleased to see other languages besides English were considered. It is one of the reasons the SGEM has gone Global and being translated and podcasted in five other languages (Spanish, Portuguese, French, German and Italian).

2. *Inter Observer Reliability*: There were two people independently screening the titles and abstracts for full-text review. The inter-observer reliability was assessed for the screening phase and had a kappa of 0.61 (moderate). The kappa increased to 0.79 (substantial) for the decision on what articles to include for full-text review. For more information on kappa and inter-rater reliability you can read these articles by McHugh ML , McGinn et al, and McGinn et al.

Commentary Continued

3. *Risk of Bias*: The Cochrane Collaboration tool for assessing risk of bias in the randomized trials was used. Only one of the nine studies had an overall low risk of bias (Beaudoin et al). The other eight had moderate to high risk of bias. Most of the bias came from lack of double blinding in six out of the nine studies. Four studies included patients who were later unaccounted for in the final results. There was also significant variability in reporting of secondary outcomes. In particular, this included the under reporting of harms.

4. *Small Studies*: These were fairly small studies with most being around 50 patients. The largest study only had 154 patients and the combined total of all nine studies was 547. We have some questions about these individual studies:

- What was the most common form of blocks done?
- What did they use for the anaesthetic and how much did they inject?
- Who did the injections?
- Were they trained to do the injections?
- Did they use ultrasound to perform the blocks?

5. *Meta-analysis*: This was a systematic review only. A meta-analysis was not performed due to the variability and heterogeneity of the studies.

Study Quality Checklist

The clinical question is sensible and answerable	
The search for studies was detailed and exhaustive	
The primary studies were of high methodological quality	
The assessment of studies were reproducible	
The outcomes were clinically relevant	
There was low statistical heterogeneity for the primary outcomes	
The treatment effect was large enough and precise enough to be clinically significant.	

Clinical Application

I am going to offer regional nerve blocks to patients who present with hip or femoral neck fractures.

CONCLUSION VS COMMENTARY

COMPARISON

We generally agree with the authors' conclusions.

WHAT DO I TELL MY PATIENT?

You have broken your hip. This is a very painful injury. We can give you pain medicine like morphine. These drugs work very well for pain but can make you sick to your stomach, hallucinate and drop your blood pressure. Another option is to inject some "freezing" in the hip that blocks the nerve. This usually works very well with few complications. It often means you do not need as much pain medication. Would you like me to do this type of nerve block?

References

Ritcey B, Pageau P, Woo MY, Perry JJ. Regional nerve blocks for hip and femoral neck fractures in the emergency department: a systematic review. Canadian Journal of Emergency Medicine. 2016 Jan;18(1):37–47.

GUEST SKEPTIC: Dr. Brandon Ritcey
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139 One things leads to another – Idarucizumab for dabigatran reversal

Case Scenario:
A 67-year-old man presents with a history of atrial fibrillation and hypertension. He takes metoprolol 50mg twice daily and dabigatran 150mg twice daily. He had been having mild epigastric pain for about one week and had one episode of coffee ground emesis that night. He arrives via ambulance with a blood pressure of 120/70, heart rate of 74 beats per minute and O2 saturation of 98% on room air.

Clinical Question:
Is idarucizumab safe and effective treatment adjunct for patients taking dabigatran with serious bleeding or who require an urgent procedure?

Bottom LINE

Idarucizumab is here (USA) and probably works but its patient oriented efficacy and safety are still pending.

Idarucizumab for dabigatran reversal

Pollack CV et al. NEJM 2015.

P

Patients 18 years of age or older, reported to have been taking dabigatran

a. Group A: Patients with overt, uncontrollable, or life-threatening bleeding
b. Group B: Patients who required surgery or other invasive procedure that could not be delayed for at least 8 hours.

I

All patients received 5g of intravenous idarucizumab in the form of two 2.5g boluses 15 minutes apart.

C

None, this was a prospective observational trial.

O

Primary Outcome: Maximum percentage reversal of the anticoagulant effect of dabigatran within four hours assessed by measurement of dilute thrombin time or ecarin clotting time.

Secondary Outcome: Reduction in the concentration of unbound dabigatran, restoration of hemostasis and suspected thrombotic events or deaths by 90 days.

Authors' Conclusion:

Idarucizumab completely reversed the anticoagulant effect of dabigatran within minutes.

Background

Dabigatran is a non-vitamin K antagonist anticoagulant that works by inhibiting thrombin. It is approved for the prevention and treatment of venous thromboembolism. It is also approved treatment of non-valvular atrial fibrillation to prevent stroke.

Life threatening bleeding can occur while taking dabigatran. Unlike warfarin that can be reversed in a variety of ways, there has been no feasible or effective method for the adjunctive treatment of these life-threatening bleeds in patients using dabigatran. The only current method of removal, hemodialysis, is impractical in the vast majority of clinical situations.

Background Continued

There has been no feasible reversal agent until now. Boehringer Ingleheim the maker of dabigatran has developed a monoclonal antibody fragmin called idarucizumab.

The FDA approved idarucizumab in October as the first reversal agent for dabigatran. As far as we know it has not yet been approved for use in Canada

Results

This is a preliminary report on an ongoing cohort study expected to recruit up to 300 patients at 400 centers in 38 countries. This report includes 90 patients with a median age of 76.5 years with 96% of patients being on dabigatran for atrial fibrillation.

Group A (Bleeding): 51 patients

- 18 intracranial hemorrhage, 20 gastrointestinal bleeds, 9 traumas and 11 other causes. This adds up to 58 rather than 51 because patients may have had more than one type of bleeding.

Group B (Surgery/Procedures): 39 patients

- Indication for surgery or urgent invasive procedure varied but the most common (8/39) was bone fractures.

Twenty-two patients were excluded from analysis because at study entry they had a dilute thrombin times that were within the normal range. This left only 68 patients in total with abnormal results, which were the focus of their analysis.

Primary outcome: Median maximum percentage reversal of the anticoagulant effect of dabigatran, assessed by both the dilute thrombin time and ecarin clotting time, within four hours was 100% (95% CI, 100% to 100%).

Secondary Outcomes:

- Reduction in the concentration of unbound dabigatran: Of patients with dabigatran levels tracked, the unbound levels dropped to a level that produces little or no anticoagulant effect in all but one patient. A handful of patients in Group B had markedly elevated dabigatran levels, and these patients never entirely normalized. Dabigatran levels dropped to their nadir in these patients after completion of the infusion, but began rising again within an hour.
- Restoration of hemostasis: Only 38 of the 51 patients in Group A could be evaluated for ongoing bleeding. The median time to reach clinical hemostasis was 11.4 hours. There were 36 out of 39 patients in Group B who underwent an urgent invasive procedure. Normal operative hemostasis was reported in 92% (33/36).
- Deaths by 90 Days: There were 18 deaths in total with 9 in each of the two groups. Half of the deaths occurred over a week after enrolment.
- Thrombotic Events: There were a total of five thrombotic events up to 90 days.
    - DVT/PE day 2, DVT/PE and left atrial thrombus day 9, DVT day 7, NSTEMI day 13 and ischemic CVA day 26

TALK NERDY TO ME

Commentary

It seems more and more patients are anti-coagulated these days with non-vitamin K antagonists. Some of these people are going to bleed and we need information on how to best treat them in the emergency department.

However, this is a disappointing publication regarding the safety and efficacy of idarucizumab for the reversal of anticoagulation in the setting of dabigatran use. It is hard to think of a good justification for the publication of these interim results.

They suggest this data reflect important insights into the clinical outcomes of patients treated with idarucizumab. However, they acknowledge a major limitation of their study was the lack of a control group.

The authors state it was unethical to perform a placebo-controlled study in the setting of life-threatening bleeding risk; this stance assumes the untested therapy is actually clinically effective and safe in a real-world setting without ever being tested.

While most reported coagulation parameters normalized within minutes, and most unbound dabigatran levels dropped to a level below detection, the median investigator-reported to hemostasis was not reported for over 11 hours in patients with overt bleeding.

It is not clear whether this reflects a lack of true clinical efficacy, or whether confounders related to individual patient condition resulted in the long delay to hemostasis. Regardless, the publication of interim results seems unwarranted given the content presented.

Such a presentation might be justified based on a safety evaluation, given the fast-track approval of this antidote, but, a cohort size of 90 is almost certainly too small to detect any pattern of adverse events.

The report of peri-procedural hemostasis is also questionable, particularly considering the procedure list. While a handful of significant surgical cases are included, several interventions are typically minimally invasive laproscopic procedures, and the list of "surgeries" also includes cutaneous abscess I&D, lumbar puncture, placement dialysis catheters, and placement of ureteral stent. No reliable conclusion can truly be drawn regarding the clinical effectiveness of idarucizumab for procedural hemostasis for urgent procedures.

Another concern regarding the trial was the 22 patients who received the drug and were subsequently found to have normal clotting levels. This means almost 25% of patients receiving a drug that was not necessary and exposed them to potential risk of adverse reactions.

Without a routinely available, rapidly feasible method for detection of therapeutic dabigatran levels, the widespread clinical usage could be fraught with waste. Especially considering the expected cost of each dose of idarucizumab is ~$3,400 USD.

Finally, it should be mention this trial was funded by the manufacturer and sponsor, Boehringer Ingelheim who also had a role in the study design. Many authors, as well as the author of the accompanying editorial, report relevant financial conflicts of interest.

Many trials are sponsored by the pharmaceutical industry. This does not make the results wrong but it probably should make us more skeptical of the results.

Clinical Application

It is too early to know how to clinically apply this preliminary research.

CONCLUSION VS COMMENTARY COMPARISON

We agree idarucizumab rapidly normalizes abnormal coagulation parameters associated with dabigatran use, but its suspected clinical effectiveness and safety cannot be confirmed at this time.

STUDY QUALITY CHECKLIST

The study addressed a clearly focused issue	*
The authors used an appropriate method to answer their question	
The cohort was recruited in an acceptable way	**
The exposure was accurately measured to minimize bias	
The outcome was accurately measured to minimize bias	***
The authors identified all important confounding factors	
The follow up of subjects was complete enough	
The results were precise and estimated risk well	
the results are believable	****
The results can be applied to the local population	
The results of this study fit with other available evidence	

*Yes and No. To measure the percentage of dabigatran reversal, a study needs no more than healthy volunteers in a controlled environment. These patients were recruited in a clinical setting more suited to providing patient-oriented outcomes, rather than pharmacokinetic data.

**No and Yes. The cohort was not recruited in an appropriate fashion with regards to their primary outcome. Regarding secondary clinical outcomes, the recruitment was reasonable and performed in an appropriate acute setting. However, there is no comparator with which to interpret any of the clinically relevant outcomes. The study protocol states each patient acts as their own control, but this is only relevant regarding pharmacokinetic data, and assumes the post-treatment baseline reflects the patients' normal baseline pre-dabigatran initiation. Patients in Group A, enrolled with supposedly overt or life-threatening bleeding necessitating emergency reversal, required packed cell transfusion only approximately half the time. Lastly, the study does not report the number of patients screened for enrollment nor the reasons regarding their lack of inclusion, resulting in an inability to assess the magnitude of selection bias.

***Yes and No. The primary outcome of dabigatran reversal was measured via surrogate, and these are reliably sampled in the relevant population. Assessments of clinical outcomes were subjectively surveyed.

****Yes and No. The measurement of thrombin time, ecarin clotting time, and unbound dabigatran are reliable and believable. The clinically relevant patient-oriented outcomes and hemostasis outcomes are poorly described and cannot be interpreted in context.

WHAT DO I TELL MY PATIENT?

You are having a serious bleed. It is made worse because of the blood thinner you take to prevent strokes. We are getting some blood for you. The gastroenterologist is on their way to take you to the operating room. If you become unstable I can give you a new drug just approved that seems effective and seems to works very quickly. However, we don't have much information on how well it works and there may be safety issues we have not yet identified.

References

Pollack Jr CV, Reilly PA, Eikelboom J, Glund S, Verhamme P, Bernstein RA, Dubiel R, Huisman MV, Hylek EM, Kamphuisen PW, Kreuzer J. Idarucizumab for dabigatran reversal. New England Journal of Medicine. 2015 Aug 6;373(6):511-20.

GUEST SKEPTIC: Dr. Ryan Radecki
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140 CT scans to rule-out subarachnoid hemorrhages in a non-academic setting

Case Scenario:
Ms. Jones is a 45-year-old woman who presents to her local community hospital with the "worst headache" of her life that started suddenly four hours ago. She has a normal neurologic exam. She gets a non-contrast head CT that is read as normal by your local radiologist.

Clinical Question:
Can a SAH be ruled out in a patient presenting to a non-academic ED within 6hrs of headache onset by a head CT read by a community staff radiologist?

Bottom LINE

These community radiologists were just as good at reading CT heads as academic radiologists when looking for blood using a third generation scanner

CT within 6 hours of headache onset to rule out subarachnoid hemorrhage in non-academic hospitals.

Blok et al. Neurology. March 2015.

P

Adult patients presenting to a non-academic emergency department with spontaneous acute headache

- ✘ Inclusion: Normal level of consciousness without focal deficits, head CT within six hours after headache onset and reported negative and lumbar puncture performed greater than 12 hours after headache onset.
- ✘ Excluded: Glasgow Coma Scale <15 at presentation, unknown time of ictus, age 16 years or younger and lumbar puncture performed earlier than 12 hours after headache onset.

I

Lumbar puncture to achieve identification of CT-negative SAH patients.

C

None

O

Negative predictive value for detection of subarachnoid blood by staff radiologists working in a non-academic hospital

Authors' Conclusion:

Our results support a change of practice wherein a lumbar puncture can be withheld in patients with a head CT scan performed <6 hours after headache onset and reported negative for the presence of SAH by a staff radiologist in the described non-academic setting.

Background

We have talked about SAH a couple of times on the SGEM with the most recent time being the Hot Off the Press paper by Sayer et al in AEM. That retrospective UK study reported a NNTap (Number Needed to Tap) to diagnose one aneurysm not picked up on CT scan was 250.

There are a couple of other studies suggesting that a LP was not automatically needed to exclude the diagnosis of a SAH in patients presenting with an acute headache as the negative predictive value of a normal head CT performed at an academic, **tertiary** care hospital within 6 hours of headache onset is 100% (Perry et al BMJ 2011and Backes et al Stroke 2012).

Dr. Jeff Perry's group came up with the Ottawa SAH Rule that we covered on SGEM#48. The bottom line from that review was the "tool" was not ready for prime time because of the need for validation studies.

There has been at least one validation study done by Bellolio et al of the Ottawa SAH Tool showing 100% sensitivity and 7.6% specificity. They concluded the low specificity and its applicability to only a minority of emergency department patients limited the potential usefulness of the Ottawa SAH Rule. This study was done at an academic center. There have apparently been no studies done at non-academic sites until now.

Box 2. The Ottawa SAH Rule

For alert patients older than 15 y with new severe nontraumatic headache reaching maximum intensity within 1 h

Not for patients with new neurologic deficits, previous aneurysms, SAH, brain tumors, or history of recurrent headaches (≥3 episodes over the course of ≥6 mo)

Investigate if ≥1 high-risk variables present:

1. Age ≥40 y
2. Neck pain or stiffness
3. Witnessed loss of consciousness
4. Onset during exertion
5. Thunderclap headache (instantly peaking pain)
6. Limited neck flexion on examination

Results

There were 760 consecutive patients who presented to one of eleven non-academic hospitals with acute headache suspected for SAH who had a head CT within six hours after headache onset reported as negative for the presence of blood by the non-academic staff radiologist and had a lumbar puncture greater than 12 hours after onset of acute headache.

The patient cohort had a median age of 45 years and 61% were women.

Negative Predictive Value 99.9% (95% CI 99.3%–100.0%)

Lumbar punctures were positive for the presence of bilirubin in 52 patients. Independent review of the community radiologists by the academics found only one patient with a perimesencephalic nonaneurysmal SAH with a benign clinical course.

Of the 51 patients with negative CTs and positive LPs 28 went on to have CTA, MRA or DSA. Eight aneurysms were identified but felt that rupture was unlikely.

Twenty patients had no aneurysm identified on further imaging and twenty-three patients did not have any other imaging on clinical grounds. None were thought to have subarachnoid hemorrhage based on a median follow-up time of 53 months

TALK NERDY  TO ME

Commentary

1. *Methods*:

- Retrospective Chart Review: There is a hierarchy of evidence and a retrospective chart review is not a very high level of evidence. This does not make the conclusions wrong but weakens the strength of any conclusions that can be made from this type of study. Just because a retrospective chart review is a lower form of evidence does not mean it should not have strong methods. There are published quality checklists for retrospective chart reviews to assist researchers (Gilbert et al and Worster et al). The chart review methods were not described well in this study. There are many questions about who abstracted the data, were they blinding to the hypothesis, what was their training and how was quality of their abstraction assessed. This information would have been helpful.
- STARD: This stands for Standards for Reporting Diagnostic accuracy studies. It is a checklist to help readers judge the potential for bias in a diagnostic study. The latest list contains 30 quality checks for the completeness and transparency of reporting diagnostic studies. There is no mention of following these guidelines. Lack of adherence to the STARD reporting standards makes it difficult to interpret the results.

2. *Negative Predictive Value (NPV)*: This is the proportion of people with a negative test who do not have the disease. The NPV is calculated by taking the true negatives and dividing them by the all negatives (true and false). This statistic depends on the prevalence of disease. Therefore the accuracy of a negative CT scan to rule out SAH cannot be interpreted without considering the per-test probability. This is getting into Bayesian thinking but is very important. A very sensitive test (even one which is very specific) will have a large number of false positives if the prevalence of disease is low. So if a CT scan is done in every headache patient (low pre-test probability for SAH) it will have a fantastic NPV. So if prevalence is low the number needed to scan will be very high. In fact, any test would look good to rule out disease if no one has the disease. All the positive tests (LP) would be false positives. The prevalence of SAH in this study was extremely low at 0.1%. This means the NPV will be close to 100% no matter what test is used.

3. *Lack of Gold Standard*: Eight patients with intracranial aneurysms had negative CT heads and positive LPs. Seven were thought to be false positive based on further CSF testing. They do acknowledge the uncertainty of this interpretation because no internationally accepted gold standard exists for the interpretation of CSF spectrophotometry.

4. *Wrong Question*: This does not answer the fundamental question we want answered. Do we need to do an LP to rule out SAH after a negative CT? This study demonstrates that non-academic radiologists are very good at identifying blood on a third generation CT scanner compared to academic radiologists. There was only one case out of 760 scans the academics felt did show blood that was not identified by the community radiologists. The blood was in the basal cistern and consistent with a non-aneurysmal perimescenphaic hemorrhage. The remaining 51 out 52 positive LPs were considered false positives.

Commentary Conti'd

5. *Harm*: When considering a diagnostic test we also need to consider the harm. LPs are not benign procedures and can cause post-LP headaches, infections, nerve damage, and bleeding around your spinal cord. It is well recognized that harm is under reported in studies. The authors did not provide any information whether or not any of the 52 patients undergoing LP experienced an adverse events due to the diagnostic tests itself. However, they did mention in their discussion: "a lumbar puncture is associated with discomfort for the patient, costs, and may induce a potentially life-threatening complication such as subdural hematoma or cerebral venous sinus thrombosis in rare cases". There are also the down stream consequences of false-positive CSF results. In this study 8 patients had aneurysms on subsequent vascular imaging. How will that knowledge affect these individuals and what impact will it have on their future healthcare?

Clinical Application

A negative CT head scan read by a community radiologist using a third-generation scanner within 6 hours of headache onset is sufficient to exclude the diagnosis of SAH in a low prevalence population.

STUDY QUALITY CHECKLIST

The clinical problem is well-defined	👍
The study population represents the target population (ie no spectrum bias)	👍
The study population included or focused on those in the ED	👍
The study patients were recruited consecutively (ie no selection bias)	👎
The diagnostic evaluation was comprehensive and applied equally to all patients (ie verification bias)	👎
All diagnostic criteria were explicit, valid, reproducible (ie no incorporation bias)	👎
The reference standard was appropriate (ie no imperfect gold-standard bias)	?
All undiagnosed patients underwent sufficiently long/comprehensive follow-up (ie no double gold-standard bias)	👎
The L.R.(s) of the test(s) in presented or can be calculated from the information provided	👎
The precision of the measure of diagnostic performance is satisfactory	👍

CONCLUSION VS COMMENTARY COMPARISON

We agree that an LP is not a useful test to diagnose SAH in a low prevalence population with a negative CT scan.

WHAT DO I TELL MY PATIENT?

Subarachnoid hemorrhages can present with sudden headaches. These types of bleeds in the brain can be devastating and even deadly. Our local radiologist looked at the CT scan of your brain and did not see any bleeding. They are just as good as radiologists at the big academic hospitals for reading these tests. CT scans are very good to rule out a bleed when done within six hours of headache onset but no test is 100%. A lumbar puncture could be done if we are really concerned. That involves sticking a needle in your back to get fluid from around your spinal column. This test can have complications. A common side effect of the test is a headache. In addition, often the test is falsely positive. That means doing even more testing that could potentially cause harm. There are studies suggesting hundreds or maybe even thousands of LPs would need to be done to find one of these serious/life-threatening bleeds not seen on CT scan. What do you want to do?

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GUEST SKEPTIC: Dr. Fareen Zaver
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Popeye and the Paperclip

Case Scenario:
A 34-year-old former sailor presents to his primary care provider for a routine employment screening. He asks if he should consider eating lots of spinach to make him strong and healthy. He is noted to enjoy pipe smoking and to have disproportionately developed forearms.

Clinical Question:
Is spinach high in iron and is that where Popeye gets his strength?

Bottom LINE

Popeye is strong to the finish because he eats spinach that contains beta carotene. Spinach is not SUPER high in iron content as suggested by SPIDES but can be part of a healthy diet.

SPINACH, IRON AND POPEYE: IRONIC LESSONS FROM BIOCHEMISTRY AND HISTORY ON THE IMPORTANCE OF HEALTHY EATING, HEALTHY SCEPTICISM AND ADEQUATE CITATION. INTERNATIONAL

DR. MIKE SUTTON. JOURNAL OF CRIMINOLOGY 2010

BACKGROUND

For many decades spinach has been promoted as a food with a super high iron content. It is also part of pop culture that Popeye the Sailor ate spinach for the iron to make him strong.

There has been a story about spinach, iron and Popeye that has been circulating for decades. It is referred to as the Spinach, Popeye, Iron and the Decimal Error Story (SPIDES). The story has been told by many academics and reproduced in many books. However, it turns out the story is complicated and not accurate.

I first heard of the story reading a book called the Half-life of Facts: Why Everything We Know Has an Expiration Date while on a cruise for my 20th wedding anniversary. Complexity scientist Samuel Arbesman wrote the book. He has been a fellow at Harvard and at the University of Colorado. He also writes for the New York Times and a few other magazines and newspapers. In the Half-Life of Facts he tells the story about Popeye and the decimal error made in the calculation of the iron content of spinach. Apparently back in the 1870's a German scientist named von Wolff was measuring the iron content of vegetables including spinach.This is where the infamous decimal point error was allegedly made changing the magnitude of iron in spinach to be ten fold greater.

This incorrect amount of iron per 100g serving would be comparable to eating a small piece of a paperclip. Arbesman goes on to say that when Popeye was created in the early 20th century he was shown to eat spinach for his strength due to its health properties.

This transcription error was supposedly corrected way back in the 1930's. But the story goes that this error wasn't corrected until after Popeye was already in the press, and that this in turn led to decades of mistaken public belief about spinach's iron content.

I have used that story to illustrate how long it takes for knowledge translation. The talk is called Popeye and the Paperclip. The story was used to demonstrate my point about knowledge translation at the SMACC conference in Chicago, on The Reality Podcast earlier this year and at other meetings.

You heard me tell this story on The Reality Check podcast and having a major in Biochemistry found it odd that a German chemist would make such a gross error. You were skeptical and did a google search to find out SPIDES was not true and that the good Dr. von Wolff was innocent. Bob contacted me and I invited him on the SGEM to clarify the story. So in the spirit of the holidays, correcting previous errors and encouraging skepticism, I wanted to do a SGEM Xtra on the Popeye and the paperclip story.

Commentary

- Who is Dr. Mike Sutton? He is a lawyer with a PhD in criminology who has a special interest in myth busting. He runs the Internet Journal of Criminology, a free open access journal.
- How did he become involved in the Spinach/Popeye story? Dr. Sutton was preparing some citations regarding the introduction to a talk on the impact of bad data on policy making he had given at Manchester University. He used the SPIDES story as an example, but when he tried to get citations for the origins of SPIDES he noticed a disturbing lack of primary sources. After a few weeks he found that all roads led to a 1981 BMJ article by Dr. TJ Hamblin, this article in turn had some very sketchy sources on the origins of this myth. He emailed Hamblin, who stated he couldn't remember who had told him about the myth in the first place, but was pretty sure he didn't make it up. Sutton then took an obsessive turn and reread all the original Popeye comics from 1928–1935.
- Was there a German scientist named Erich von Wolf mentioned in the book the Half-Life of Facts? Yes and No. There appears to have been a typo from the book you had read, the real name of the German scientist was Emil Theodor von Wolff spelt with two "f"s.
- Did he calculate the iron content in spinach? Yes, he calculated the iron content from burnt spinach residue.
- Is there evidence that von Wolff made a transcription error? There is no any primary evidence of this error. Also, there is no secondary or tertiary evidence of von Wolff making this error prior to the BMJ article.
- So how did this error get into the literature at the end of the 19th and beginning of the 20thcentury? According to Sutton's investigation, it appears this was actually based on a confusing table in a 1934 paper from the University of Wisconsin by Sherman et al (J Biol Chem 1934). They reported iron contents for dry and fresh spinach.
- What about the dry vs. fresh measurements? As spinach's iron content is measured based on 100 g of spinach, the dry measurements of spinach's iron content are much higher since the water content is gone. The paper by Sherman et al is very confusing as to whether it is referring to dried or fresh spinach, but does report a value of iron in spinach that is more consistent with the current values seen in dried spinach.
- Do we know who corrected the error in the 1930s? Kohler et al (J Biol Chem 1936) issued a paper two years later. They modified the chemical method of extracting the iron and also used fresh spinach. Their results are consistent with our current fresh spinach values.
- Tell us about the 1981 BMJ article by Dr. TJ Hamblin called "Fake". The BMJ puts out a holiday article every year that is light hearted and less meticulously researched like the Parachute Trial. They approached Hamblin asking for a humorous piece and didn't ask him to provide references. He did in fact give 13 references to the article, but none specifically referenced the SPIDES story.
- Who was Dr. Hamblin? He was a well-published immunohematologist who specialized in his work on chronic lymphocytic leukaemia.
- Where did he get his information for the story? This is very unclear. When Sutton emailed Hamblin in 2010, he was unclear, stated he couldn't recall his source, but was sure he had heard it once or read it in the Reader's Digest.

Commentary cont'd

- Apparently the story may have come form a Professor Arnold E. Bender? Yes, it appears that in 1972 during an inaugural lecture and an article in The Spectator in 1977. Professor Bender reiterated the SPIDES story but stated the error was fixed in 1937 by professor Schupan. There is no record of who this professor Schupan was or where his correction came from. Bender incorrectly cites a paper that measures the iron oxide, not iron content, of spinach.
    - *"For a hundred years or more spinach has been (and clearly still is) renowned for its high iron content compared with that of other vegetables, but to the joy of those who dislike the stuff this is quite untrue. In 1870 Dr E. von Wolff published the analyses of a number of foods, including spinach which was shown to be exceptionally rich in iron. The figures were repeated in succeeding generations of textbooks – after all one does not always verify the findings of others – including the 'Handbook of Food Sciences' (Handbuch der Ernahrungslehre) by von Noorden and Saloman [1] 1920. In 1937 Professor Schupan eventually repeated the analyses of spinach and found that it contained no more iron than did any other leafy vegetable, only one-tenth of the amount previously reported. The fame of spinach appears to have been based on a misplaced decimal point."*
- Does spinach even contain iron? Yes. Here is the quote from Dr. Sutton's paper:
    - *"Iron levels for fresh spinach contains around 2.75mg per 100gm (USDA 2009). Once dried, however, spinach contains substantially more mg of iron per 100gm, just as dried herbs contain far more concentrated flavour by weight and volume than when fresh."*
- Who Popeye and when was he created? Popeye started as a character in a comic strip in 1929 by Segar. He was added into an already existing comic strip that had been around since 1919 called Thimble Theatre. Perhaps this is why Sutton's analysis of the cartoons started one year prior to Popeye's debut in 1929. He is a strong sailor man who is well known for having a gruff way of talking and a deep love of spinach–although this love of spinach was not added to the comics until 1932.
- So where does Popeye get his strength? Segar actually goes out of his way in the first comic panel to point out that Popeye eats spinach. *"Spinach is full of vitamin "A" an' tha's what makes hooman's strong an hefty".* Spinach does contain a large amount of beta-carotene, which in turn becomes vitamin A.
- Where does the idea come from of Popeye being "iron man"? In another panel, Popeye's doctor says he has a *"cast iron interior"* and Popeye later states he is an *"iron man"* in the sense of being a tough guy.

Reference

Sutton M. Spinach, Iron and Popeye: Ironic lessons from biochemistry and history on the importance of healthy eating, healthy scepticism and adequate citation. Internet Journal of Criminology. 2010 Mar:1-34.

GUEST SKEPTIC: Dr. Bob Edmonds
3rd year EM resident at University of Missouri, Kansas City, MO

142 We need asthma education

Case Scenario:

A 21 year old with asthma since he was five years old and a prior intubation when he was eight presents to your ED with wheezing that is improved with two short (5 mg Albuterol) nebulizer treatments + Prednisone. You note that he has had 15 visits to your ED for asthma exacerbations over the last 12 months. You ask him if he is following with his PCP and filling the asthma medication prescriptions that he receives at each ED visit. He notes that he has no PCP with whom to follow-up, no money to pay for prescriptions, and no transportation to get to either a doctor's office or the pharmacy.

Clinical Question:

Can an educational intervention done in the emergency department prior to discharge improve follow-up with primary care providers in asthma patients?

Bottom LINE

Educating asthma patients about warning signs, acute medical management, follow-up recommendations, and indications to return to the ED for re-evaluation are important components of quality emergency care. Available studies indicate that a variety of pre- or immediate post-discharge efforts by research personnel improve PCP follow-up rates, but whether these efforts reduce short-term asthma-related morbidity (relapsing symptoms, emergency department returns, hospitalization) remains unproven.

Effectiveness of educational interventions to increase primary care follow-up for adults seen in the emergency department for acute asthma: a systematic-review and meta-analysis

Villa-Roel et al. AEM. Dec 2016.

P Original studies of adult patients discharged from the emergency department after treatment for asthma exacerbation.

I RCT (or controlled studies) of asthma-related educational intervention occurring w/in 1 week of the index ED visit for asthma. Interventions ranged from post-ED phone call reminding patients of f/u appointment (or arranging f/u appointment), 5-day course of steroids + transport voucher, fax from ED to PCP w/ tailored asthma care recommendations, and/or "asthma action plan" constructed in ED with patient prior to discharge.

C All studies evaluated the effectiveness of educational interventions compared to usual care (discharge instructions + medication prescriptions at discretion of the treating emergency physician).

O Primary outcome: Percentage of PCP (family physician, general practitioner, general internist, nurse) office f/u visits.

Secondary outcomes: Percentage of unscheduled revisits to the office or ED for asthma relapse, hospital admissions, time to first PCP office visit, time to first relapse. The authors also attempted to evaluate the fidelity of the reported educational interventions.

Authors' Conclusion:

ED-directed educational interventions targeting either patients or providers increase the chance of having office follow-up visits with PCPs after asthma exacerbations. Their impact on health-related outcomes (e.g., relapse and admissions) remains unclear.

Background

Asthma is a common presentation to the emergency department. Listen to Dr. Brian Rowe discuss the following:

- Asthma's impact on the health care system
- Asthma's impact on the individual
- What happens to most emergency department patients who present with asthma
- What the guidelines say about post-emergency department discharge
- Patient education and teachable moments in the emergency department

Results

Five eligible studies totaling 825 patients were identified, all from the U.S. (2) or Canada (3). The risk of bias across studies was qualified as "unclear", mostly due to the possibility of selective outcome reporting secondary to the lack of registered protocols or full-text publications. The authors were unable to assess the risk of publication bias due to the small number of eligible studies.

Using the Treatment Fidelity Assessment Grid, the authors noted that none of the trials used any behavioral adaptation theory for their educational intervention. In addition, details about the educator training protocols and methods to ensure participant receipt of the educational materials were largely lacking. None of the studies assessed patient compliance with individual recommendations from the educational intervention.

Primary Outcome: Post-emergency department primary care provider follow-up was improved compliance with the educational intervention RR=1.6 (95% CI: 1.31–1.87) with minimal statistical heterogeneity (I2 = 0%)

NNT of 6 for one patient to follow-up with their primary care provider after emergency department encounter.

Secondary Outcomes: No significant differences were noted between the educational intervention and usual care for

- asthma relapse (RR 1.3; 95% CI 0.82–1.98),
- time to asthma relapse (median 45 days in the educational arm vs. 28 days in the usual care arm),
- time to first primary care provider visit (median 18 days in education arm vs. 16 days in the usual care arm)
- admission rate (RR 0.51; 95%CI 0.24–1.06)
- Most studies reported no difference in medication compliance between their comparison groups.

One study reported more patients with a written asthma action plan (46% vs. 25%) and higher quality-of-life scores in the educational arm at 6-months follow-up.

TALK NERDY TO ME

Commentary

Patient education is the basis for effective and meaningful shared decision making. Unfortunately, emergency department providers manage patients with widely varying levels of health literacy (Carpenter et al, Griffey et al, and McNaughton et al) everyday in chaotic settings with scant access to personnel or resources that enable focused pre-discharge educational efforts.

Nonetheless, enhancing pre-discharge care must be a priority for efficient, patient- centric emergency department operations for medical, psychiatric, surgical, and trauma patients. Therefore, understanding the effectiveness of pre-discharge interventions in asthma patients provides valuable lessons for researchers, clinicians, and educators across multiple conditions. This systematic review suggests that a variety of pre- or immediate post-discharge patient-focused interventions improve primary care provider follow-up rates (Disease Oriented Outcomes) without compelling evidence of reduced asthma relapse rates, emergency department returns, or hospital admissions (Patient Oriented Outcomes).

Differentiating these outcomes is important because increasing follow-up rates (NNT = 6) drives up healthcare costs and resource utilization, which should derive improved health via less asthma-related morbidity, but this cause-effect relationship has yet to be established.

There were a number of limitations to this study that we discussed with the authors. Here are five issues and their responses. Listen to the podcast to hear the full responses from Dr. Rowe and Dr. Villa-Roel

1. *Labor Intensive*: The studies used non-clinical personnel to perform the educational intervention (trained research assistants, study coordinators, or research nurses). Using resources that are not widely available in most EDs limits the external validity of research findings so more pragmatic research designs will be needed in the future.

- Author's Response: *That is an excellent point. Emergency physicians and most nurses likely don't have the time (nor the training) to accomplish this. Ideally, the use of clinical resources available in the emergency department (e.g., specialized nurses, respiratory therapists) or health professional liaisons in transitions of care (e.g., asthma educators, pharmacists, nurse practitioners) should be guided by the needs of patients and local primary care providers.*

2. *Theoretical framework*: None of the studies reported a theoretical framework for the educational intervention. Adapting behavior is complex and implementation science mandates use of an established framework to guide these interventions.

- Author's Response: *That is correct. The unclear theoretical foundation of many educational trials in asthma has been strongly criticized; difficulties in replication and limited applicability may be associated with this issue.*
    - In addition, implementation science frameworks indicate the need to contemplate, measure, and report cultural capacity for change, essential stakeholders and opinion leaders, intervention adaptability, and sustainability, none of which was evaluable in this systematic review.

TALK NERDY TO ME

Commentary cont'd

Author's Response: *That is also correct and it is unfortunate that we couldn't summarize these elements in our article. Clearly, these steps should be performed before implementation; however, in their defense the authors may have completed this work prior to starting the trial and just not reported it. The identification of potential facilitators/barriers for implementation contributes to incorporating evidence into practice particularly when aiming an improvement of self-care and professional practices.*

3. *Fidelity of the Intervention*: None of the studies reported fidelity of the intervention. What I mean by that is the vigor, timing, engagement and clarity of the asthma education. There was not enough detail to differential which interventions were effective vs. ineffective.

- Author's Response: *In our article, we made considerable efforts to describe the fidelity of the interventions; however, we failed to identify detailed fidelity information. Consequently, we called for standardized description and evaluation of the proposed interventions in future reports. Analyses focused on one or more of the fidelity domains could reveal important changes in effect sizes.*

4. *Health Literacy*: The NNT was 6 for the intervention but none of the studies reported whether patients understood or followed the ED educational recommendations. Nor did they assess what happened during the PCP office follow-up visit. Better understanding these events will be essential to establishing a cause-effect relationship between ED education efforts and patient-oriented outcomes.

- Author's Response: *The issue of literacy needs to be determined BEFORE the intervention is implemented and was not reported in these trials. We are similarly concerned that simply being seen by a PCP is as effective as seeing a PCP with and interest and training in asthma education. The effectiveness of the intervention does depend to some degree on the skills and resources available to PCPs at the time of the follow-up.*

5. *Texting*: What about using technology for the asthma education and encourage follow-up? You could text asthma information while at the same time reminding patients of their primary care provider follow-up.

- Author's Response: *Texting has been shown to be an effective delivery method for educational interventions; however, you need to consider your "target population" and the purpose of your intervention. We have learned lots from engaging patients and knowledge users (PCPs) in our research initiatives in asthma and from exploring their perceived needs and expectations. In our research, patients appear to prefer having one-on-one discussions, and text was not a preferred method. We concur; however, this is an area, which deserves more focused attention.*

Clinical Application

Working with my nurse educator, our emergency department develops a nurse-led asthma discharge education protocol that includes teach-back understanding of asthma care received in the emergency department, prescriptions provided, indications for each prescription, available primary care provider, and access to transportation for both prescriptions and primary care provider office follow-up.

STUDY QUALITY CHECKLIST

The clinical question is sensible and answerable	
The search for studies was detailed and exhaustive	
The primary studies were of high methodological quality	
The assessment of studies were reproducible	
The outcomes were clinically relevant	
There was low statistical heterogeneity for the primary outcomes	
The treatment effect was large enough and precise enough to be clinically significant.	

CONCLUSION VS COMMENTARY

COMPARISON

A variety of emergency department educational interventions appear to improve primary care provider follow-up rates, but which interventions applied to which patients in what settings remain nebulous. The external validity of these findings in emergency departments without dedicated research personnel is unknown, as is the link between asthma education and asthma-related morbidity in the months following an asthma exacerbation episode of care.

WHAT DO I TELL MY PATIENT?

Asthma is a common lung disease. An asthma attack can happen throughout your life. Sometimes we are able to find what triggered the attack (cold, weather changes, medication changes, exposure to smoke or chemicals), but often we cannot. If you understand your asthma better you can have less attacks, which could be less severe. This can mean fewer trips to the emergency department, better quality of life, less sick days lost from work and even prevent you from being admitted to hospital. Our asthma nurse is going to talk with you about:

1. What would mean your asthma is getting worse
2. How to treat your asthma if it is getting worse
3. What treatments you received in the emergency department today
4. When you should follow-up with your primary care provider?
5. What situations you should return immediately to the emergency department?

References

Villa-Roel C, Nikel T, Ospina M, Voaklander B, Campbell S, Rowe BH. Effectiveness of educational interventions to increase primary care follow-up for adults seen in the emergency department for acute asthma: A systematic review and meta-analysis. Academic Emergency Medicine. 2016 Jan 1;23(1):5–13.

GUEST SKEPTIC: Dr. Chris Carpenter
Deputy Editor of Academic Emergency Medicine; faculty member of Emergency Medical Abstracts

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Call me Maybe for bystander CPR

Case Scenario:
A 78-year-old man with a history of hypertension and coronary artery disease suddenly collapses at home in front of his wife. She calls 911 but is unable to get on her knees and provide CPR due to her comorbidities.

Clinical Question:
Can using a mobile-phone positioning system to dispatch lay volunteers who were trained in CPR increase the rate of bystander-initiated CPR for patients with OHCA?

Bottom LINE

Using mobile phones to increase bystander CPR for OHCA is a cool use of technology but we would want to see it externally validated and demonstrate survival with good neurologic outcome.

Mobile-phone dispatch of laypersons for CPR in Out-of-Hospital cardiac arrest Ringh et al. NEJM. June 2015.

P

Cases suspected by 911 dispatcher to be out-of-hospital cardiac arrest that occurred during daytime hours (6am-11pm) in Stockholm, Sweden and ended up getting treated by EMS.

✘ Patients less than 8 years of age, hazardous environment, and cases of OHCA caused by drowning, trauma, intoxication, or suicide.

I

Volunteer within 500m radius called to scene of possible cardiac arrest, with the assumption that CPR should likely be performed.

C

Usual care. No volunteer called to the scene. EMS called as usual.

O

Primary: Bystander-initiated CPR before the arrival of EMS (ambulance, fire, and police services).

Secondary: Bystander-initiated CPR, including CPR that was given only with the help of instructions given over the telephone, findings of ventricular fibrillation or ventricular tachycardia at the first electrocardiographic assessment, return of spontaneous circulation, and 30-day survival.

Authors' Conclusion:

"A mobile-phone positioning system to dispatch lay volunteers who were trained in CPR was associated with significantly increased rates of bystander-initiated CPR among persons with out-of-hospital cardiac arrest."spi

Background

Sudden cardiac arrest is common with approximately 500,000 cardiac arrests each year in the USA. More than half of these cardiac arrests are out of hospital cardiac arrests (OHCA) and the survival rate is pretty poor.

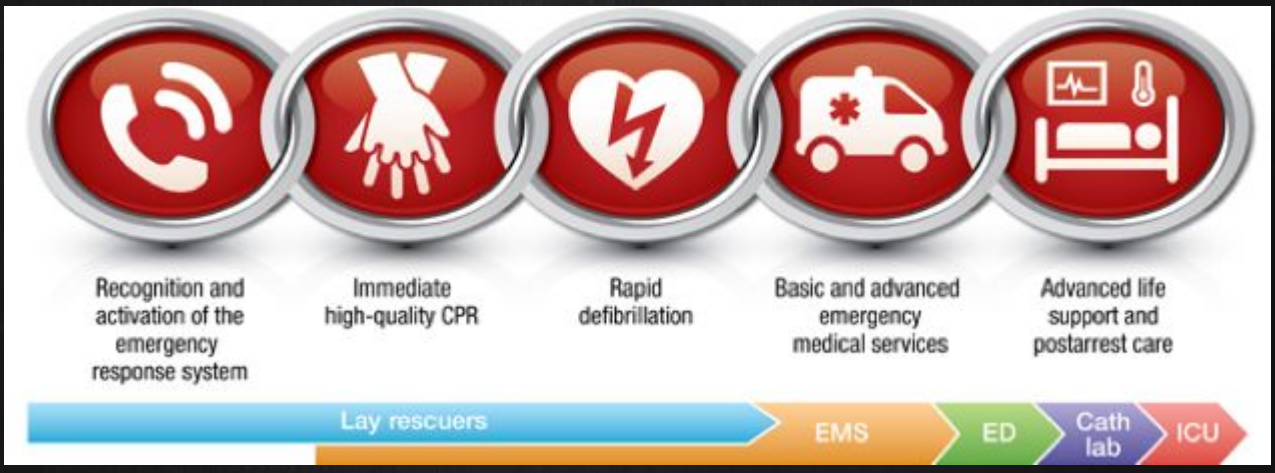
The American Heart Association came out with updated CPR & ECC Guidelines in 2015 that included its "Chain-of-Survival". There are five steps in the Chain-of-Survival for OHCA.

- Step One – Recognition and activation of the emergency response system
- Step Two – Immediate high-quality CPR
- Step Three – Rapid defibrillation
- Step Four – Basic and advanced emergency medical services
- Step Five – Advanced life support and post arrest care

The fourth step in the chain was covered with the EM Swami on SGEM#64. This was the classic OPALS trial done by Ian Stiell and his group in Ottawa, Canada. It demonstrated ACLS did not increase survival to hospital discharge over BLS for patients with OHCA.

In contrast, step two has been associated with a significant increase in survival. Bystander-initiated CPR improves chances of survival compared to those people who did not receive such help. A major barrier to improved survival of OHCA remains the low rates of bystander-initiated CPR.

There has been a dramatic increase in mobile phones over the last few years. These devices are becoming tools used in health care. One fascinating application has been automated text messaging to remind discharged emergency department patients of their follow-up appointments. This was a study published in AEM by Sanja Arora showed the NNT (number needed to text) was 10 (SGEM#102).



Results

They recruited close to 10,000 lay volunteers and trained them in CPR for the study. For perspective, Stockholm County has a population of 2 million covering an area of 6,500 square kilometres.

The mobile-phone positioning system was activated in 667 out-of-hospital cardiac arrests: 46% (306 patients) in the intervention group and 54% (361 patients) in the control group.

First responders (police or fire vehicle) arrived on scene before an ambulance in close to 40% of all the OHCA. The median time to arrival of EMS or first responders was 7.5 minutes. Bystander CPR was performed for at least two minutes in almost 50% of the cases and up to five minutes in over 80% of the cases.

Results

Primary Outcome: The rate of bystander-initiated CPR was 62% (188/305 patients) in the intervention group and 48% (172/360 patients) in the control group (absolute difference for intervention vs. control, 14 percentage points; (95% CI 6 to 21; P<0.001).

Number Needed to Text = 7

If you included the cases in which instructions for how to perform CPR were provided over the telephone were counted as bystander-initiated CPR the rate increased to 64.3% in the intervention group and 54.7% in the control group. So about a 10% improvement in CPR rates if they got instructions over the phone giving a NNT of 10.

Secondary Outcome: None of the secondary outcomes were statistically significant (return of spontaneous circulation, initial cardiac rhythm, and 30-day survival).

Commentary

This was a very interesting study using technology in a way that was probably never conceived when it was being designed. The merging of mobile phones, texting, and global positioning can be a powerful force. How we use our tools is a statement of what kind of society we live in. This idea of crowd sourcing layperson CPR is fascinating way to use this modern tool.

There were a few issues with this study to discuss in more detail:

1. *Consecutive*: Not all patients with OHCA were randomized. There were 237 patients where the dispatcher suspected OHCA but did not activate the system for one reason or another, which we don't really know. These patients represent a significant proportion (¼) of all eligible patients, but in the authors' defense they were similar to the group who were randomized (mostly older men at home), so unlikely to change much. About 40% of these non-randomized daytime OHCA patients received bystander CPR.

2. *Blinding*: Bystanders and EMS would know if a responder arrived on scene first and started CPR. However, the investigators were unaware of group assignment until after the study was analyzed. Bias may have been introduced by this lack of blinding but its effect is unknown.

3. *Patient Oriented Outcomes*: The primary outcome was the rate of bystander-initiated CPR, which is a surrogate marker and not patient oriented. One of their secondary outcomes was 30-day survival rate but their study was underpowered to detect a statistical difference. This is also not really patient oriented. What we really care about in these OHCA studies is survival with good neurologic function. Nobody calls it a "win" if you have improved 30 day survival but the survivors were all completely brain dead. A larger study will need to be performed to determine if mobile-phone dispatching of lay volunteers trained in CPR will be superior to usual care for survival with good neurologic outcome.

4. *Exclusions*: There were a number of exclusions with the biggest one being nighttime. The system did not operate from 11pm until 7am. Over 200 patients had OHCA at night. They excluded children under eight years of age, hazardous environment, and cases of OHCA caused by drowning, trauma, intoxication, or suicide. Would the same improvement in layperson-initiated CPR occur at night and in these other circumstances?

Commentary

5. *External Validity*: This is one of the very big concerns about this study. It represented one dispatch system in one health care system with a dense population. Whether or not these results would be replicable in other settings is unclear. Stockholm is a very developed, well-educated, progressive city with only ~10% foreign-born residents. Does this reflect the community you work in currently?

- Rural vs. Urban: EMS response times tend to be longer in rural areas but the population is less dense. So the professional would take longer to arrive but so probably would the layperson. There is also a lack of cell phone signal in some rural areas. So would this work better or worse in rural communities?

- Los Angeles: LA is a very large, ethnically, socioeconomically diverse city with varying degrees of health literacy and language. LA has ~40% foreign born as opposed to 10%, with a diaspora of languages spoken, compared to Stockholm which has near total Swedish fluency and even over 90% English proficiency. Not to mention in LA the amount of cultural and other barriers to communication separating people. It makes you wonder, would people allow strangers into their homes? Stockholm's crime rate pales in comparison to LA. What would be the reaction of the neighbours in these cases? Would responders have some badge or identification displayed on their mobile phone? What about safety of the provider and of the individual? Would trained volunteers in CPR also carry protection or guns? What would be the legal implications if the volunteer is injured or the patient is harmed?

Clinical Application

None, as we do not have a mobile phone dispatch system of laypersons trained in CPR at this time. However, high-quality bystanders CPR should be initiated immediately for people with an OHCA.

Study Quality Checklist

The study population included or focused on those in the ED	👎
The patients were adequately randomized	👍
The randomization process was concealed	👍
The patients were analyzed in the group to which they were randomized	👍
The study patients were recruited consecutively (ie., no selection bias)	👎
The patients in both groups were similar with respect to prognostic factors	👍
All participants (patients, clinicians, outcome assessors) were unaware of group allocation	👎
All groups were treated equally except for the intervention	👍
Follow-up was complete (i.e., at least 80% for both groups)	👍
All patient-important outcomes were considered	👎
The treatment effect was large enough and precise enough to be clinically significant	?

CONCLUSION VS COMMENTARY

COMPARISON

We agree that this system can improve layperson CPR in Stockholm, Sweden without improving 30-day survival for patients with OHCA.

WHAT DO I TELL MY PATIENT?

After they have survived their OHCA, I would encourage them to get trained in CPR because someday they may save a life. In addition, their life may be saved in the future by a layperson trained in CPR sent to their location by a text message if they have another OHCA.

References

Ringh M, Rosenqvist M, Hollenberg J, Jonsson M, Fredman D, Nordberg P, Järnbert-Pettersson H, Hasselqvist-Ax I, Riva G, Svensson L. Mobile-phone dispatch of laypersons for CPR in out-of-hospital cardiac arrest. New England Journal of Medicine. 2015 Jun 11;372(24):2316-25.

GUEST SKEPTIC: Dr. Dave Harrison
EM resident at Keck School of Medicine, USC, Los Angeles, CA.

144 That smell of isopropyl alcohol for nausea in the Emergency Department

Case Scenario:
A 34-year-old male presents to your ED with complaints of severe nausea for the past 24 hours. He's vomited a number of times at home and on a scale of zero to ten (ten being the worst nausea he's ever experienced), he rates his current nausea at an eight. As the triage nurse brings him back to get settled into his room, you observe him holding an emesis basin and dry heaving. He has no significant past medical history and no known drug allergies.

Clinical Question:
Does nasally inhaled isopropyl alcohol reduce nausea in adult emergency department patients?

Bottom LINE

For patients presenting to the emergency department with complaints of nausea and vomiting, a nasal inhalation of isopropyl alcohol is a quick, inexpensive way that may transiently improve symptoms without evidence of harm.

Isopropyl alcohol nasal inhalation for nausea in the emergency department: a randomized controlled trial

Beadle et al. Ann Emerg Med. 2015.

P

Adult patients presenting to an urban tertiary care emergency department with chief complaint of nausea or vomiting.

✘ Exclusion Patients with an allergy to isopropyl alcohol, were unable to inhale through the nares, if they were unable to read or write in English, or had altered mental status (including intoxication). Other exclusions included patients who had received an antiemetic (including nasally inhaled isopropyl alcohol) or psychoactive drug or a medication known to potentially produce nausea when exposed to alcohol (eg, disulfiram, metronidazole, cefoperazone).

I

Nasal inhalation of an isopropyl alcohol pad for no more than 60 seconds (at study start, after two minutes and after four minutes). If nausea was relieved at any time, subjects were instructed to not further inhale.

C

Nasal inhalation of a pad saturated in normal saline

O

Primary outcome: Nausea score at 10 minutes post treatment using an 11-point verbal numeric response scale (0 being "no nausea" to 10 being "worst nausea imaginable").
Secondary outcomes: Patient satisfaction scores on a 5-point Likert scale (1 being "very unsatisfied" to 5 being "very satisfied"), pain verbal numeric response scale score at 10 minutes post-intervention, and receipt of subsequent rescue antiemetics.

Authors' Conclusion:

"We found that nasally inhaled isopropyl alcohol achieves increased nausea relief compared with placebo during a 10-minute period."

Background

Nausea and vomiting is a very common complaint for patients presenting to the emergency department, accounting for almost five million visits in the US each year.

Currently available antiemetic treatments include ondansetron, droperidol, metoclopramide, promethazine, and prochlorperazine. Ondansetron is the most commonly administered medication in US emergency departments. Despite this, it takes about 30 minutes for intravenous ondansetron to work, which isn't ideal in patients on the verge of vomiting.

There are studies showing commonly used antiemetic drugs are not superior to placebo in undifferentiated emergency department patients. We covered one of those studies with Eve Purdy on SGEM#101 called Puke – Antiemetics in Adult Emergency Department Patients.

A number of studies have evaluated the use of isopropyl alcohol inhalation for nausea, but these have primarily been in the postoperative setting. A recent Cochrane Review by Hines et al found that isopropyl alcohol inhalation was more effective than placebo in reducing the number of subjects requiring rescue anti-emetics but not as effective as standard anti-emetic therapy.

That Cochrane review also found that other aromatherapies like peppermint oil did not have any good evidence to support their use in treating postoperative nausea and vomiting.

Results

Eighty patients were enrolled in this study and underwent randomization (37 to treatment and 43 to control).

Primary Outcome: The isopropyl alcohol arm had lower verbal numeric response scale nausea scores at 10 minutes than placebo (Median score of 3 vs. 6 on an 11 point scale, $p<0.001$). This gave an effect size of 3 (95% CI 2 to 4).

Secondary Outcomes: No significant difference between groups in median pain verbal numeric response scale scores or subsequent receipt of rescue antiemetics. Patients randomized to the isopropyl alcohol arm reported higher satisfaction scores. Median satisfaction score was 4 in the isopropyl alcohol arm vs. 2 in the placebo arm. This gave an effect size of 2 (95% CI 2 to 2). There were no serious adverse events were documented in either group.

Commentary

This paper, although small, is the first to evaluate this intervention in an emergency department population of patients presenting with nausea and vomiting-related complaints.

Isopropyl alcohol inhalation may affect neurotransmission at sites affecting the chemoreceptor trigger zone, and represents an inexpensive and safe intervention for the treatment of nausea, a common presentation to the emergency department.

TALK NERDY  TO ME

Commentary Continued

There were a number of limitations:

1. *Single Center*: This was done at the San Antonio Military Medical Center. It serves active-duty military personnel, retirees and beneficiaries. The mean age was in the mid thirties and about 2/3 were women. This may or may not reflect your patient population presenting to your emergency department with nausea and vomiting.

2. *Convenience Sample:* These were not consecutive patients presenting with nausea and vomiting but a convenience sample. This could introduce selection bias. They tried to minimize this potential bias by having study personnel available to recruit patients at varying times (days, nights, and weekends).

3. *Blinding*: The investigators tried hard to blind the subjects and evaluators. This included obscuring the two types of pads with opaque brown tape, holding the packages at arms length from the investigators and telling the patients not to describe the pad scent. Despite these efforts, I think there probably was some un-blinding. Because isopropyl alcohol provides a stronger olfactory stimulation compared to normal saline it could trigger a placebo effect. This would bias the study toward the treatment group. The authors could have addressed this in the study design by having three groups; isopropyl alcohol, placebo (normal saline pad) and sham group (peppermint oil). The investigators could then inform patients about the possibility of being randomized into a placebo group. After the study, patients and investigators could be asked which group they felt they were assigned. This would serve two purposes. It would help minimize the olfactory component associated with the isopropyl alcohol and confirmed if blinding was maintained.

4. *Patient Oriented Outcomes*: A decrease in nausea scores at 10 minutes is important but there are other possibly important patient oriented outcomes. It would have been nice to see how many patients in each group actually vomited after the intervention. Receiving an antiemetic and the number of doses are indirect markers for the patient-oriented outcome that really matters (i.e. did you vomit?). The primary outcome of nausea scores on a verbal rating scale is certainly a subjective measure, but measuring individual episodes of vomiting may have provided a more objective endpoint to measure. Additionally, the duration of the study period was relatively short at 10 minutes. You wouldn't necessarily expect that the effectiveness of isopropyl alcohol nasal inhalation to last longer than 10 minutes, but further detail evaluating what happened to these patients further on in their emergency department stay might have been valuable to measure and describe. The onset of action for many of our commonly used anti-emetics isn't immediate; ondansetron takes around 30 minutes to have a notable effect on nausea. So if you have a patient who is acutely nauseous in front of you, the use of isopropyl alcohol via nasal inhalation might in theory represent a "bridge" therapy until the other anti-emetics can kick in. However, when prophylactic isopropyl alcohol was evaluated along with ondansetron versus ondansetron alone for postoperative nausea and vomiting, the study investigators weren't able to detect a benefit (Radford et al).

5. *Harm*: This study is too small and too short a time period (10min) to give any strong statement about safety. It is a common mistake to assume the lack of evidence of harm equals evidence of safety. I am not saying that nasal inhalation of isopropyl alcohol is harmful but the conclusion cannot be that it is safe. The authors seem to acknowledge this limitation.

Clinical Application

Emergency department physicians may consider using isopropyl alcohol nasal inhalation as a very inexpensive intervention for transient relief of nausea symptoms for patient presenting to the emergency department.

CONCLUSION VS COMMENTARY COMPARISON

We agree that isopropyl alcohol nasal inhalation appears to transiently decrease nausea compared with placebo.

Study Quality Checklist

The study population included or focused on those in the ED	👍
The patients were adequately randomized	👍
The randomization process was concealed	👍
The patients were analyzed in the group to which they were randomized	👍
The study patients were recruited consecutively (ie., no selection bias)	👎
The patients in both groups were similar with respect to prognostic factors	👍
All participants (patients, clinicians, outcome assessors) were unaware of group allocation	?
All groups were treated equally except for the intervention	👍
Follow-up was complete (i.e., at least 80% for both groups)	👍
All patient-important outcomes were considered	👎
The treatment effect was large enough and precise enough to be clinically significant	?

WHAT DO I TELL MY PATIENT?

It sounds like you're experiencing some pretty severe nausea and discomfort. I would like you take a few deep breaths of this alcohol swab. There is some evidence it can help with nausea. This will give us 10 minutes to set up an IV and start you on some IV fluids and other medications for your nausea.

References

Beadle KL, Helbling AR, Love SL, April MD, Hunter CJ. Isopropyl alcohol nasal inhalation for nausea in the emergency department: a randomized controlled trial. Annals of emergency medicine. 2016 Jul 1;68(1):1-9.

GUEST SKEPTIC: Meghan Groth, PharmD, BCPS
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145 Topical anesthetics for ED patients with corneal abrasions

Case Scenario:

A 23-year-old healthy woman presents with right eye pain. She felt a foreign body sensation yesterday. Overnight it became painful. Her visual acuity is 20/20 bilaterally; she doesn't wear corrective lenses. Tetracaine drops results in complete resolution of the pain. On slit lamp exam, there is a small corneal abrasion outside of the visual axis with no evidence of ulceration or foreign body. You update the patient's tetanus, prescribe an antibiotic drop, and prepare to discharge her when she states, "The pain is starting to come back. Can I have that bottle of medicine you used before to take home with me?"

Clinical Question:

Can emergency department patients with simple corneal abrasions be safely discharged home with a prescription for a topical anesthetic drop?

Bottom LINE

The best evidence that we currently have demonstrates that dilute topical anesthetic drops of either proparacaine or tetracaine are safe for use in ED patients with simple corneal abrasions to provide analgesia. The studies are small but the data contained in them is far superior to the case series published 50 years ago which led to the dogma that using them is dangerous.

The safety of topical anesthetics in the treatment of corneal abrasions: a review

Swaminathan et al. J Emerg Med. 2015.

P Population: Adult patients with a corneal abrasion
- ✘ Excluded: Animal studies, case reports, case series and non-English

I Topical anesthetic drops (proparacaine, tetracaine or bupivacaine)

C Placebo

O Pain control and adverse events

Authors' Conclusion:

Limited available data suggests that the use of dilute topical ophthalmologic proparacaine or tetracaine for a short duration of time is effective, though their safety for outpatient use is inconclusive.

Background

Corneal abrasions account for approximately 10% of eye related visits to the Emergency Department, making them one of the most common eye related presentations (Verma and Kahn). The cornea is highly innervated, and even small abrasions can cause significant pain. Pain control is one of the fundamental goals of emergency medical care. The first documented use of topical ophthalmologic anesthetics was in 1818. A cocaine derivative was employed to effectively block nerve conduction in the superficial cornea and conjunctiva (Rosenwasser).

However, a number of proposed dangers limit the use of topical anesthetic agents for the treatment of corneal abrasion associated pain. These dangers include delayed healing secondary to mitosis inhibition and decreased corneal sensation

Background Cont'd

The latter issue is of concern because of the potential for the abrasion to progress to an ulcer without the patient noticing. Additionally, these agents may have direct toxicity to corneal epithelium with prolonged use, leading to increased corneal thickness, opacification, stromal infiltration, and epithelial defects. The fear of these complications has led to the pervasive teaching that topical anesthetics should never be used for outpatient management of corneal abrasions. This is reflected in the condemnation of their use in major Emergency Medicine textbooks including Rosen's and Tintinalli's.

Based on this, we have been reluctant to give these agents to patients in spite of the fact that we know they'll improve pain levels.

Results

Our systematic review found that topical anesthetics provided good pain control with no adverse outcomes if used for 48 hours and having physician follow up.

Emergency Department Studies of Topical Anesthetics for Corneal Abrasions

Author	Years of Study	Number of Patients	Intervention	Outcomes
Ball et al	2010	33	0.05% Proparacaine vs. placebo (both arms: 2-4 drops prn x 7 days)	No observed adverse events with efficacious analgesia
Waldman et al	2014	116	1.0% tetracaine vs. saline drops (both arms: 1 drop q30min x 24h)	24h use was safe with effective analgesia

Photorefractive Keratectomy Studies of Topical Anesthetic Agents

Author	Years of Study	Number of Patients	Intervention	Outcomes
Verma et al	1995	44	1.0% tetracaine vs. placebo (both arms: 1 drop q30 min while awake x 24h)	Tetracaine group had significantly less pain and full epithelial closure within 72h
Verma et al	1997	38	Bupivacaine 0.75% vs. 1% tetracaine (both arms: 1 drop q30 min while awake x 24h)	Tetracaine had better pain control with full epithelial closure in all patients at 72h
Shahinian et al	1997	10	0.05% proparacaine (1 drop q15 min x 12h day 1, then 1 drop q1h x 6 days)	Dilute 0.05% proparacaine can be used safely for 1 week after PRK
Brilakis and Deutsch	2000	49	0.5% tetracaine (10 drops during a 3-day period)	All eyes healed within 3 days and effective for analgesia

TALK NERDY TO ME

Commentary

Dr. Chris Carpenter discussed with lead authors Drs. Kara Otterness and Salim Rezaie on primary outcomes, comparison of other systematic reviews, high risk of bias, and other topics, which can be found SGEM #145

Clinical Application

Was not in article...

Study Quality Checklist

The clinical question is sensible and answerable	
The search for studies was detailed and exhaustive	
The primary studies were of high methodological quality	
The assessment of studies were reproducible	
The outcomes were clinically relevant	
There was low statistical heterogeneity for the primary outcomes	
The treatment effect was large enough and precise enough to be clinically significant.	?

CONCLUSION VS COMMENTARY COMPARISON

Since we're the authors, we agree with our conclusion. We'd love to see more robust data on the topic and, we may see that soon. As part of our research, we were able to contact Neal Waldman and he let us know that they are currently enrolling patients in a larger, prospective study. We'll have to keep our eyes out for that one.

WHAT DO I TELL MY PATIENT?

You have a corneal abrasion, which is a scratch on the surface of your eye. This scratch can be quite painful. There are various options available to help control your pain once you leave the ED, including topical eye drops and oral pain medications. The advantage of the eye drops is that their effects are limited to the eye, so they cause less body-wide side effects compared to the oral medications. While we don't have robust evidence regarding their use and further research is needed, recent studies suggest that they are effective and probably safe, as long as you use them as prescribed and for a short amount of time. Furthermore, it is very important that you follow up with an ophthalmologist within two days for your eye to be re-checked.

References

Swaminathan A, Otterness K, Milne K, Rezaie S. The safety of topical anesthetics in the treatment of corneal abrasions: a review. Journal of Emergency Medicine. 2015 Nov 1;49(5):810-5.

GUEST SKEPTICS:
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Dr. Salim Rezaie
Associate Clinical Professor of Emergency Medicine Internal Medicine, University of Texas Health Science Center

146 The HEAT is on – IV Acetaminophen for fever in the ICU

Case Scenario:

Case Scenario:
A 64-year-old woman presents to the emergency department with fever, urinary symptoms, and altered mental status. You diagnose her with sepsis with a probable urinary source. You rapidly provide empiric antibiotics and initiate fluid resuscitation. You are ready to send her up to the ICU for monitoring when your nurse asks, "Shouldn't we give her some acetaminophen for her fever?"

Clinical Question:

Does regular administration of intravenous acetaminophen in febrile ICU patients being treated for a known or suspected infection impact the number of ICU-free days?

Bottom LINE

The routine use of IV acetaminophen for the treatment of fever in ICU patients thought to be due to infection cannot be recommended at this time.

Acetaminophen for fever in critically ill patients with suspected infection.

Young P et al. NEJM. 2015.

P

Population: ICU patients 16 years or older with a temperature of 38° C or higher and being treated for a known or suspected infection.

✘ Exclusion criteria: Acute brain disorders; liver dysfunction; post cardiac arrest where current or anticipated temperature control was required; rhabdomyolysis; pregnancy; previous enrolment.

I

Acetaminophen 1 gram intravenous every six hours

C

Placebo (5% dextrose in water) intravenous every six hours

O

Primary outcome: ICU free days at day 28 (death counted as zero ICU free days)

Secondary outcomes: All cause mortality at 28 and 90 days, number of days alive, ICU and hospital length of stay, hospital free days, number of days free from inotropes or vasopressors, mechanical ventilation, and renal replacement therapy. Physiological and laboratory-related outcomes.

Authors' Conclusion:

Early administration of acetaminophen to treat fever due to probable infection did not affect the number of ICU-free days.

Background

If you work in emergency medicine, you are aware of the continuous debate about fever. Is it harmful? Is it helpful? Should it be treated? We did a great episode (SGEM#95) on pediatric fever with Dr. Anthony Crocco from SketchyEBM.

When it comes to children, the American Academy of Pediatrics says: *"...fever, in and of itself, is not known to endanger a generally healthy child. In contrast, fever may actually be of benefit; thus, the real goal of antipyretic therapy is not simply to normalize body temperature but to improve the overall comfort and well-being of the child."*

Dr. Crocco also did a great RANThony on the whole fever fear topic a few years ago. However, we are not talking pediatric fever today but rather adult ICU patients with fevers.

There are two opposing schools of thought about the value of fever in infection. One side argues that fever causes an increased metabolic stress than might be detrimental to already sick patients. The other side points out that fever is a natural immune response designed to fight infection. So eliminating this natural line of defense could make sick patients even sicker. Unfortunately, there has been little high quality evidence to answer this question – until now.

Results

They enrolled 700 patients of which 690 were available for assessment. The mean age was in the late 50's, two-thirds of the patients were male and the peak temperature was in the high 38C.

Primary Outcome: No statistical difference in ICU free days to day 28

About half had a pulmonary source of infection, about half needed inotropic or vasopressor support and about half had invasive ventilation.

- 23d (IQR 13–25) in the acetaminophen group vs. 22d in the placebo group (IQR 12–25)
- Hodges–Lehmann estimate of absolute difference, 0 days (96.2% CI 0 to 1; P=0.07)

Secondary Outcomes: No statistical differences

- All cause mortality at 28 days: 13.9% with acetaminophen vs. 13.7% with placebo
- All cause mortality at 90 days: 15.9% with acetaminophen vs. 16.9% with placebo (relative risk, 0.96; 95% CI, 0.66 to 1.39; P = 0.84)
- ICU length of stay: 4.1 days with acetaminophen vs. 4.2 days with placebo
- Hospital length of stay: 13.7 days with acetaminophen vs. 13.8 days with placebo

However, in a pre-specified subgroup analysis, acetaminophen was associated with a shorter ICU length of stay among survivors, but with a longer ICU length of stay among non-survivors.

- Non-survivors: 10.4 (IQR 4.1 – 16.9) vs. 4.0 (1.7 – 9.4); P<0.001
- Survivors: 3.5 (IQR 1.9 – 6.9) vs. 4.3 (2.1 – 8.9); P< 0.01

There was a statistically but not clinically significant different in the mean daily peak body temperature (38.4±1.0°C vs.38.6±0.8°C; absolute difference, −0.25°C, 95% CI −0.38 to −0.11; P<0.001) and mean daily average body temperature (37.0±0.6°C vs. 37.3±0.6°C; absolute difference, −0.28°C (95% CI −0.37 to −0.19; P<0.001)

TALK NERDY  TO ME

Commentary

It is great to have some data in the adult population on whether or not treating a fever is beneficial. Knowing the pediatric literature we were not surprised with the primary result demonstrating no statistical difference with acetaminophen.

They did a number of things very well that strengthened the study. In particular they published their statistical analysis plan and crunched the numbers before un-blinding the study-group assignments.

There were a few issues to discuss:

1. *Consecutive Patients*: They excluded over 1,000 patients or almost 1/3 of the eligible population. We could not find in the article or the supplemental material why these patients were not randomized into the study. This could have led to selection bias and had an unknown impact on the results.

2. *Pre-Enrollment Exposure:* They did not track how many patients had acetaminophen prior to ICU admission. Two-thirds of these admissions came from the emergency department or the ward. How many of them had acetaminophen or another antipyretic prior to being transferred? How would this affect the results? We do not know.

3. *Protocol Violators*: Almost one out of every five patients in the treatment and the control group had protocol violations. The most common reasons were about 10% of patients missing a dose and 10% receiving an extra dose in both arms of the study. All the protocol violations were listed in Table S6 of the supplemental material. With so many violations it makes it harder to interpret the data.

4. *Length of Use*: The median number of doses of the study drug was only eight in the acetaminophen group and nine in the placebo group. The two most common reasons for discontinuing the study in both groups were discharge from the ICU (46% vs. 47%) or the fever had resolved (23% vs. 17%). Although I think unlikely, it is possible that the lack of difference seen was the result of not being on the acetaminophen long enough.

5. *Open Label Post-Trial*: While we do not know anything about acetaminophen use prior to randomization in the ICU we do know about what happened after the study concluded. Open label acetaminophen was used after the study drug was stopped in 30% of both arms. The effect of this on the primary outcome or any of the secondary outcomes is not known and again, makes it more difficult to interpret the data.

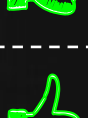
Clinical Application

There does not appear to be any benefit to providing routine acetaminophen to febrile ICU patients. However, it remains reasonable to provide acetaminophen to any patient for whom fever is causing distress or for pain control.

CONCLUSION VS COMMENTARY COMPARISON

We would agree with the authors' conclusion that intravenous acetaminophen to treat fever in ICU patients thought to be due to an infection did not affect the number of ICU-free days.

Study Quality Checklist

The study population included or focused on those in the ED	
The patients were adequately randomized	
The randomization process was concealed	
The patients were analyzed in the group to which they were randomized	
The study patients were recruited consecutively (ie., no selection bias)	
The patients in both groups were similar with respect to prognostic factors	
All participants (patients, clinicians, outcome assessors) were unaware of group allocation	
All groups were treated equally except for the intervention	
Follow-up was complete (i.e., at least 80% for both groups)	
All patient-important outcomes were considered	
The treatment effect was large enough and precise enough to be clinically significant	

WHAT DO I TELL MY PATIENT?

Like many patients, you may have heard that fever requires treatment. Fever doesn't seem to be harmful, and it may even be helping you fight off your infection. The best study we have so far shows that treating fever with acetaminophen does not improve your health, and therefore I don't think it is required. However, if your fever causes you any discomfort, we can give you acetaminophen to make you feel better.

References

Young P, Saxena M, Bellomo R, Freebairn R, Hammond N, van Haren F, Holliday M, Henderson S, Mackle D, McArthur C, McGuinness S. Acetaminophen for fever in critically ill patients with suspected infection. New England Journal of Medicine. 2015 Dec 3;373(23):2215–24.

GUEST SKEPTIC: Dr. Justin Morgenstern
EM Physician and Director of Simulation Education at Markham Stouffville Hospital, Ontario, Canada

147

The is SVT and I'm gonna REVERT it using a modified Valsalva manoeuvre

Case Scenario:
A 24-year-old female presents to the ED with palpitations. She feels anxious but is hemodynamically stable and her ECG demonstrates supraventricular tachycardia (SVT). This condition has happened several times before and she hates the medication she is usually given in the ED that makes her feel like she is dying.

Clinical Question:
Can a modified Valsalva manoeuvre help convert stable patients presenting to the ED with SVT to a sinus rhythm more often than a standard Valsalva manoeuvre?

Bottom LINE

Try modifying the Valsalva manoeuvre to REVERT you next stable patient with SVT to a sinus rhythm.

Postural modification to the standard valsalva manoeuvre for emergency treatment of supraventricular tachycardia (REVERT): a randomised trial

Appelboam et al. Lancet. 2015.

P

Population: Adult patients presenting to the ED with SVT (Ten Hospitals in the United Kingdom: two teaching hospitals, eight district general hospitals).

Inclusion: Over 18 years of age with a narrow complex tachycardia (QRS duration less than 0.12 seconds on ECG).

Excluded:

- ✘ Unstable patients with systolic blood pressure less than 90mmHg
- ✘ Patients with an indication for immediate cardioversion
- ✘ Those in atrial fibrillation or flutter
- ✘ Suspected atrial flutter requiring a trial of adenosine
- ✘ Any contraindication to the Valsalva manoeuvre (aortic stenosis, recent MI, glaucoma, or retinopathy)
- ✘ Inability to perform Valsalva, lie flat, or have legs lifted
- ✘ 3rd trimester pregnancy
- ✘ Previous inclusion in the study

I

A modified Valsalva manoeuvre

C

The standard valsalva manoeuvre

O

Primary: Return to sinus rhythm at one minute confirmed by ECG.

Secondary: Use of adenosine, use of any anti-arrhythmic, discharge home, length of stay in the emergency department and adverse events.

Authors' Conclusion:

"In patients with supraventricular tachycardia, a modified Valsalva manoeuvre with leg elevation and supine positioning at the end of the strain should be considered as a routine first treatment, and can be taught to patients."

Background

Patients with SVT often present to the emergency department. Life in the Fast Lane has a good blog posting about SVT.

Restoring patents back to a sinus rhythm can be done in a number of ways, including electrical, pharmacologic, and non-pharmacologic. For the hemodynamically unstable patient, synchronized cardioversion is usually the preferred treatment.

If they are not hemodynamically unstable, a variety of drugs have been used to stop SVT such as adenosine, calcium channel blockers, and beta blockers. It is the adenosine that people find particularly upsetting and is probably why the woman in this case is anxious about having her heart temporarily stop again.

Another way to convert patients that does not include drugs or electricity uses the mammalian dive reflex. This is used more often in children than in adults. Smith et al also published a review article on this method. The patient puts their face in an ice-cold bath. I have used this one time successfully on a patient who did not want to have adenosine again.

Carotid massage can also be tried but has the risk of adverse outcomes in elderly patients.

The Valsalva manoeuvre is a non-invasive way to convert patients from SVT to sinus. It increases the myocardial refractory period by increasing intrathoracic pressure, thus stimulating baroreceptors in the aortic arch and carotid bodies increasing vagal tone.

The effectiveness of the Valsalva manoeuvre for conversion of SVT was on SGEM#67. It was a systematic review by Smith et al that included three studies. Only one was from the emergency department setting and demonstrated a conversion rate of only 19%.

Results

N=428 with mean age in the mid 50's, approximately 40% being male and just less than half had a history of SVT.

The modified Valsalva manoeuvre resulted in an increased frequency of conversion out of SVT to a sinus rhythm, compared to the standard Valsalva manoeuvre. The primary outcome of return to sinus rhythm had an adjusted odds ratio (AOR) = 3.7 (95% CI: 3.3, 5.8, P<0.0001); NNT = 4 (95% CI: 3, 7)

Return to sinus rhythm at one minute: 43% vs. 17%, NNT = 4

Secondary Outcomes (modified vs. standard):

- Less use of adenosine (50% vs. 69%): AOR=0.45 (95% CI: 0.30, 0.68; P=0.0002);
- Less use of anti-arrhythmic treatment (57% vs. 80%): AOR=0.33 (95% CI: 0.21, 0.51; P<0.0001);
- No difference discharge home (63% vs. 68%): AOR= 0.79 (95% CI: 0.51, 1.21; P<0.28);
- No difference in time spend in the emergency department (2.82hrs vs. 2.83hrs): AOR=0.90 (95% CI: 0.75, 1.10; P=0.32)
- No difference in adverse events (6% vs. 4%): AOR= 1.61 (95% CI: 0.63, 4.08; P<0.31)

TALK NERDY TO ME

Commentary

This was a very well done, pragmatic study looking at a common problem. It provided a simple and cheap treatment option that was well tolerated and had impressive NNT of 4.

Blinding: As mentioned in the checklist section, it was not possible to blind the patient or the treating physician to treatment group. The participants were not aware of which treatment was the "new"method so that should have help with blinding the patients. The investigators also had the analysis of the ECG blinded. An independent cardiologist who was masked to the treatment group allocation retrospectively assessed the ECGs. They even had an independent eletrophysiologist also blinded to treatment group assignment arbitrate any disagreements with the treating physician's ECG interpretation.

Clinical Application

This new information is enough to convince me to try the modified Valsalva manoeuvre for the next hemodynamically stable patient presenting with SVT.

CONCLUSION VS COMMENTARY COMPARISON

We agree with the authors that a modified Valsalva manoeuvre should be tried first as routine care for stable SVT patients presenting to the ED and patients can be taught this technique.

STUDY QUALITY CHECKLIST

The clinical problem is well-defined	👍
The study population represents the target population (ie no spectrum bias)	👍
The study population included or focused on those in the ED	👍
The study patients were recruited consecutively (ie no selection bias)	👍
The diagnostic evaluation was comprehensive and applied equally to all patients (ie verification bias)	👎
All diagnostic criteria were explicit, valid, reproducible (ie no incorporation bias)	👍
The reference standard was appropriate (ie no imperfect gold-standard bias)	👍
All undiagnosed patients underwent sufficiently long/comprehensive follow-up (ie no double gold-standard bias)	👍
The L.R.(s) of the test(s) in presented or can be calculated from the information provided	👍
The precision of the measure of diagnostic performance is satisfactory	👍

WHAT DO I TELL MY PATIENT?

There is new and simple way that can slow your heart rate down to normal. It does not involve any drugs or electricity. It is successful in over 4 out of 10 patients. We have a short video for you to watch to show you how it's done. After you have watched the video we can give it a try.

References

Appelboam A, Reuben A, Mann C, Gagg J, Ewings P, Barton A, Lobban T, Dayer M, Vickery J, Benger J. Postural modification to the standard Valsalva manoeuvre for emergency treatment of supraventricular tachycardias (REVERT): a randomised controlled trial. The Lancet. 2015 Oct 31;386(10005):1747–53.

GUEST SKEPTIC: Dr. Bob Edmonds
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148 Stuck on you – Skin glue for peripheral IVs

Case Scenario:
In the middle of an ED shift, your nurses asks you to resite an IV on an 80-year-old lady with confusion and urosepsis. You had placed the IV yourself under ultrasound guidance earlier and it took some time and effort. The line has 'fallen out' and she needs re-siting before heading off to the ward. Your nursing colleague asks if you want to glue this one to stop it from getting pulled out?

Clinical Question:
Does the addition of skin glue decrease the failure rate of emergency department inserted peripheral intravenous catheters compared to standard peripheral intravenous catheter care?

Bottom LINE

Skin glue does appear to decrease the failure rate of IVs in patients admitted to hospital from the ED at 48 hours. We do not know if this is a good idea for all ED patients and we do not know the true effect size, but for high stakes cannulas that we really want to stay in this intervention should be considered.

Skin glue reduces the failure rate of emergency department-inserted peripheral invtravenous catheters: A randomized Controlled Trial

Bugden et al. Ann Emerg Med. 2015.

P

Adult emergency department patients requiring IV cannulation for therapeutic intervention.

✘ Excluded: Allergy/irritation to skin glue or standard IV catheter securement material; presence of infection near the IV site, upper limb phlebitis, or venous thrombosis; high likelihood of intentional IV removal (ex: agitated patient); and non-English speaking patients without an interpreter.

I

Fixation of the IV with one drop of glue at the peripheral IV skin site and one drop of glue under the peripheral IV catheter hub. There is a YouTube video demonstrating the technique.

C

Fixation of the IV with standard dressing (details and figures are in the paper).

O

Primary: PIV failure at 48 hours, defined as one or more of:

1. Infection: Clinical impression of cellulitis or pus
2. Phlebitis: Two or more symptoms of pain, redness, swelling or palpable venous cord
3. Occlusion: Inability of flush 10ml of saline or history of IV being removed because "it was not working"
4. Dislodgement: Subcutaneous extravasation or history of "it fell out"

Secondary: Modes of PIV (infection, phlebitis, occlusion, dislodgment)

Authors' Conclusion:

"This study supports the use of skin glue in addition to standard care to reduce peripheral intravenous catheter failure rates for adult emergency department patients admitted to the hospital."

Background

Placement of an IV is arguably the most common invasive procedure in the emergency department. It is almost routine for our sicker patient and yet it is not without risk.

IVs can act as a source of infection, are restrictive to patient movement, require monitoring and can fall out requiring replacement. All of these factors take time away from other aspects of clinical care and put patients at risk.

It is also fair to say that every clinician will remember the IV that took them ages to site, only for it to fall out later.

Back in 2012, Cliff Reid on the Resus.me site reviewed two papers looking at the use of tissue glue to secure central venous catheters and the results looked good. I am also aware of the use of glue amongst our anaesthetists to secure arterial lines in young children. These are both examples of "high stakes" lines. Glue is used to secure the line as it will be difficult and potentially dangerous for them to be removed and it makes sense to me and others to use it for securing them.

The glue used is cyanoacrylate glue, or skin glue as we know it. For peripheral IVs the question is slightly different.

We still need to question whether we need to place as many IVs in the ED as we do. A paper reviewed on the St.Emlyn's website back in 2013 showed that in an Australian ED fewer than 60% of peripheral IVs were used for anything more than taking blood. So clearly they are not as high stakes as our CVC and arterial lines.

However, some clearly are and in the case described we really do not want our IV to fall out and our patient may come to harm if they have delays in IV fluids or antibiotics.

The bottom line is that for many of our patients the securing of the IV is an important clinical intervention.

Results

A total of 369 patients were enrolled and had data to be analyzed (179 in the intervention group and 190 in the control group). The most common cannula was 20 gauge with the most common site being the antecubital fossa.

Failure rate at 48hrs: 17% (glue) vs. 27% (standard) NNT=10

Secondary Outcomes: Mode of peripheral IV failure was similar in both groups except for dislodgement. Peripheral IV dislodgement was 7% less frequent by 48hrs (95% CI –13% to 0)

TALK NERDY TO ME

Commentary

We like this study. It is a simple question, a simple design and an important question so first up we want to say thanks to all the people who put a lot of hard work into getting us to where we are now and for giving us the opportunity to discuss it. Anyone and everyone who has ever conducted an RCT in an emergency department will know – it's jolly hard work.

So on to the nerdy stuff. The bits that we need to discuss not to wreck a paper, but to understand how we can interpret the results in the paper and also for the applicability to our own practice.

1. *External Validity*: This is a paper from Australia, which has a similar EM practice to the UK and much of the developed world, including Canada. This means that the decisions about IVs and the reasons for their placement are likely to be similar to our practice.

2. *Single Centre*: This will always limit the generalizability of the findings. We do not know much about the patients in this study; they are likely to be similar to ours but we do not really know.

3. *Most ED Patients*: We need to think deeper about the patients. The patients in this study are those admitted for more than 48 hours. That's a subset of my patients who get IVs and so I'm not sure that we can apply this to every patient who might need an IV at the door of the ED. The patients themselves looked similar in table 1 in terms of their characteristics but there are only 360 patients in that table yet they randomised 380. It is unclear where the missing 20 are.

4. *Exclusion:* They excluded agitated patients and yet suggested these patients may have benefited the most. However, agitated patients often have super human strength and I am not sure a little dab would do ya.

5. *Randomization:* Randomization process itself was good in terms of the process; they used a computer generated randomisation sequence but there is some work out there that tells us that certain sites and uses of IVs are likely predisposed to failure. For example some studies suggest that the use of antibiotics increases the failure rate. The authors could have stratified their randomisation for factors such as this though that may have led to the need for a larger study.

6. *Consecutive Patients*: This was not consecutive recruitment and that may bias the results. Admittedly they recruited 16 hours/day 7 days a week, which is better than most EM studies, but there are problems with this. Firstly, patients overnight (I am guessing that's where those missing 8 hours were) are different. Secondly, the fact that it had to be when the research nurses were present may have influenced the cases. I can not see any data on the number of patients "screened" for inclusion in this trial and so it is possible that patients deemed "unsuitable" for whatever reason may have had different outcomes.

7. *Blinding*: As this is a therapeutic trial and an RCT a key question is blinding, or masking as we like to say in my house. Ideally, in a therapeutic trial everyone should be unaware of which group the patient has been assigned to until right at the end. Now clearly patients and staff could not be blinded here as it is obvious who gets the glue. However, they could have blinded those doing the data analysis, just giving them data but not telling them which group they were allocated. This is Nerd level – EXPERT but is increasingly seen in RCTs.

Commentary

8. *Follow-Up:* Follow-up was fantastic at over 97%. In Virchester we wound struggle to find 97% of my patients 48 hours after seeing them in the ED! You could question the outcome measure of 48hrs as many admitted patients require an IV for more than two days. In addition, 209/369 (57%) of patients were discharged home before being reviewed by the research nurse. These patients did not have direct visualization of their IV but rather a telephone interview with a standardized questionnaire, chart review and discussion with ward staff.

9. *Harm*: Harm is often underreported in studies. They did not report any incidents of adverse skin events but patients did comment on a "pulling" feeling during removal. This seemed to occur when the glue was not wiped off properly or patients with very hairy arms.

10. *Cost*: It's also worth mentioning that there is no assessment of cost here. Wound glue is expensive and the wipes to remove it similarly so. Having said that, the time, effort and equipment required to re-site IVs is also expensive and so there is a balance here. We simply don't know from the data presented how that would pan out in different health economies. In the UK the ED would bear the increased cost, and the wards would reap the benefits with the patients stuck in the middle. Such insanities exist in the financial world of medicine and so this would need to be a carefully negotiated intervention if we were to take it forward.

11. *Effect Size and Precision*: Lastly we need to think about the size of this study and I think the final question on the checklist is telling. The effect size is great, really great. The failure rate in the glue group was 17% as compared to 27% in the standard care group. That is an absolute reduction of 10% and thus a number needed to treat of just 10. If this study is true then we would save one resiting of a cannula for every ten that we put in. That effect size is huge as compared to most of the interventions that we deliver in the ED. So it is a big effect, but sadly it is not a very precise one. If we look at the confidence intervals for the effect they are pretty broad, ranging from an absolute risk reduction of 18% (an NNT of just over 5) through to 2% (an NNT of 50). That range would have a real impact on whether this is a worthwhile, routine, ED intervention.

Clinical Application

I think that the evidence here does not convince me to do this in every single patient, and of course if we are to start doing this we would need to consider resource and training implications. However, for some IVs, ones where I would consider them "high stakes" then yes I will consider and will probably use this technique in the ED.

CONCLUSION VS COMMENTARY COMPARISON

We generally agree with the authors' conclusions that skin glue reduces failure rate of peripheral IVs for adult ED patients admitted to the hospital.

STUDY QUALITY CHECKLIST

The study population included or focused on those in the ED	
The patients were adequately randomized	
The randomization process was concealed	
The patients were analyzed in the group to which they were randomized	
The study patients were recruited consecutively (ie., no selection bias)	
The patients in both groups were similar with respect to prognostic factors	
All participants (patients, clinicians, outcome assessors) were unaware of group allocation	
All groups were treated equally except for the intervention	
Follow-up was complete (i.e., at least 80% for both groups)	
All patient-important outcomes were considered	
The treatment effect was large enough and precise enough to be clinically significant	*

*Yes/unsure. It's a large enough treatment effect, but not sure about precision.

WHAT DO I TELL MY PATIENT?

We know that about 1 in 5 IVs fail in the first 48 hours. It looks as though you will need one for at least a couple of days. Putting a little skin glue on the IV site can make it less likely to fail. The skin glue makes it a little trickier to remove but we think it is a good idea to use it in your case.

References

Bugden S, Shean K, Scott M, Mihala G, Clark S, Johnstone C, Fraser JF, Rickard CM. Skin glue reduces the failure rate of emergency department-inserted peripheral intravenous catheters: A randomized controlled trial. Annals of emergency medicine. 2016 Aug 1;68(2):196-201.

GUEST SKEPTIC: Dr. Simon Carley
Professor of Emergency Medicine in Manchester, England.

149 Share Decision Making for Pain Control in Older ED Patients

Case Scenario:
78-year-old female with history of osteoporosis trips and falls, and presents with right wrist pain after which an x-ray revealed a Colles' fracture with no other injuries. After you assess her response to emergency department analgesia and splint the fracture, you prepare to discharge her and you contemplate the pros and cons of various pain meds. You ask the patient for her pain management preferences, but you wonder what the role is for ED shared decision making in geriatric patients.

Clinical Question:
Does shared decision making for analgesic selection in older adults discharged home from the ED with acute musculoskeletal pain improve pain relief?

Bottom LINE

SDM in selecting pain relief medications in older adult musculoskeletal pain patients is preferred to varying degrees by most patients, but in this study is not associated with faster recovery (less pain), less side effects, or a predisposition to any particular analgesic.

A Prospective Evaluation of Shared Decision-Making Regarding Analgesics Selection for Older Emergency Department Patients with Acute Musculoskeletal Pain.

Holland et al. Acad Emerg Med 2016

P

Adults >60 years old with acute, moderate-to-severe (pain greater than or equal to 4/10 on a 0-10 scale) musculoskeletal pain discharged home from the emergency department.

✘ Exclusion: Cognitive impairment (Six Item Screener score of 3 or less), pain for >1 month, daily use of opioid pain medication prior to current pain onset, headache, chest pain, or abdominal pain, lack of telephone for follow-up, or non-English speaking.

I

No intervention, but rather a descriptive, prospective, convenience-sample observational study of patient's preferences for shared decision-making, perceptions of shared decision-making with their musculoskeletal pain related ED visit, amount of analgesic information received, and ED care satisfaction within 24 hours of discharge via telephone. Another telephone interview at 1-week assessed effectiveness of pain relief and functional recovery.

C

No comparator group.

O

Primary Outcome: Change in pain severity from the time of ED arrival to the 1-week follow-up phone interview.

Secondary Outcomes: Satisfaction with the decision made in the ED about how to treat pain at home and satisfaction with the recommended or prescribed pain medication, and medication side effects.

Authors' Conclusion:

"In this sample of older adults with acute musculoskeletal pain, the reported desire of patients to contribute to decisions regarding analgesics varied based on both patient and provider characteristics. SDM was not significantly related to pain reduction in the first week or type of pain medication received, but was associated with greater patient satisfaction."

Background

Most clinicians are familiar with informed consent or informed decision making but may not be as familiar with the concept of shared decision making (SDM). Valerie Billingham in 1998 is credited with proclaiming *"nothing about me without me" at* the Salzburg Global Seminar. This statement succinctly captures the vision that medicine must always consciously respect human dignity. Her statement is credited as the genesis for *"Shared Decision Making"*(SDM) in medical decision-making.

- Key elements to SDM (Barry and Edgman-Levitan NEJM 2012):
  - Patient and the doctor *collaborate* on reaching a decision about a management strategy for a given problem
  - It first requires a situation where *more than one reasonable option exists*
  - SDM also requires that a patient be given the information they need to choose among the competing acceptable strategies
  - It shifts focus from *"disease"* and towards understanding patients' experience of illness
  - Barry states that SDM is *the pinnacle of patient-centered care*

The Affordable Care Act of 2010 in the United States emphasizes SDM that includes communication strategies to help patients collaboratively choose the best treatment option.

Although the 3-prongs of Evidence Based Medicine include research evidence, clinician expertise, and patient preferences, medicine has too often underemphasized the unique perspectives of patients and caregivers.

Results

Patients were mostly female (62%) with mean age 70 years and 74% were white and in severe pain (69%) at triage. There was an overall mean pain score reduction of 2.1 (6.6 to 4.5) between the ED visit and 1-week follow-up.

- *Preferences for SDM* were:
  - Active (16%): dering patient's opinions or wanted to leave all treatment decisions to the doctor. Patient makes the decision independently or make the decision after seriously considering input from the doctor.
  - Collaborative (37%): Share the decision with the doctor.
  - Passive (47%): Have the doctor make the final decision about treatment after considering patient's opinions or wanted to leave all treatment decisions to the doctor.

Results cont'd

Characteristics associated with greater desire for active role in decision making included: college graduate, care received from nurse practitioner, and care received from a female provider.

No significant association between 1-week pain improvement and any perceived degree of SDM was noted.

In addition, no difference in number of analgesic medication side effects or type of pain medication (acetaminophen, NSAID, or opioid) was observed.

However, patients who perceived receiving more SDM noted more satisfaction with the pain medication that they received (2.7 vs. 3.9 on a 1-5 Likert scale with 5 representing "completely satisfied").

Commentary

Adults over age 65 represent 18%-20% of ED patients in most hospitals nationwide. Surveys of ACEP membership in 1992 and in 2006 indicated that EM providers believe geriatric patients are more challenging to diagnose and manage, and consume more time and resources. Yet older adults often leave the ED feeling dissatisfied with the care received. Tim and I co-authored GED Guidelines that have been endorsed by ACEP, SAEM, AGS, ENA, and last week by CAEP in an effort to attain the Triple Aim for these patients (improved healthcare experience at same or lesser cost with improved outcomes). Prompt, effective analgesia is obviously essential for an improved patient experience.

1. *Screening Tool for Occult Cognitive Dysfunction*: One of the confounders for geriatric SDM is the presence of occult cognitive dysfunction. Multiple studies indicate that delirium and dementia are usually unrecognized in ED elderly. Therefore, these authors used the Six Item Screener as one exclusion criterion in order to reduce the impact of occult cognitive dysfunction. However, multiple ED validation studies have demonstrated that the Six Item Screener is inaccurate to either rule-in or rule-out occult dementia (positive likelihood ratio [LR+] =3.3, negative likelihood ratio [LR-]= 0.33). More accurate dementia screening instruments like the AD8, the Ottawa 3DY, or the Short Blessed Test, could be used in the future (Carpenter et al and Wilding et al). In addition, ultra brief screening instruments for acute delirium could also be used (Han et al and Han et al).

TALK NERDY  TO ME

Commentary cont'd

- *RESPONDS: Ottawa 3DY asks patients to report the day of the week, the year, and the date, plus spelling the word WORLD backward, with a three or less being cognitively impaired. I usually check my phone to see what the date is, sometimes multiple times a day. So…I'd probably fail this. Six item screener uses day of the week, the year, and the month (plus remembering apple, table, and penny), which seems a bit more friendly, plus you are allowed to miss two. For a clinical trial, the question is not how really well you can measure it but whether we think SDM could help patients with mild cognitive impairment? I think the answer is yes, so I'd pick a measure which is more inclusive for deciding who gets included in the study. Delirium is definitely missed in the ED, but I think less so in patients with acute MSK pain. Probably would be good to screen for delirium and exclude in the trial.*

2. *Health Literacy*: Another patient-level factor that can negatively impact the effectiveness of SDM is health literacy, which is based upon the gold standard of the S-TOFHLA is limited in about 25% of urban ED patients in the United States. Studies have shown that ED clinicians do not detect health literacy subjectively. Furthermore, health literacy is exacerbated by cognitive dysfunction so in older adult studies, both health literacy and cognitive impairment should be measured concurrently as these authors did. However, the choice of the REALM-R (LR+ = 2.1, LR- = 0.3) is not the best choice based on ED research indicating that the Newest Vital Sign is more accurate to identify a subset of patients at less risk of limited health literacy with LR+ 1.8 and LR- 0.04.

- *RESPONDS: The Newest Vital Sign was developed by a team including physicians at UNC (Dewalt, Pignone). We initially considered using the Newest Vital Sign (NVS) as an assessment of health literacy, but noticed that it was much more difficult and time-consuming to administer in the ED compared to the REALM-R. The NVS questionnaire includes six questions based on the information provided in an example nutrition label. Some of the questions are rather long and require basic mental math and reasoning skills, which may be too intensive for regular use in the ED. Additionally, the NVS is reported to take over three minutes on average to complete for adults aged 18 and older. This is much longer than the REALM-R, which can be easily finished in less than 30 seconds since it only involves reading ten words aloud. There is no free lunch – if you use a more accurate tool that takes 3 minutes and has 6 word problems, you are likely to lose some patients, which introduces selection bias. I think REALM-R was good choice in this case.*

TALK NERDY  TO ME

Commentary

3. *Descriptive Studies*: Descriptive studies are limited by the measures employed to capture, define, and characterize a phenomenon. The current study tries to evaluate a nebulous activity called *"shared decision making"*, a process that many experts still cannot reach consensus about how to define. They use the Control Preferences Scale to characterize the extent to which patients wish to lead or follow in reaching a medical decision with physicians. The authors then use the Shared Decision-Making Questionnaire (SDM-Q-9) to explore patient's perceptions of how effectively or ineffectively their ED provider used SDM while managing their current musculoskeletal pain. As with any instruments (see the studies about dementia, delirium, and health literacy referenced above), the performance of measures that work in primary care clinics, post-op settings, or nursing homes may differ markedly from how unwell they perform in ED settings. Using appropriate methods, instruments like these should be validated in ED settings before they can be confidently applied and interpreted in ED settings. For example, the SDM-Q-9 assesses only perceptions of SDM, but does not try to evaluate what actually occurred. The authors note that the "Observing Patient Involvement in Decision Making" (OPTION) scale assesses SDM using a third person or video camera thereby removing the uncertainties of patient memory or subjective interpretations. SDM is inherently subjective, though, so even if pristine methods were used by providers to engage willing and able patients in SDM, if the patient's next day perceptions are that SDM attempts were sub-optimal than it may not matter what a third party observer believes.

- *RESPONDS: It would be interesting to watch what happens in patient rooms, and try to do objectives assessments of SDM. However, to quote Eisenhower, I would make the problem bigger here. The tool we used to measure SDM is a problem, but the presence of unmeasured or poorly measured confounders is also a problem. In some lines of research, you only have observational studies. You can't randomize patients to smoking or not smoking to see an effect on cancer. For understanding whether an SDM approach improves outpatient pain management for older adults, we can do clinical trials, which would allow us to overcome many of these limitations. So…I am happy to accept all the limitations described, including this particular one about the SDM-Q-9. The real value of this research, is I hope, that it inspires a research group (perhaps ours, perhaps another group) to do a clinical trial to evaluate SDM for the outpatient treatment of acute musculoskeletal pain in older adults. I think it also provides some of the background needed to design such a trial in terms of which patients might be included and what outcomes might be considered. I will add however, that SDM in this setting has a ton of face validity. We know there are pain medication options, we know these medications have risks, and we know that physicians often don't get enough information from patients about what they should or shouldn't take and many patients don't even know the difference between acetaminophen and ibuprofen.*

Commentary

4. *Adjusting for Multiple Covariates*: Another aspect of this study that leave significant uncertainty are the attempt to adjust for multiple covariates (age, gender, race, initial pain severity, health literacy) with a sample size of 94.

    - *RESPONDS: Agreed. As you start to adjust for covariates you need a bigger sample. In the article we showed unadjusted and adjusted estimates – and they are fairly similar – which makes me think that there wasn't a lot of confounding going on. The biggest confounder is probably education – educated patients are more likely to engage in SDM and also probably more likely to do a number of behavioral things to make them recover (like get good sleep, stay active, take medications appropriately).*

In addition, the authors made no attempt to educate providers about techniques or barriers to SDM, nor how to evaluate patient comprehension. For example, how did individual providers communicate comparative effectiveness estimates for acetaminophen vs. NSAIDS vs. opioids? Did they use studies or generalized gestalt?

    - *RESPONDS: Right – We didn't intervene on providers. If we could effectively teach SDM to all our ED providers, that would probably be a good thing for patients, but we wouldn't have any variance in the exposure so we wouldn't know if it was helpful. In truth, we have an outstanding group of physicians at UNC – I think as good as anywhere in the country. But, most providers are not giving much information to patients about these options.*

5. *Statistical vs. Clinical Significance*: Finally, the adjusted difference in *"satisfaction with pain medication"* (2.7 in low SDM vs. 3.9 in high SDM, p=0.006) may be statistically significant, but whether this is clinically relevant or important to patients is unknown.

    - *RESPONDS: Also a good question. Having a satisfaction score of 3 meant they were "somewhat satisfied"; having a score of 4 meant the patient was "quite a bit satisfied." Seems like an important difference for this outcome, but not sure. I agree with the broader sentiment implied here, that for the clinical trial, I'd like to see an impact on pain and function, which strike me as much more important than satisfaction with the medication.*

Clinical Application

Uncertain. Since the authors did not assess the actual delivery of SDM real-time in the ED or provide any control group, the cause-effect relationship of SDM for these patient-centric pain outcomes cannot be elucidated by these results. How and when SDM should be used on whom and by which ED personnel cannot be determined by this study design. As the authors note, a clinical trial is required to confirm this benefit (as well as to better understand the how/when/who issues of SDM delivery).

CONCLUSION VS COMMENTARY COMPARISON

We agree with the authors' conservative conclusions. In this single center, convenience sampling of older adults without overt cognitive impairment and with acute or sub-acute musculoskeletal pain, the majority of patients desire some SDM in selecting outpatient analgesia. Perceived receipt of ED SDM is associated with improved patient satisfaction about the analgesic prescribed and is not associated with an increased use of opioids, but is not associated with either less pain or less medication side effects at 1-week.

STUDY QUALITY CHECKLIST

The study addressed a clearly focused issue	👍
The authors used an appropriate method to answer their question	?
The cohort was recruited in an acceptable way	👎
The exposure was accurately measured to minimize bias	👎
The outcome was accurately measured to minimize bias	👍
The authors identified all important confounding factors	?
The follow up of subjects was complete enough	👎
The results were precise and estimated risk well	?
The results are believable	👍
The results can be applied to the local population	👍
The results of this study fit with other available evidence	?

WHAT DO I TELL MY PATIENT?

Shared Decision-Making is the process by which patients and healthcare providers mutually review treatment options in deciding upon the optimal choice for the individual patient. This small study indicates that in older adults with acute pain in the ED, patients who receive SDM in selecting a pain medication are more satisfied with the choice of pain medicine received, but do not obtain faster pain relief or less side effects. Would you like me to review the effectiveness and side effects of different pain medications available?

References

Holland WC, Hunold KM, Mangipudi SA, Rittenberg AM, Yosipovitch N, Platts-Mills TF. A Prospective Evaluation of Shared Decision-making Regarding Analgesics Selection for Older Emergency Department Patients With Acute Musculoskeletal Pain. Academic Emergency Medicine. 2016 Mar 1;23(3):306–14.

GUEST SKEPTIC: Dr. Tim Platts-Mills
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150 Hypertonic Saline for Traumatic Brain Injury

Case Scenario:
21-year-old male is standing on the corner, minding his own business when he is hit in the head with a bat and suffers a severe traumatic brain injury. He's brought into the trauma room and appears to have an isolated head injury. His GCS is 6 and after intubating him, his left pupil is sluggish and 5 mm while his right is 3 mm and reactive. You decide to give a hyperosmolar solution for his suspected increased intracranial pressure while he is being transported to the CT scanner. You ask for a bag of mannitol, but someone asks whether hypertonic saline will be more effective for him.

Clinical Question:
What are the clinical benefits and harms associated with the use of hypertonic saline when compared to any alternative solution in patients with severe traumatic brain injury?

Bottom LINE

No significant mortality benefit or improved control of ICP compared to any other solution

Hypertonic saline in severe traumatic brain injury: a systematic review and meta-analysis of randomized controlled trials.

Pelletier et al. CJEM March 2016

P Population: Adults (aged 18 years and older) suffering from severe traumatic brain injury (Glasgow Coma Scale ≤ 8)

✘ Exclusions: For case-mix population studies, those with less than 80% adult patients were excluded

I Hypertonic saline

C Any other type of solution (e.g. Mannitol or normal saline)

O Primary outcome: Death and control of intracranial pressure
Secondary outcomes: Neurological outcomes at discharge, length of stay in the intensive care unit and hospital, and the occurrence of adverse events (including plasmatic osmolality and natremia).

Authors' Conclusion:

"We observed no mortality benefit or effect on the control of intracranial pressure with the use of hypertonic saline when compared to other solutions. Based on current level of evidence pertaining to mortality or control of intracranial pressure, hypertonic saline could thus not be recommended as a first line agent for managing patients with severe traumatic brain injury".

Background

Severe traumatic brain injury (TBI) is associated with a high morbidity and mortality and is a common injury seen in Canada (Turgeon et al and Zygun et al). In severe cases, increased intracranial pressure (ICP) may happen and generate secondary cerebral injuries following decreased cerebral perfusion pressure and ischemia. Increased ICP is strongly associated with mortality and unfavorable neurological outcomes (Giulioni and Ursino).

- Several interventions have been proposed to manage ICP:
  - Cerebrospinal Fluid Drainage (Bullock et al) – This is basically where an external ventricular drain is inserted into one of the ventricles of the brain to drain off CSF when the ICP is increasing.
  - Decompressive Craniectomy (Bullock et al) – This removes a piece of skull to allow the swollen brain to expand and thus reduce ICP.
  - Barbiturate Coma (Guidelines) – This is a last ditch effort when all other medical and surgical therapies have failed. Barbiturates are postulated to decrease ICP by a number of mechanisms such as lowering vascular tone and cerebral metabolism. Unfortunately, the RCTs of barbiturate comas were all done in the 80s, when standard care was prolonged hyperventilation, fluid restriction and steroids.

One therapeutic intervention to treat increased ICP is the use of hyperosmolar solutions. Mannitol is the most frequently administered hyperosmolar solutions and is the solution recommended by the clinical practice guidelines (Guidelines). Mannitol is considered the gold standard for hyperosmolar therapy in the treatment of ICP (Guidelines, Brown et al, and Sakowitz et al).

Recently, hypertonic saline solutions have been receiving support in treatment of increased ICP in TBI because of their volume expansion properties and osmotic effect (Mattox et al).

Results

Eleven studies were included in the systematic review for a total of 1,820 patients.

- Primary Outcomes:
  - Four studies had data on mortality (n=1,638). There was no significant difference in mortality RR 0.96 (95% CI, 0.83 to 1.11) I2=0%.
  - Six studies had data on ICP which also showed no significant difference WMD –0.39 (95% CI –3.78 to 2.99) I2=79%.

No significant mortality benefit or improved control of ICP compared to any other solution

- Secondary outcomes: No difference
  - Glasgow Outcome Scales extended– Two studies: no statistical difference
  - Disability Rankin Scale – Two studies: could not be pooled, no effect of the intervention
  - Functional Independence Measure (FIM) – One study: no clinical and statistical difference
  - Cerebral Performance Category – One study: no clinical and statistical difference
  - Ventilator– Free Days – One study: no observed benefit
  - Days Alive Out of ICU – One study: no observed benefit
  - Days Alive Out of Hospital – One study: no observed benefit
- Adverse Events: Hypernatremia was seen in all studies. No difference in seizures or nosocomial infections. Only one study reported on renal insufficiency.

TALK NERDY TO ME

Commentary

This is the largest systematic review on hypertonic saline for TBI to date and has strict methodological standards. In particular, we really liked how exhaustive the search strategy was to find the included articles. You searched multiple electronic databases, looked for the grey literature and reviewed the references of included studies.

- *Our team wanted to be thorough, we searched Medline, Embase, SCOPUS, Cochrane, Web of science, Biosis. There was no language restriction. We also contacted authors of studies that only the abstract was available to obtain additional unpublished data.*

Now a few questions for Elyse to help us better understand the paper.

1. *Primary Outcomes*: You had not one but two primary outcomes. They were death and intracranial pressure. Death is a very important patient oriented outcome but ICP is a disease-oriented outcome. Why the two primary outcomes?

- *Response: The decision to use two co-primary outcomes was based on the main reasons why clinicians justify their use of hyperosmolar therapies; death is a clinically relevant outcome while ICP control is the main mechanism behind a potential clinically significant benefit.*

One of your secondary outcomes was good neurological outcome at discharge. Some may argue that that would be even more patient oriented. Why not have good neurological outcome as your primary outcome for the study?

- *Response: We agree that neurological functional outcome measures are the best outcome measures to use in severe TBI. When we designed the study, we feared that very little data were published using such outcome measures and that readers will consider ICP control and death as more relevant of their practice, for good or bad reasons.*

2. *Compare to other Systematic Reviews*: There have been six systematic reviews looking at the efficacy of hypertonic saline. How did your study compare to the other systematic reviews?

- *Response: Our study is the most recent and the largest systematic review. Most of the others reviews included studies that were not randomized or that included patients with a variety of pathologies that create intracranial hypertension (e.g. stroke, spontaneous hemorrhage). We included studies solely with severe TBI population and randomized design, as well as we did not restrict our comparators to mannitol.*

Why do you think some of the other systematic reviews came to different conclusions?

- *Response: Mostly because positive systematic reviews included studies with various design (retrospective) and population (e.g. stroke, head injury, and tumor). Finally, they did not report clinically significant outcomes such as mortality, but rather used surrogate outcomes as their primary.*

TALK NERDY TO ME

Commentary cont'd

3. *High Risk of Bias*: You used the Cochrane Collaboration's Tool for assessing the risk of bias. Nine out of the eleven included studies were deemed to have high risk of bias. Only two of the included studies were felt to have low risk of bias based on the Cochrane Collaboration's tool. What impact do you think the bias should have on our interpretation of the results?

- *Response: The quality and the risk of bias of included studies in a systematic review may for sure have an impact on the quality of the evidence that is generated. Despite the conduction of a thorough systematic review following high methodological standards, we must deal with included studies of various methodological quality. In our review, the two studies (Bulger and Cooper) with low bias have a large part of all patients included in the meta-analysis (1511 patients).*

4. *Concentrations of Hypertonic Saline Solutions*? This varied in the different studies. Did it seem to make any difference depending on concentration used?

- *Response: We did not observe any impact on the concentration used. However, the small number of studies limited our ability to detect an effect.*

5. *Sensitivity Analysis*: There were only a few studies that could be pooled for analyses. What impact did that have on the systematic review?

- *Response: In our protocol, we planned a series of sensitivity analyses that could not be performed (e.g. different types of hypertonic saline concentrations) due to the limited number of studies. The absence of these sensitivity analyses did not impact the overall result of our systematic review, but precluded to generate hypotheses that could explain the findings.*

6. *Difference in Management*: What are the differences from a management perspective when using hypertonic saline solutions versus mannitol in terms of ongoing hour-to-hour treatment of the patient in the ICU (e.g. measuring serum osmolalities, urine output differences, etc.)?

- *Response: Both solutions are hyperosmolar solutions; management and monitoring following their administration are thus comparable regardless of the solution used.*

Commentary cont'd

7. *What about the Harm*? Trials are usually powered to find benefit and often under report harms. You could not do a meta-analysis on adverse events due to lack of standardization. Can you expand and comment on the adverse events or harms observed in the included trials.

- *Response: Most studies measured variation in natremia and osmolality but reported it in various ways that were difficult to appropriately evaluate. More importantly, most studies did not report clinical adverse events (e.g. hypotension, dialysis, etc) nor if they monitored it at all. We can thus say that adverse events in relation with the use of hypertonic saline solutions are potentially underreported.*

Clinical Application

Chris will continue to use mannitol for the management of elevated ICP in traumatic brain injury patients

STUDY QUALITY CHECKLIST

The clinical question is sensible and answerable	
The search for studies was detailed and exhaustive	
The primary studies were of high methodological quality	
The assessment of studies were reproducible	
The outcomes were clinically relevant	
There was low statistical heterogeneity for the primary outcome of mortality	
There was low statistical heterogeneity for the primary outcome of ICP	
The treatment effect was large enough and precise enough to be clinically significant	

CONCLUSION VS COMMENTARY COMPARISON

We agree with the author's conclusion.

WHAT DO I TELL MY PATIENT?

In this case we'd likely be speaking to the family members. I would tell them the patient had sustained a serious life threatening brain injury. We are doing everything we can to help. The CT scan shows a serious bleed in the brain. The neurosurgeons are taking him for emergency surgery now. They will be able to explain more once he is out of surgery.

References

Berger-Pelleiter E, Émond M, Lauzier F, Shields JF, Turgeon AF. Hypertonic saline in severe traumatic brain injury: a systematic review and meta-analysis of randomized controlled trials. Canadian Journal of Emergency Medicine. 2016 Mar;18(2):112-20.

GUEST SKEPTIC: Dr. Chris Bond
Clinical Lecturer, Emergency Medicine
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151 Groove is in the HEART Pathway

Case Scenario:
40-year-old male arrives to the ED via EMS with substernal chest pain that has lasted for 3 days without any relief. He denies SOB, radiation, nausea/vomiting, diaphoresis, or palpitations. He has no past medical history, does not smoke, but states his father died of a MI at the age of 70, which is why this chest pain concerned him. He runs 4 times/week without any difficulty, but has had some increased stress at work. The ECG showed normal sinus rhythm without any other abnormalities and cardiac troponin testing was negative both at arrival and at 3 hours after arrival. You go to speak to your patient about objective/provocative testing. What will your conversation be?

Clinical Question:
Does the HEART Pathway identify ED patients with acute chest pain who are safe for early ED discharge without objective cardiac testing?

Bottom LINE

The HEART Pathway appears to have the potential to safely decrease objective cardiac testing, increase early discharge rates and cut median length of stay in low risk chest pain patients presenting to the ED with suspicion of ACS.

The HEART Pathway Randomized Trial

Identifying Emergency Department Patients with Acute Chest Pain for Early Discharge.

Mahler SA et al. Circ Cardiovasc Qual Outcomes 2015

P

Population: Patients ≥21 years of age presenting with symptoms suggestive of ACS that providers ordered an ECG and troponins

- ✘ Key Exclusions: STEMI, hypotension, life expectancy <1 year, and non-cardiac medical, surgical or psychiatric illness needing admission

I

The HEART Pathway (Combination of HEART Score with 0- and 3-hr cardiac troponin testing)

C

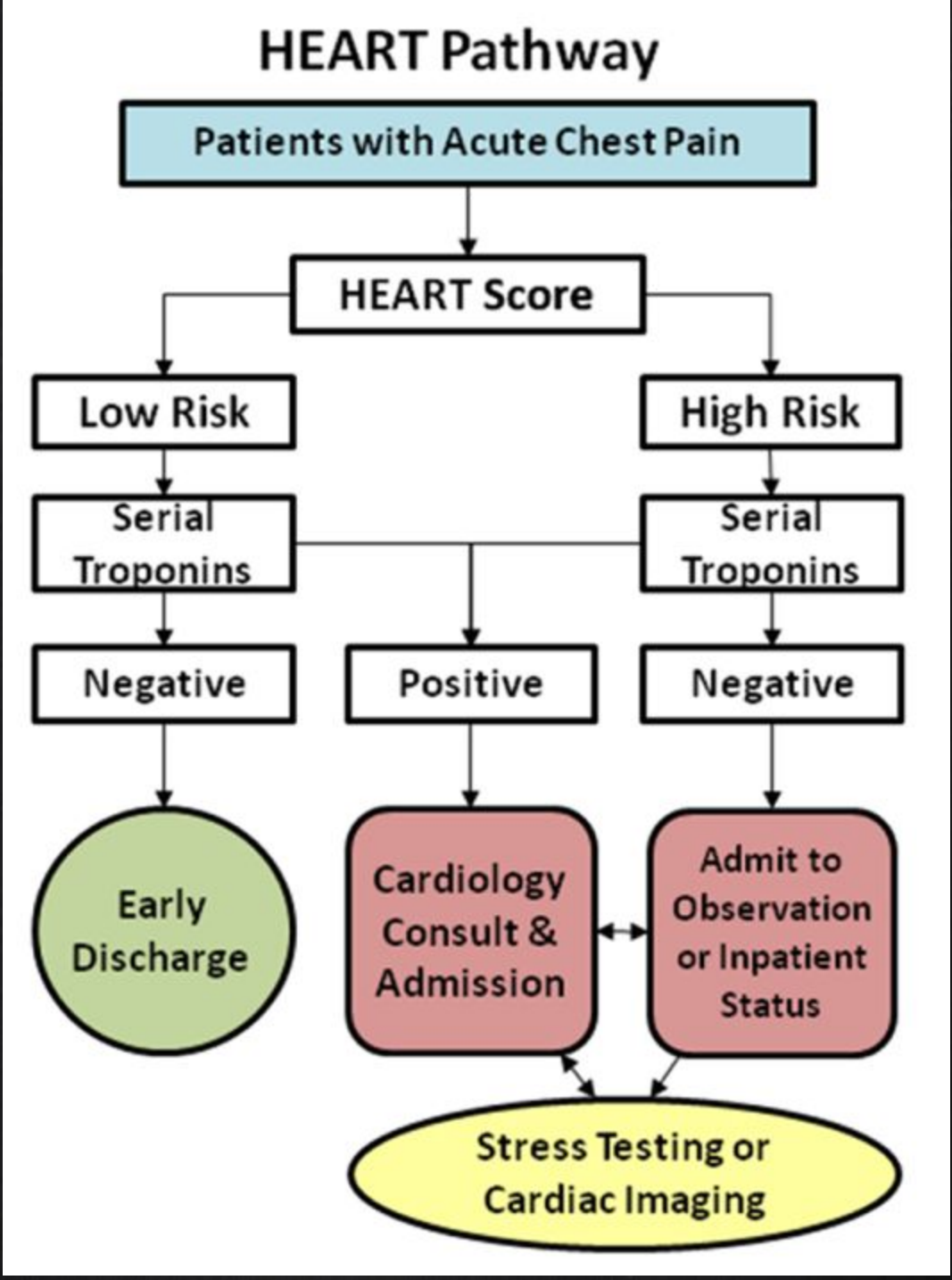
Usual Care (American College of Cardiology/American Heart Association Guidelines) – Serial cardiac biomarkers and objective cardiac testing before discharge

- Objective cardiac testing was a stress test or angiography

O

Outcome:

- Primary Outcome: Rate of objective cardiac testing within 30 days of presentation (Any stress testing modality, coronary computed tomographic angiography, or invasive coronary angiography)
- Secondary Outcomes: Index length of stay, early discharge (discharged from ED without objective cardiac testing), and major adverse cardiac events (all-cause mortality, myocardial infarction, or coronary revascularization) at 30 days.



Authors' Conclusion:

"The HEART Pathway reduces objective cardiac testing during 30 days, shortens length of stay, and increases early discharges. These important efficiency gains occurred without any patients identified for early discharge suffering MACE at 30 days."

Background

There are approximately 8 to 10 million patients complaining of chest pain coming to emergency departments in the United States annually. In the US, a very liberal testing strategy is used in order to avoid missing acute coronary syndrome (ACS) in patients with chest pain. This results in over 50% of emergency department patients with acute chest pain receiving serial cardiac biomarkers, stress testing, and/or cardiac angiography at an estimated cost of $10 to $13 billion annually and yet fewer than 10% of these patients are diagnosed with ACS. To add further angst to emergency department providers the American College of Cardiology/American Heart Association (ACC/AHA) recommends that chest pain patients with concern for ACS should receive serial cardiac markers followed by some sort of provocative/objective cardiac testing.

Using this strategy amongst a low-risk chest pain population unnecessarily uses resources on those least likely to benefit. Low risk chest pain patients have ACS rates of <2%. Provocative/objective cardiac testing is associated with a significant amount of *"downstream"* testing (i.e. cardiac catheterization) due to false positive tests. These false positives expose patients to potential harms from the testing and treatment.
The value of chest pain characteristics to predict ACS has been studied. None of these individual elements have been shown to have +LR>10 or –LR <0.1 to help us rule-in or out ACS.

Pain that INCREASES the Likelihood of MI	Likelihood Ratio
Radiation to Right Arm/Shoulder	4.7 (1.9 - 12)
Radiation to Both Arms/Shoulders	4.1 (2.5 - 6.5)
Exertional	2.4 (1.5 - 3.8)
Radiation to Left Arm	2.3 (1.7 - 3.1)
Associated with Diaphoresis	2.0 (1.9 - 2.2)
Associated with Nausea or Vomiting	1.9 (1.7 - 2.3)
Worse than Previous Angina or Similar to Previous MI	1.8 (1.6 - 2.0)
Described as Pressure	1.3 (1.2 - 1.5)
Pain that DECREASES the Likelihood of MI	**Likelihood Ratio**
Pleuritic	0.2 (0.1 - 0.3)
Positional	0.3 (0.2 - 0.5)
Sharp	0.3 (0.2 - 0.5)
Reproducible with Palpation	0.3 (0.2 - 0.4)
Inframammary Location	0.8 (0.7 - 0.9)
Non-Exertional	0.8 (0.6 - 0.9)

Swap CJ & Nagurney JT. JAMA 2005. PMID: 16304077

Background Continued

The HEART Score for Chest Pain Patients in the ED		
History	• Highly Suspicious • Moderately Suspicious • Slightly or Non-Suspicious	• 2 points • 1 point • 0 points
ECG	• Significant ST-Depression • Nonspecific Repolarization • Normal	• 2 points • 1 point • 0 points
Age	• ≥ 65 years • > 45 - < 65 years • ≤ 45 years	• 2 points • 1 point • 0 points
Risk Factors	• ≥ 3 Risk Factors or History of CAD • 1 or 2 Risk Factors • No Risk Factors	• 2 points • 1 point • 0 points
Troponin	• ≥ 3 x Normal Limit • > 1 - < 3 x Normal Limit • ≤ Normal Limit	• 2 points • 1 point • 0 points
Risk Factors: DM, current or recent (<one month) smoker, HTN, HLP, family history of CAD, & obesity		
Score 0 – 3: 2.5% MACE over next 6 weeks → Discharge Home Score 4 – 6: 20.3% MACE over next 6 weeks → Admit for Clinical Observation Score 7 – 10: 72.7% MACE over next 6 weeks → Early Invasive Strategies		

Cardiac risk factors like the Framingham Criteria can predict future risk but do not help in the emergency department whether or not the patient is having ACS.

Combining various aspects like: the risk factors, history, physical, labs and ECG findings into a score like the TIMI Score or GRACE Score have been used. A problem with TIMI and GRACE scores is they were not designed to assess whether patients presenting to the emergency department with chest pain are due to ACS. They were designed to risk stratify patients once the diagnosis of ACS had already been made.

A new score has recently been developed in the emergency department to help risk-stratify patients who present with chest pain into who will have a Major Advserse Cardiac Event (MACE) in the next 6 weeks and who will not have a MACE. This new score is called the HEART Score and has five different elements.

To date the HEART Score has examined > 13,000 patients and demonstrated a high negative predictive value for major adverse cardiac events (MACE) at 6 weeks exceeding 98%; but to many providers, a 2% risk is still too high.

Results

They enrolled 282 patients into the study with 141 in each group. The mean age of the patients was about 53 years with 57% being women. The overall MACE rate was 6% (17/282).
Of the 141 patients randomized into the HEART Pathway there was close to a 50/50 split between patients stratified as low risk (47%) and those stratified as high risk (53%).
There was some significant non-adherence to the HEART Pathway (29% of low-risk patients and 13% of high-risk patients).

- Primary Outcome: Objective testing with 30 days

HEART Pathway 56.7% vs. Usual Care 68.8% NNT=8

Results continued

- Secondary Outcomes:
  - Early Discharge Rate*: HEART Pathway 39.7% vs. Usual Care 18.4% (Absolute Early
  - Discharge Increase of 21.3%) NNT = 5
  - Median LOS: Heart Pathway 9.9 hrs vs. Usual Care 21.9 hrs
  - MACE: ZERO patients identified as low risk by HEART Pathway had an index or non-index MACE.

Commentary

We reached out to the lead author Dr. Simon Mahler from Wake Forest School of Medicine in Winston-Salem North Carolina. He agreed to come on the SGEM and answer some of our questions to get a deep understanding of his research. This 18 minute extra segment takes place between 14-32 minutes of the podcast. You will need to listen to the PODCAST to hear Dr. Mahler's responses to our questions.

1. *Setting*: This was a randomized clinical trial, which makes it a superior design to the previous observational trials and was on a US population rather than European population and so it's more applicable to North Americans. However, the study was conducted at a single center and this limits the generalizability to other community settings.
   - Listen to Podcast for Response:

2. *Sample Size/Power*: The methods say the study was powered to detect a 15% reduction in objective cardiac testing within 30 days with 90% power at the 5% 2-sided level of significance with an expected loss to follow-up rate of 10%. I could not find in the manuscript how many people you needed to recruit but you enrolled 282?
   - Listen to Podcast for Response:
   - You powered your study to find a 15% difference, which you considered clinically significant a priori. Yet only found a 12% effect size. Does that not leave your study a little short of the mark?
   - Listen to Podcast for Response:
   - A 12% absolute reduction in objective testing may be very important to the patient and to the health care system but the p value does not tell us is the precision of the point estimate. For that we need 95% confidence intervals can you provide those.
   - Listen to Podcast for Response:
   - The final thing about sample size and power was about your secondary outcomes. Specifically you make if very clear that the study was not powered to a detect difference in MACE.
   - Listen to Podcast for Response:

TALK NERDY TO ME

Commentary cont'd

3. *Non-Adherence:* You left things open in both arms to provide care at the discretion of the provider. In other words you did not mandate the care by the protocol. Why did you make that choice?
    - Listen to Podcast for Response:
    - The non-adherence to the HEART Pathway occurred in 29% (19/66) of low risk patients and 13% of high-risk patients. What would the results have been if there was perfect adherence?
    - Listen to Podcast for Response:
    - So if the physicians strictly followed the HEART Pathway almost half of patients could have been discharged home without objective testing being done prior to emergency department discharge. Do you think this non-adherence represents a more accurate determination of "real world" practice of using clinical decision instruments?
    - Listen to Podcast for Response:

4. *Not all Low Risk HEART Scores are Low Risk:* It is possible to have an elevated troponin and all other aspects of the HEART Score be 0 and by definition this would be deemed a low risk patient. Similarly, significant ST-depressions alone would be considered low risk. However, I think some physicians would be uncomfortable stratifying those patients as low risk.
    - Listen to Podcast for Response:
    - Clinical Decision Aids help give us a structure to risk stratify, but the art of medicine is to use clinical judgment. The clinical decision instruments are tools not rules and we need to know how to use the tools to guide our care for individual patient needs.

5. *Shared Decision Making:* Evidence based medicine (EBM) is not just about the literature. Evidence based medicine is our clinical judgment, relevant scientific evidence, and patient values/preferences. Dr. Sackett defined EBM as "The conscientious, explicit and judicious use of current best evidence in making decisions about the care of individual patients." The issue of patient values and preferences was not discussed in this paper but represents an important component of chest pain evaluation and disposition.

Clinical Application

Evaluation of low risk chest pain does not live in the bubble of this one study. Even though this study was not powered to detect the patient oriented outcome of MACE. There have been many studies looking at the use of the HEART Score in the evaluation of chest pain and the sum of these studies shows that we can do amazingly well in a low risk patient with a 30d MACE rate of <2%.

Clinical Application cont'd

Jellema 2013:The results of the entire population of HEART Score 0 – 3 were not included in this manuscript making it hard to know what the exact MACE rate was in this population. There was a subcohort of patients that were admitted to the hospital, for a second troponin test, that were included. Using this population creates a huge selection bias in that although these patients were HEART Scores of 0 – 3, they were admitted because they were thought to be higher risk.

Marcoon 2013: The definitions of patient history and ECG used in Marcoon's paper are different than the original HEART Score definitions.

- History: Patients with 2 elements typical for ACS (oppressive, burning, left sided, substernal chest pain, radiation, diaphoresis, vomiting, short of breath) were scored as atypical instead of intermediate/suspicious and patients with 3–4 elements typical for ACS were scored as intermediate instead of highly suspicious.
- ECG: Only ECGs showing ST elevations were scored as a 2, while t-wave inversions/ST depression were scored as a 1, and nonspecific changes were scored as a 0. Again these definitions would result in underscoring of the ECGs.

CONCLUSION VS COMMENTARY COMPARISON

We differ a little from the authors. We think using the HEART Pathway in chest pain patients presenting to the ED with suspicion of ACS has the potential to decrease objective cardiac testing, increase early discharge rates, and cut median length of stay. However, based on this study alone it is unclear if it truly results in a zero MACE rate at 30 days.

STUDY QUALITY CHECKLIST

The study population included or focused on those in the ED	
The patients were adequately randomized	
The randomization process was concealed	
The patients were analyzed in the group to which they were randomized	
The study patients were recruited consecutively (ie., no selection bias)	
The patients in both groups were similar with respect to prognostic factors	
All participants (patients, clinicians, outcome assessors) were unaware of group allocation	
All groups were treated equally except for the intervention	
Follow-up was complete (i.e., at least 80% for both groups)	
All patient-important outcomes were considered	Yes & no*
The treatment effect was large enough and precise enough to be clinically significant	

*The HEART Pathway produced a meaningful reduction in objective cardiac testing, doubled ED rate of early discharge, and reduced the hospital LOS by half a day but was not powered to detect differences in MACE.

WHAT DO I TELL MY PATIENT?

At this point in your workup with a low risk HEART Score, non-ischemic ECG, and negative zero and three hour cardiac troponins, for every 100 patients who come in to the ED with chest pain, 1 in 100 will have a heart attack or pre-heart attack diagnosis in the next 30 days. Would you like to stay in the hospital for a stress test or schedule an appointment as an outpatient to see your primary care physician?

References

Mahler SA, Riley RF, Hiestand BC, Russell GB, Hoekstra JW, Lefebvre CW, Nicks BA, Cline DM, Askew KL, Elliott SB, Herrington DM. The HEART Pathway randomized trial: identifying emergency department patients with acute chest pain for early discharge. Circulation: Cardiovascular Quality and Outcomes. 2015 Mar 1;8(2):195-203.

GUEST SKEPTIC: Salim Rezaie, MD
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152

Movin' on Up – Higher Floors, Lower Survival for OHCA

Case Scenario:

43-year-old male calls with chest pain from 14th floor of a high-rise apartment. After the dispatcher gets the address and details of the chest pain, the patient stops responding. The paramedic response time is 4 minutes to the apartment, but the patient doesn't answer the buzzer. They then attempt to buzz the building superintendent and it goes to voicemail, thus they start buzzing random names until someone lets them in. After they take the elevator to the 14th floor, the apartment door is locked. One medic goes back down to get the superintendent's number and after a few minutes, they arrive at the 14th floor to open the door. 10 to 15 minutes after arrival of the paramedics, they gain access and meet their patient, a 43-year-old male, vital signs absent, with the phone in his hand.

Clinical Question:

Is there an association between floor of patient contact and survival of out of hospital cardiac arrest?

Bottom LINE

We need to find ways to maximize bystander CPR, improve access to AEDs and eliminate barriers for first responders.

Out-of-hospital cardiac arrest in high-rise buildings: delays to patient care and effect on survival. Drennan et al. CMAJ 2016.

P Population: Adults with OHCA of not obvious cause at private locations

✘ Excluded: Children, witnessed arrests by first responders, traumatic arrests or with another obvious cause, or in a public location

I (prognostic factor) On or above the 3rd floor

C Below the 3rd floor

O Primary Outcome: Survival to hospital discharge
Secondary Outcomes: Subgroup analyses

Authors' Conclusion:

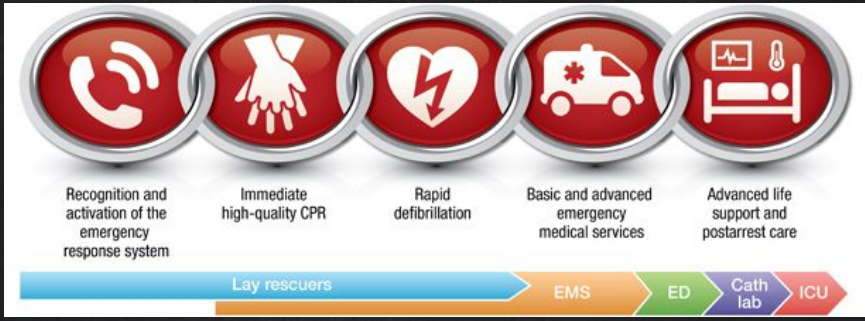
"In high-rise buildings, the survival rate after out-of-hospital cardiac arrest was lower for patients residing on higher floors. Interventions aimed at shortening response times to treatment of cardiac arrest in high-rise buildings may increase survival."

Background

Recent data from the AHA estimates about 350,000 EMS-assessed OHCA happen in the United States each year. The median age is 65 years. Half of these arrests are witnessed (bystander 38% and EMS provider 12%) with the other half being unwitnessed. The majority of these cardiac arrests happen at a home or residence (70%). Of those EMS-treated patients with OHCA about ¼ have an initial shockable rhythm. Survival to discharge from hospital for adults with OHCA assessed by EMS is around 6% (AHA Statistical Update 2016).

The American Heart Association came out with updated CPR & ECC Guidelines in 2015 that included its "Chain-of-Survival". There are five steps in the Chain-of-Survival for OHCA:

- Step One – Recognition and activation of the emergency response system
- Step Two – Immediate high-quality CPR
- Step Three – Rapid defibrillation
- Step Four – Basic and advanced emergency medical services
- Step Five – Advanced life support and post arrest care



Results

7,842 cases of OHCA met inclusion. 5,998 (76.5%) were below the 3rd floor and 1,844 (23.5%) were on the 3rd floor or higher. There were baseline differences between the two groups. Those on or above the 3rd floor were more likely to be female; less often witnessed; took EMS longer to reach; and were less likely to have a shockable rhythm. Overall survival to hospital discharge was 3.8% regardless of what floor you were on.

- Primary Outcome: Lower survival was associated with 3rd floor or above OR 0.70 (95% CI 0.50-0.99).

  Survival below 3rd floor vs. 3rd floor or above: 4.2% vs. 2.6%
  p=0.0002

- Subgroup Analysis: A subgroup analysis was done based on building type. They found 2,363 cases of OHCA in adults living in apartment buildings. Survival was 35/667 (5.2%) for those cases below a 3rd floor apartment and 46/1,696 (2.7%) for those cases above the 3rd floor apartment.
- Time to Patient Contact: They measured the time of arrival of 911-initiated first responders on scene to actual patient contact and found a difference of almost two minutes longer for patients on the higher floors (4.9min vs. 3.0min; p=0.01)
- Variables Associated with Lower Survival to Hospital Discharge (Adjusted):
  - Older Age OR 0.96 (95% CI 0.95-o.97)
  - Male Sex OR 0.72 (95% CI 0.54-0.95)
  - Longer 911 Response Time OR 0.86 (95% CI 0.79-0.92)
- Variables Associated with Higher Survival to Hospital Discharge (Adjusted):
  - Initial Shockable Rhythm OR 10.68 (95% CI 7.98-14.29)
  - Witnessed Arrest OR 2.93 (95% CI 2.16-3.98)
- Other Results:
  - Survival rate above the 16th floor was 0.9% (2/216).
  - Survival rate was zero percent for those above the 25th floor (0/30).

TALK NERDY  TO ME

Commentary

Listen to the podcast to hear the lead author, Ian Drennan's full responses to the questions.

1. *Observational Trial:* The biggest limitation to this study is that it was an observational trial. In this type of study design only associations can be demonstrated, not causation.
   - *You are absolutely right, as with all observational research designs there are inherent limitations that are associated with this type of study design. Although we found an association between higher floors and decreased survival after controlling for some well-known predictors of survival, we are unable to determine a cause and effect relationship with observational research. This is because we are unable to account for all possible confounding variables that may affect the relationship between our variables and outcome of interest.*
   - *I would not think that there is anything physically about the higher floors that all of a sudden you survive less if you cross over the third floor so there must be other confounders, beyond what we controlled for in our analysis, that are at least partially responsible for the result.*
   - *I think the reasons why this association was seen need to be further investigated, but it is interesting that there was an association in our data between having a cardiac arrest on higher floors and poor outcome.*

2. *Associations Beyond Elevation*: You found other associations besides elevation with increasing or decreasing chance of survival.
   - *Yes, as part of the analysis we examined the effect of the floor of the arrest and survival while controlling for some other known predictors of survival such as age, initial cardiac rhythm, witness status, bystander CPR, and 911 response time.*
   - *What we found was that after controlling for these variables, older age, male sex and longer 911 response times were all independently associated with worse outcomes.*
   - *We also found that initial shockable cardiac rhythms and bystander-witnessed cardiac arrests were associated with higher rates of survival. All of these factors are typically found to be associated with patient outcomes after out-of-hospital cardiac arrest so none of these results were surprising.*

3. *CPR Rates*: What was your overall rate of CPR in this study?
   - *Overall we had about 35% bystander CPR rate, however rate of AED use was <1%.*

You did not find a difference in survival with bystander CPR? Was that just a no difference between above and below the 3rd floor or no difference in CPR in general for survival? (OR 1.07, 95% CI 0.83–1.39)?

TALK NERDY TO ME

Commentary cont'd

- *No that is correct. The rate of bystander CPR was actually the same on higher and lower floors. When we looked at bystander CPR on survival, the unadjusted analysis was significant but when we adjusted for other variables there was a non-significant effect.*
- *Now I wouldn't suggest based on this one study then that bystander CPR is not important. My interpretation is that first survivors and non-survivors both had relatively decent rates of bystander CPR (45% vs 35%), second it appears in our adjusted analysis that much of the effect on survival is run by the variables initial rhythm, and witness status, which is common in OHCA research, and that these can sometimes overpower some of the other variables.*

4. *Overall Survival to Hospital Discharge*: You found the overall survival to hospital discharge for adult OHCA was 3.8%. This is less than the 5% found in the OPALS study. Why do you think there was a difference?

- *Good question. So a few reasons why the survival was slightly lower in our study. First, our population was different than OPALS as we required a specific population to answer our research question; specifically private residences (which are known to have lower survival than public cardiac arrests) and we excluded EMS witnessed cases (again a group known to have higher survival than non-EMS witnessed cases).*
- *Second, some of the other factors that are associated with higher survival such as witnessed arrests and initial shockable rhythm were lower in our study as well.*

5. *Patient Oriented Outcome*: You reported survival to discharge but not survival to discharge in good neurologic condition. Wouldn't that be a very important patient oriented outcome?

- *Correct, so we only reported on survival to hospital discharge (yes/no) and did not specifically look at neurological outcomes of our patients at hospital discharge.*

Patients not only want to survive but they want to be neurologically intact. If the increase in survival to hospital discharge was just to be institutionalized in a long-term facility with poor neurologic function it would not be considered by most to be a positive outcome.

- *I can tell you from our research that the vast majority of patients who survive do so with a good neurologic status, but this would be an interesting and important outcome to look at as well.*

Clinical Application

Listen to the podcast for Ian's full response.

1. *Maximize CPR (Bystander)*
2. *Access to AEDs (Place in Elevators)*
3. *Minimize Delays for 911– Responders (Universal Keys)*

CONCLUSION VS COMMENTARY

COMPARISON

We generally agree with the authors' conclusions.

Study Quality Checklist

The study addressed a clearly focused issue	
The authors used an appropriate method to answer their question	
The cohort was recruited in an acceptable way	
The exposure was accurately measured to minimize bias	
The outcome was accurately measured to minimize bias	
The authors identified all important confounding factors	
The follow up of subjects was complete enough	
The results were precise and estimated risk well	***
The results are believable	
The results can be applied to the local population	
The results of this study fit with other available evidence	

*** Point estimates were provided for OR with 95% confidence intervals.

WHAT DO I TELL MY PATIENT?

The patient is dead Ken. However, on the way out, the neighbor says; "what took you so long to get up here? I saw your ambulance parked outside long before you came up here. What were you doing?" A short discussion takes place regarding what the paramedics were doing, and how they were trying to gain access, but simply could not get into the building. The building superintendent overhears the discussion, and now we are working with the city to create a bylaw for Paramedic access into buildings.

References

Drennan IR, Strum RP, Byers A, Buick JE, Lin S, Cheskes S, Hu S, Morrison LJ. Out-of-hospital cardiac arrest in high-rise buildings: delays to patient care and effect on survival. Canadian Medical Association Journal. 2016 Apr 5;188(6):413-9.

GUEST SKEPTIC: Jay Loosley, RN
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153 Simulation for Ultrasound Education

Case Scenario:
An emergency medicine resident in your institution has learned some basics of ultrasound training, but feels uncomfortable performing ultrasound in a crashing patient. They come to ask you how they can learn to use their ultrasound skills in critically ill patients, other than doing it in real time.

Clinical Question:
What ultrasound simulation method is preferred by trainees and instructors in high fidelity simulation?

Bottom LINE

Consider integrating PoCUS into your high fidelity simulation program.

Ultrasound during Critical Care Simulation: A Randomized Crossover Study.

Olszynski et al. CJEM 2016

P Emergency Medicine residency program trainees and 8 instructors (5 staff physicians, 3 senior emergency medicine trainees with significant U/S experience)

I 1) edus2 PoCUS simulator, which is comprised of a modified ultrasound probe and laptop and 2) Laptop with ultrasound videos placed on an audiovisual cart

C Previous PoCUS with HFS

O Trainee and instructor preference

Authors' Conclusion:

The edus2 was identified as being a superior teaching intervention, as it allowed for greater functional integration of PoCUS into critical care, better assessment of trainee skills and had greater impact on session debriefing and formative feedback.

Background

Point of care ultrasound (PoCUS) can be broken down into two main categories – diagnostic applications and procedural applications. There are simulators and trainers for both types.

Diagnostic Applications: When it comes to diagnostic ultrasound simulation the case is most compelling for the more invasive applications. These include things like transesophageal echo in shock and arrest states or transvaginal ultrasound in first trimester bleeding.

Procedural Applications: The procedural side of ultrasound simulation is where we find the most compelling evidence. In one study by Barsuk et al, trainees who were trained to mastery on Central Venous Line trainers with the use of ultrasound and performed far better on real patients than those trained with the more traditional approach of *"go read about it, then see one – do one."*

There is now a movement towards hybridized simulation experiences where either diagnostic or procedural trainers are introduced into broader simulation environments. This type of "bridging" from simple task training to clinical integration (in a simulated setting) is now being explored more and more, especially as we move towards competency based training.

Assessing competency is not a one–time event. Seeing a trainee perform a skill like PoCUS in one instance is insufficient to say they have achieved competence. Assessment of competence requires thoughtful assessment of several instances spaced over time and ranging in complexity. It is here where these types of hybrid simulation offer a window for assessment.

Seeing when the trainee decides to reach for the transducer, how they hold it, how long they allow themselves to scan, how they interpret and then integrate the findings into care. This can serve as one of many touch points making the case for that trainee's PoCUS competence. Eventually, with multiple assessment points over the duration of their training with the formative feedback that is associated with it, they will achieve competence in PoCUS.

Resuscitative PoCUS can be divided into three parts:

1. Firm Grasp of Indications – Knowing when and where to scan
2. Image Generation with Interpretation – Generating the images and knowing when the image is adequate for interpretation and data extraction
3. Integration into Clinical Care – Making decisions based on the all the data (history, physical and PoCUS images).

High–fidelity simulation (HFS) can then be combined with PoCUS to teach residents.

The purpose of this study was to evaluate two comparable ultrasound simulation interventions as used during HFS. Comparing two somewhat similar but distinct interventions allowed the study team to assess and isolate for the potential value of basic probe handling and other logistical aspects associated with the use of either intervention.

Results

25 trainees with an average pre-intervention multiple choice question exam of 72% based on the American College of Emergency Physician's EMSONO online exam. This means they were familiar with PoCUS

Twenty-one out of twenty-five already had their level I PoCUS course or equivalent. However, they reported their HFS to date had been poor (3.26 out of 10)

Trainees and instructors rated these two studied interventions superior over-previous critical care ultrasound simulation with edus2 being the prefer method of the two.

Trainees rated edus2 and laptop as a quantitatively better experience than previous experience on a Likert scale in five categories. There was also no significant difference between the two teaching interventions.

Two weeks after the course the trainees completed a **qualitative** assessment. All the respondents indicated they preferred the edus2. Reasons included primarily the themes of *"real-time"* handling of the U/S probe with the edus2 and *"hands-on use"*. The laptop alone was felt to be a more artificial intervention.

The instructors were also asked about intervention. Both the quantitative and qualitative data support a preference for the edus2 over the laptop intervention as well as previous experiences.

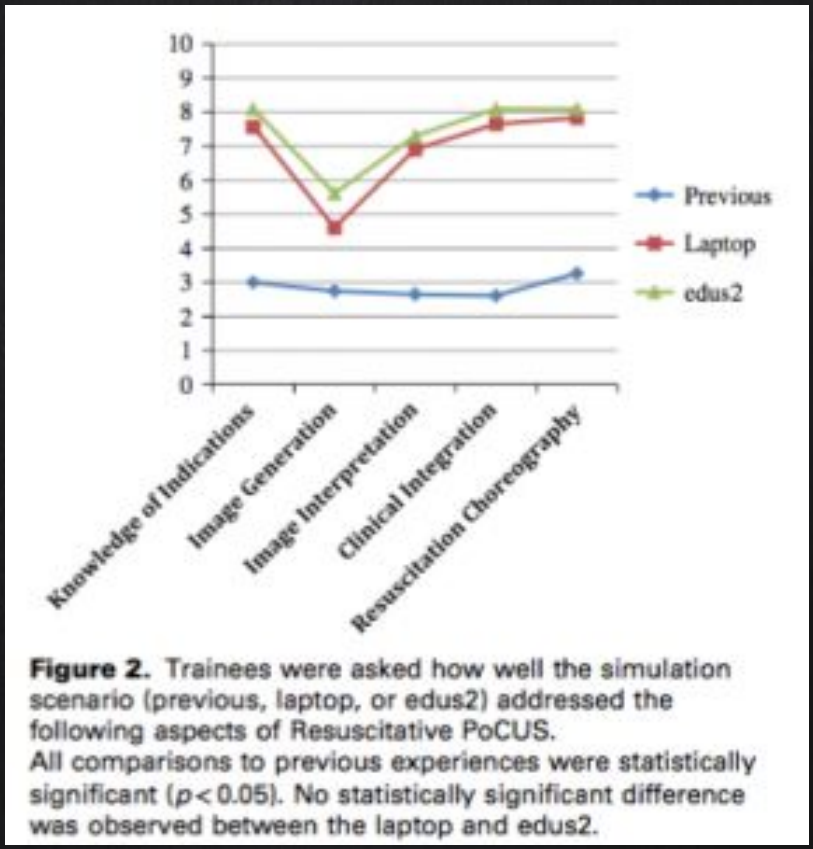


Figure 2. Trainees were asked how well the simulation scenario (previous, laptop, or edus2) addressed the following aspects of Resuscitative PoCUS.
All comparisons to previous experiences were statistically significant ($p < 0.05$). No statistically significant difference was observed between the laptop and edus2.

TALK NERDY TO ME

Commentary

Listen to the podcast for lead author, Dr. Paul Olszynski's full responses.

1. *Randomization*: You just allocated every other trainee based on arrival

– *The challenge with randomization was that we never really knew who was coming on a given day. So we decided that we would use their order of arrival to the simulation center at Whipps Cross Hospital as part of our randomization. As they walked into the center, we provided them with an envelope that included their group allocation. We had arranged our envelopes to alternate from group A to B to A and so forth as a means of ensuring that we would have balanced groups in terms of size. It was somewhat reassuring to see that our process did result in 2 generally similar groups. In the end there were no statistically significant differences between the two groups in terms of POCUS and simulation experience so I guess our randomization worked?*

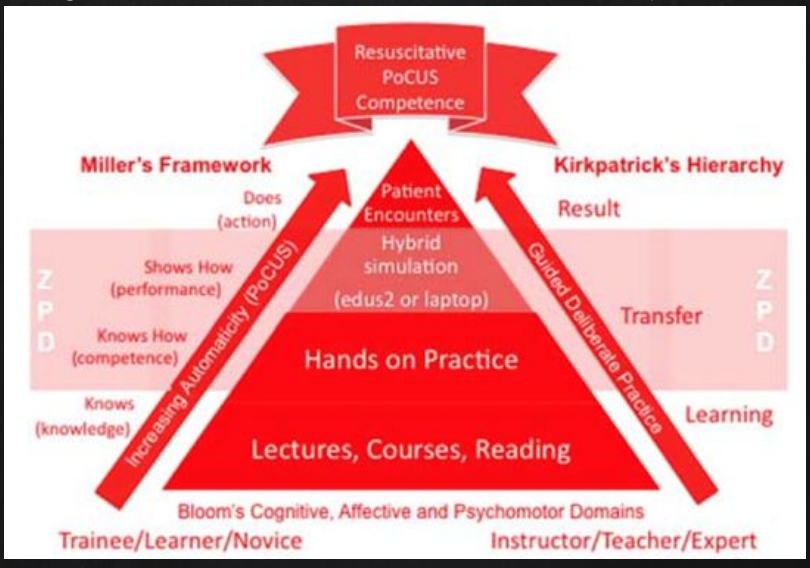
2. *Quantitative vs. Qualitative Data*. You used both tools. Why and what do you think they tell us about your study?

– *When it comes to education research, I think combining the two forms of data really enriches the study. It adds insight to the numbers. In our study, it also highlighted how tricky research on students and instructors can be. For example, the trainees initially rated the two interventions very similarly. Yet on the exit survey, every one of them stated they preferred the edus2 to the laptop intervention.*

3. *Personal Bias*: You were the lead author but also were involved in the teaching sessions. How did you try to minimize this bias?

– *Early on we realized I could not act as a teacher/instructor with any of the groups. In the end, my job was to briefly introduce the trainees to the two interventions (explaining how they work and how they would be able to activate the clips they desired during the scenarios). I was also the voice of the patient for all scenarios.*

4. *Resuscitative PoCUS Competence Model.* You give a conceptual framework illustrating the key concepts supporting the use of PoCUS simulation in HFS. Can you take us through that model?



TALK NERDY TO ME

Commentary cont'd

Bloom's cognitive, affective psychomotor domains:
- The cognitive domain (knowledge-based)
- The Affective domain (emotive-based)
- The Psychomotor domain (action-based)

Miller's Framework:
- *In my mind it represents the earliest work around assessment of competency in Medicine. First the trainee is simply asked to "write it down" but as they move along in their training, we expect them to describe how to do it and show us how they would do it. Until finally, near the end of their residency we observe them do it completely independently. The hybrid simulation experience we studied represents the "shows how" in Miller's framework*

Kirkpatrick's Hierarchy:
- *This is about the meaningfulness of outcomes as they relate to an educational intervention. Ideally, studies like mine would show clinically significant outcomes (better patient outcomes). But to get there, we often have to first make our way up the pyramid. I think introducing PoCUS into resuscitation simulation provides us with the opportunity to "glimpse" at transfer of knowledge into practice (albeit in a simulated setting) where we can see things like improved diagnostic accuracy or shorter time to diagnosis.*

Zone of Proximal Development (ZPD):
- *Going back to those residents of ours – the ones who are nervous about reaching for the transducer when facing a critically ill patient: You could think of that "reach" as representing their zone of proximal development – that space between what they know how to do (for example: scanning a stable trauma patient) and what they have not done yet (but have some of the basic skills already) like performing resuscitative PoCUS. The ZPD is the space the trainee could move through IF they have the proper guidance. Practicing resuscitative POCUS in HFS offers a safe environment for them to reach into their ZPD prior to doing so in real life.*

5. *Patient Oriented Outcomes*: Do you have any plans for demonstrating this PoCUS HFS has a positive impact on patient oriented outcomes?
- *It keeps coming up but it would have to be multi-centered. If anyone is interested, please get a hold of me.*

Is there anything else you wanted to mention Paul?

- *The CAEP Emergency Ultrasound Committee's Education Working Group is working hard to establish some national objectives and milestones for PoCUS EM in Canadian EM residency. We're also hoping to introducing CAEP first ever SONOGAMES to CAEP17! We'll be meeting at CAEP16 to review our progress thus far while also setting our compass for the coming year. Check us out at CAEPultrasound.ca to get in touch with us whether you are interested in being involved or just interested in being kept up to date!*

Clinical Application

PoCUS skills are useful at the bedside in real patients and this integration into high fidelity simulation is the last step prior to using them in real patient encounters.

CONCLUSION VS COMMENTARY

COMPARISON

We agree with the authors' conclusions.

STUDY QUALITY CHECKLIST

The study addressed a clearly focused issue	👍
The authors used an appropriate method to answer their question	👎
The cohort was recruited in an acceptable way	👎
The exposure was accurately measured to minimize bias	👍
The outcome was accurately measured to minimize bias	👍
The authors identified all important confounding factors	👍
The follow up of subjects was complete enough	👎
The results were precise and estimated risk well	👍
The results are believable	👍
The results can be applied to the local population	👍
The results of this study fit with other available evidence	?

WHAT DO I TELL MY PATIENT?

We know that use of PoCUS during simulation is beneficial for your learning and will help develop your knowledge of PoCUS indications, and your skills of image interpretation, clinical integration of ultrasound images and resuscitation choreography.

References

Olszynski PA, Harris T, Renihan P, D'Eon M, Premkumar K. Ultrasound during critical care simulation: a randomized crossover study. Canadian Journal of Emergency Medicine. 2016 May;18(3):183–90.

GUEST SKEPTIC: Dr. Chris Bond
Clinical Lecturer, Emergency Medicine
University of Calgary, Calgary, Alberta, Canada

154 Here I Go Again, Kidney Stone

Case Scenario:
48-year-old man presents to the emergency department complaining of right flank pain radiating to his groin. He states the pain comes in "waves," and he has associated nausea without vomiting. On exam, he is afebrile and appears very uncomfortable while grabbing his right flank.

Clinical Question:
1) Does medical expulsive therapy with tamsulosin or nifedipine increase the likelihood of spontaneous stone passage measured by the absence of need for further intervention?
2) What is the efficacy and safety of tamsulosin in patients with stones less than or equal to 10mm in the distal ureter?

Bottom LINE

Expulsive therapy is unnecessary for ureteric stones < 5mm. There is some weak evidence that tamsulosin may help passage of larger stones (5 to 10 mm).

Question 1: Does medical expulsive therapy with tamsulosin or nifedipine increase the likelihood of spontaneous stone passage measured by the absence of need for further intervention?

Medical expulsive therapy in adults with ureteric colic: a multicentre, randomised, placebo-controlled trial. Pickard et al. Lancet 2015

P

Patients between the age 18-65 undergoing expectant management for single ureteric stone 10mm or less identified by CT

✘ Excluded: Patients with suspected sepsis, GFR<30, stones >10mm and age >65yrs

I

Tamsulosin 400µg daily x 4 weeks or nifedipine 30mg daily x 4 weeks

C

Placebo and each other

O

Primary: Need for further treatment to achieve stone clearance in 4 weeks.

Secondary: Number of days for analgesic use, time to stone passage, and health status between the groups

Authors' Conclusion:

"Tamsulosin 400 µg and nifedipine 30 mg are not effective at decreasing the need for further treatment to achieve stone clearance in 4 weeks for patients with expectantly managed ureteric colic."

Background

We have covered renal colic a number of times on the SGEM. The last time it was a systematic review on tamsulosin from 2012. The SGEM Bottom Line from that episode was: *"Tamsulosin is useless in most ED patients with ureteral colic unless their stone size exceeds at least 4mm."*

- SGEM#71: Like a Rolling Kidney Stone
- SGEM#4: Getting Un-Stoned (Renal Colic and Alpha Blockers)

Results

1136 patients were enrolled (378 in the tamsulosin group, 379 in the nifedipine group and 379 in the control group). Mean age was in the low 40's, 20% women, one-third of patients had a history of stones, two-thirds of stones were in the lower ureter and 75% were <5mm.

Primary outcome: Need for additional intervention at four weeks

- 19% for tamsulosin, 20% for nifedipine and 20% for control

No statistical difference in spontaneous stone passage at 4 weeks.

Secondary outcomes:

- No difference in any of the secondary outcomes for days of analgesia use, time to stone passage, and health status between groups
- Patients used pain medication for about median of 7-10 days and the median time to stone passage was about 14 days
- There were three serious adverse events in the nifedipine group; 1 in the placebo group

Commentary

This was a large and well-done study.

1. *ED Patients*: The study never explicitly stated that these patients were from the emergency department. The study simply state a routine care setting.

2. *Adherence to Trial Medication*: They did not verify adherence to trial medication. This weakens the conclusions that medical expulsive therapy does not work but probably is more pragmatic and representative of the "real world".

3. *Confirmation of Stone Passage*: The study design did not require CT confirmation of stone passage. They rationalize this by saying ultrasound and plain films would not be accurate enough while CT scans come with a financial cost and radiation exposure. They also say that routine clinical care would involve further imaging based upon clinical concerns.

Commentary

4. *Patient Oriented Outcome:* It could be argued that need for urologic intervention may not be the most important patient oriented outcome. Usually what patients want is to just pass the stone.
5. *Secondary Outcome*: Patients self reported whether or not they passed the stone and their VAS pain scores and number of days of analgesic use at four weeks. They also self reported their heath status using a questionnaire at four and twelve weeks. The response rate was only 62% at four weeks and 49% at twelve weeks. There were no measured differences between the groups who completed the survey and those who did not. However, this seriously limits the interpretation of these secondary outcomes.

CONCLUSION VS COMMENTARY COMPARISON

We agree with the author's conclusion that medical expulsive therapy does not change the percentage of patients that required further intervention.

Study Quality Checklist

The study population included or focused on those in the ED	👍
The patients were adequately randomized	👍
The randomization process was concealed	👍
The patients were analyzed in the group to which they were randomized	👍
The study patients were recruited consecutively (ie., no selection bias)	👍
The patients in both groups were similar with respect to prognostic factors	👍
All participants (patients, clinicians, outcome assessors) were unaware of group allocation	👍
All groups were treated equally except for the intervention	👍
Follow-up was complete (i.e., at least 80% for both groups)	👍
All patient-important outcomes were considered	👍
The treatment effect was large enough and precise enough to be clinically significant	👎

Question 2: What is the efficacy and safety of tamsulosin in patients with stones less than or equal to 10mm in the distal ureter?

Distal Ureteric Stones and Tamsulosin: A Double-Blind, Placebo-Controlled, Randomized, Multicenter Trial. Furyk et al. Annals of EM 2016

P

Patients >18yo with symptoms suggestive of utereric colic and a calculus less than or equal to 10mm demonstrated on CT.

✘ Excluded: Temperature >38C, GFR<60, stone>10mm, solidary kidney, transplanted kidney, history or ureteral strictures, know allergic reaction to study medication, current calcium channel blocker or alpha-blocker, or systolic blood pressure <100mmHg

I

0.4mg of tamsulosin daily for 4 weeks.

C

Placebo

O

Co-Primary: Stone passage demonstrated on CT at 4 weeks and time to stone expulsion

Secondary: Unplanned re-presentation to the ED or hospital admission, total analgesia use, pain scores, need for urological intervention, complications, days off work, and adverse effects.

Authors' Conclusion:

"We found no benefit overall of 0.4 mg of tamsulosin daily for patients with distal ureteric calculi less than or equal to 10 mm in terms of spontaneous passage, time to stone passage, pain, or analgesia requirements. In the subgroup with large stones (5 to 10 mm), tamsulosin did increase passage and should be considered."

Results

n=393 (198 in the tamsulosin and 195 in the placebo group). The median age was 45years old and about 20% women. The median stone size was 4mm with about 75% being <5mm.

- Co-Primary Outcome: Stone passage at four weeks and median time to stone passage
  - 87% tamsulosin vs. 82% placebo (difference 5% [95% CI −3.0% to 13.0%])
  - 7 days tamsulosin (95% CI 5 to 10 days) vs. 11 days placebo (95% CI 6 to 14 days)

No significant difference in stone passage or time to stone passage.

- Secondary Outcomes: There were no differences in any of the measured secondary outcomes (Unplanned re-presentation to the ED or hospital admission, total analgesia use, pain scores, need for urological intervention, complications, days off work, and adverse effects).

- Subgroup Analysis Stones 5-10mm:
  - 83% (30/36) tamsulosin vs. 61% (25/41) placebo
  - Difference of 22% (95% CI 3.1% to 41.6%) NNT=4.5

Commentary

This was another well-done study.

1. *Consecutive Patients*: It was not consecutive patients and this could have introduced some selection bias into the study.
2. *Co-Primary Outcomes:* This is a pet peeve (co-primary or composite outcomes). It assumes both or all components are equally important. What do patients care more about, time to passage or if it passes?
3. *Lost to Follow-up*: The result section says 18.7% in the treatment group and 20.5% in the placebo group did not have a follow-up CT yet in the discussion they say 17%? This large number of patients missing from the primary outcome introduces another possible source of bias.
4. *Compliance*: This was self-reported and found to be poor. While it weakens the results of no superiority of tamsulosin vs. placebo it is probably a more accurate/pragmatic representation of what would happen in general practice.
5. *Subgroup Analysis of Stones 5-10mm*: They report superiority with tamsulosin but this should be interpreted with skepticism for a variety of reasons:
   - The study was designed for this subgroup analysis but they needed 98 patients in total to find an increase of stone passage from 5% to 25% with an alpha of 0.05 and a power of 0.8. They ended up only having 77 patients in total not 98.
   - Stone passage was much higher than the 5% to 25% anticipated. They observed stone passage of 61% with placebo vs. 83% with tamsulosin. This was a 22% absolute difference with an impressive NNT of 4.5.
   - Wide confidence interval around their point estimate 22% (95% CI 3.1% to 41.6%). So their point estimate is not very precise. The NNT could be as low as 2 and as high as 32.

Clinical application

No indication to start on medical expulsive treatment in most cases of renal colic.

CONCLUSION VS COMMENTARY COMPARISON

We agree with the authors' conclusion that medication medical expulsive therapy is not needed for uncomplicated ureteral stones less than 10mm.

Study quality checklist

The study population included or focused on those in the ED	
The patients were adequately randomized	
The randomization process was concealed	
The patients were analyzed in the group to which they were randomized	
The study patients were recruited consecutively (ie., no selection bias)	
The patients in both groups were similar with respect to prognostic factors	
All participants (patients, clinicians, outcome assessors) were unaware of group allocation	
All groups were treated equally except for the intervention	
Follow-up was complete (i.e., at least 80% for both groups)	
All patient-important outcomes were considered	
The treatment effect was large enough and precise enough to be clinically significant	

WHAT DO I TELL MY PATIENT?

You have a small 4mm kidney stone that is down near your bladder. The good news is about 80% of these stones will pass on their own. The bad news is it can take an average of 1–2 weeks for it to pass and this can be painful. However, we can treat your pain with some anti-inflammatories drugs. If that does not work you can also use some opioid pain pills as a back up plan. We will also give you some anti-nausea medications. There another medication you may hear about that has been tried called tamsulosin. It unfortunately has not show to help patients with small stones like yours <5mm in size.

References

Pickard R, Starr K, MacLennan G, Lam T, Thomas R, Burr J, McPherson G, McDonald A, Anson K, N'Dow J, Burgess N. Medical expulsive therapy in adults with ureteric colic: a multicentre, randomised, placebo-controlled trial. The Lancet. 2015 Jul 25;386(9991):341–9.

Furyk JS, Chu K, Banks C, Greenslade J, Keijzers G, Thom O, Torpie T, Dux C, Narula R. Distal ureteric stones and tamsulosin: a double-blind, placebo-controlled, randomized, multicenter trial. Annals of emergency medicine. 2016 Jan 1;67(1):86–95.

GUEST SKEPTICS:
Dr. Anthony Seupaul, Chairman of Dept. of EM at University of Arkansas
Dr. Mark Phan, PGY-3 EM resident at University of Arkansas

155 Girls Just Want To Have Fun – Not Appendicitis

Case Scenario:
15-year-old female presents to the ED with a worsening RLQ abdominal pain for 2 days that started around her umbilicus. She had a temp this morning of 101F, an episode of non-billious, non-bloody emesis, and says the bumps in the road worsened her pain. She denies any dysuria, discharge, diarrhea, and constipation. She just finished her menstrual cycle and is not sexually active. A medical student also noticed pain over McBurney's point and wants to CT scan her. You start to tell him about limiting radiation in pediatric patients and the Pediatric Appendicitis Score (PAS) but can't help to wonder, is this clinical prediction rule as helpful in this female adolescent as other peds patients?

Clinical Question:
How well does the Pediatric Appendicitis Score (PAS) perform for adolescent female patients?

Bottom LINE

The PAS has similar utility in adolescent females patients compared to other pediatric patients.

Utility of Pediatric Appendicitis Score in Female Adolescent Patients. Scheller et al. AEM May 2016

P Female patients 13–21 years old presenting with symptoms suggestive of appendicitis

I Use of the Pediatric Appendicitis Score

C Pathology proven appendicitis

O Diagnostic metrics (Sensitivity, Specificity, PPV, NPV) including comparison of these metrics to All other patients presenting with symptoms of appendicitis

Authors' Conclusion:

"Our study demonstrates that the PAS score, as commonly used clinically (i.e. with cutoffs of >=3 and >=8), showed better specificity and equivalent sensitivity for female adolescent patients compared to all other patients, as well as a good NPV in both groups."

Background

Abdominal pain is a common complaint in any emergency department, as is true in a pediatric emergency department. Appendicitis is usually on the differential in a pediatric patients presenting with abdominal pain and is a common surgical emergency.

Female adolescents pose a unique diagnostic dilemma due to having competing gynecologic diagnoses, such as urinary tract infections, sexually transmitted infections or ovarian cysts or torsion. Being accurate about diagnosis of appendicitis is important to avoid complications of missed appendicitis as well as complications of negative appendectomies.

The PAS is a clinical prediction tool which uses elements of the history and physical examination such as symptoms of right lower quadrant pain and fever and combines this with laboratory findings such as the white blood cell count (WBC) to predict the risk of acute appendicitis.

The PAS score was initially developed with a single cutoff, but validation studies showed better performance with two cutoffs: one at the low end to identify patients with a low risk of appendicitis who may not need further evaluation, and one at the high end to identify patients with a high risk of acute appendicitis on clinical grounds alone.

PAS
(Pediatric Appendicitis Score)

- (1 point) anorexia
- (1 point) fever
- (1 point) nausea/vomiting
- (1 point) migration of pain
- (2 points) pain with cough, percussion, or hopping
- (2 points) RLQ tenderness
- (1 point) WBC > 10,000*
- (1 point) ANC > 6750*

With a possible score of ten, scores at the lower cutoff, such as less than or equal to two are used to discharge a patient home without further work up due to low suspicion for appendicitis, thus making sensitivity important at this cutoff. Scores at the higher end, such as greater than or equal to seven or eight are used to predict high suspicion for appendicitis, thus making specificity important at this cutoff.

There are not any studies to our knowledge that compare the PAS performance at both different ages and genders which is an important consideration in caring for pediatric patients.

Results

n=901 with 28% pathology-proven appendicitis. Of the total population enrolled in the study, 30% were adolescent females (age 13-21).

There was no significant difference in the sensitivity for the cutoff value of three or the specificity for the cutoff value of seven.

The specificity of the cutoff value of eight was significantly better in the adolescent female group compared to the pediatric non-adolescent female group.

PAS Score	Female 13-21	All other Patients	P value
Cutoff ≥ 3	**N=250**	**N=596**	
Sensitivity	97.7% (87.9-99.6)	99.5% (97.3-99.9)	0.226
Specificity	9.2% (5.4-12.9)	7.6% (5.0-10.2)	0.478
PPV	16.8% (12.7-21.9)	34.4% (30.7-38.3)	<0.001
NPV	95.5% (78.2-99.2)	97% (84.7-99.5)	0.772
Cutoff ≥ 7	**N=87**	**N=303**	
Sensitivity	58.1% (43.3-71.6)	76.7% (70.5-82)	0.012
Specificity	72.9% (66.8-78.3)	65.5% (61.1-70.1)	0.060
PPV	28.7% (20.3-39)	52.2% (46.5-57.5)	<0.001
NPV	90.3% (85.3-93.8)	85.3% (81.0-88.7)	0.105
Cutoff ≥ 8	**N=46**	**N=206**	
Sensitivity	48.8% (34.6-63.3)	55.8% (49.0-62.4)	0.401
Specificity	89.0% (84.2-92.5)	78.1 (73.9-81.8)	<0.001
PPV	45.7% (32.2-59.8)	55.8% (49.0-62.4)	0.215
NPV	90.2% (85.6-93.5)	78.1% (73.9-81.8)	<0.001

Commentary

Lead author of this study was Dr. RoseAnn Scheller. RoseAnn is a pediatric emergency physician and assistant professor at the Children's Mercy Hospital and Clinics in Kansas City, MO. Her career goals are to improve the quality of emergency care of pediatric patients through improvements on resuscitation and trauma, and research in pediatric emergency management, resuscitation, and violence prevention. Her study was done at the Cincinnati Children's Hospital Medical Centre. We asked RoseAnn five questions and her responses are in *italic.*

1. *Sub-group Analysis*: This is a retrospective cohort study, effectively a sub-group analysis of a previously done study on the PAS. Was this study adequately powered for the diagnostic metrics you were investigating?
   - *As we stated in our limitation,s it was possible that the sample size in regards to age and sex may have not been sufficient. We did do a prospective power calculation for this study before complete enrolment of the parent study. Using the expected prevalence estimates we had at the time, we determined that 222 female adolescents would allow us to detect a difference in the areas under the ROC curves for the two groups. Our study included 250 adolescent females.*

TALK NERDY TO ME

Commentary cont'd

2. *Consecutive or Convenience*: The manuscript says the clinical research coordinators identified a convenience sample of patients. Does this mean it was not consecutive patients presenting with abdominal pain suspected of appendicitis? If not consecutive, how do you think this may have impacted the results?

- *Research assistants were present 12–18 hours/day and enrolled study patients consecutively during these times. Because of this convenience sample, our results may not have clear generalizability. There may be sample bias and sampling error due to the nature of convenience sampling. It is possible that patients that present during times that the research assistants were not present may be different than patients that present other times of day.*

3. *Clinical Appendicitis Pathway*: Physicians were given a new clinical appendicitis pathway prior to the start of the study. This diagnostic pathway, which included the PAS, was added to your electronic medical record halfway through the study period. What impact, if any, do you think that had on your results?

- *I think that having the clinical pathway and computerized decision support tool introduced may have increased awareness and may have influenced the physicians consideration and identification of symptoms as well as the overall score.*

4. *Incomplete Follow-up*: You defined *"negative appendicitis"* to include all patients who did not undergo appendectomy one month after emergency department presentation. What about patients who sought care at another hospital or after one month?

- *We felt that it would be likely that a pediatric patient with appendicitis would follow up at our facility because it is the only hospital with pediatric surgeons in our catchment area. One month was chosen due to the probability that a case of appendicitis from an ED visit would likely present within one month of initial presentation allowing for full capture of data even with a delayed presentation or antibiotic therapy. However this is a potential limitation that we identified in the article.*

5. *PPV and NPV*: These are dependent on prevalence of disease. The pathology proven appendicitis in the female adolescent cohort was 16% while in the comparison group it was 33%. While this difference does not impact the PPV and NPV that much, did you think about calculating the likelihood ratios, which are not dependent on prevalence of disease?

- *We had considered likelihood ratios however we wanted our study to be comparable to other studies of the PAS, which reported PPVs and NPVs more often. Additionally, we do report the primary outcomes of sensitivity and specificity, which are not dependent on prevalence and can be used to calculate the likelihood ratios*

Commentary cont'd

Is there anything else about the project you would like to mention?

- *I do think this difference in prevalence between the groups is interesting and would like to see research in the future address this discrepancy. One possibility is that adolescent females are more likely to have other abdominal pathology, which can mimic appendicitis, such as urinary tract infections, sexually transmitted infections or ovarian pathology, so clinicians suspect it, and test for it more. Since our study population was based on clinician concern for appendicitis, it is possible that we had high number of adolescent females with other final diagnoses, thus decreasing the prevalence in this group compared to the "all patients" group.*

Clinical Application

In children presenting to the emergency department with abdominal pain, where there is clinician concern for acute appendicitis, the PAS can be used, even if the patient is an adolescent female.

Study Quality Checklist

The study population included or focused on those in the ED	👍
The patients were adequately randomized	👍
The randomization process was concealed	👍
The patients were analyzed in the group to which they were randomized	?
The study patients were recruited consecutively (ie., no selection bias)	👍
The patients in both groups were similar with respect to prognostic factors	👍
All participants (patients, clinicians, outcome assessors) were unaware of group allocation	👍
All groups were treated equally except for the intervention	👍
Follow-up was complete (i.e., at least 80% for both groups)	👍
All patient-important outcomes were considered	👍
The treatment effect was large enough and precise enough to be clinically significant	👍

CONCLUSION VS COMMENTARY COMPARISON

We agree with the authors' conclusions. It appears that the PAS is at least as good a tool in adolescent female patients as it is for the rest of the pediatric population.

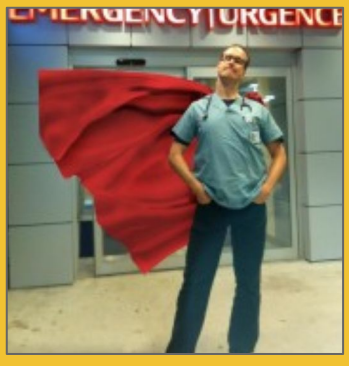
Clinicians have the option of using the PAS or the Alvarado score to help risk-stratify children with abdominal pain with regards to appendicitis risk. Both scores require laboratory investigations, specifically a CBC. Neither of these tools is perfect, however, and both should be used with caution. For patients with low risk who are being sent home, adequate discharge planning is paramount. For patients with intermediate risk, clinicians should adopt a strategy of investigation that minimizes radiation exposure.

WHAT DO I TELL MY PATIENT?

We are going to use a score called the Pediatric Appendicitis Score to help us understand your risk of having appendicitis, to guide our testing and treatment.

References

Scheller RL, Depinet HE, Ho ML, Hornung RW, Reed JL. Utility of pediatric appendicitis score in female adolescent patients. Academic Emergency Medicine. 2016 May 1;23(5):610–5.



GUEST SKEPTIC: Dr. Anthony G. Crocco
Medical Director & Division Head of the Division of Pediatric Emergency at McMaster's Children's Hospital

156 Working at the Abscess Wash – Irrigation of Cutaneous Abscesses?

Case Scenario:
A 30-year-old female with a history of cutaneous abscesses comes to your emergency department stating she thinks she has another one developing on her arm. She tells you she wants to do as little as possible to treat the abscess using an incision and drainage because she hates the pain from the procedure, especially the irrigation.

Clinical Question:
Does irrigation of a cutaneous abscess after incision and drainage reduce the need for further intervention?

Bottom LINE

Irrigation of a cutaneous abscess after an initial incision and drainage is probably not necessary.

Irrigation of Cutaneous Abscesses Does Not Improve Treatment Success.

Chinnock and Hendey. Ann Emerg Med 2016.

P Population: Emergency department patients >18 years old with a cutaneous abscess

✘ Excluded: Pregnant, police custody, prison resident, admitted to hospital, taken to the OR, inability to follow-up in 48hrs or to provide contact information for 30-day follow-up.

I Incision and drainage plus irrigation

C Incision and drainage alone

O Need for further intervention in the next 30 days after the initial incision and drainage (Interventions include: repeat incision and drainage, antibiotic change, or abscess related hospital admission within the next 30 days).

Authors' Conclusion:

"Although there were baseline differences between groups, irrigation of the abscess cavity during incision and drainage did not decrease the need for further intervention."

Background

Cutaneous abscesses are a very common complaint in the emergency department and there is much debate about the management of abscesses. The mainstay management of an abscess is incision and drainage. Other management may include wound culture and sensitivity, pain control, packing and antibiotics.

There is lots of dogma around wound care and we have covered some of these issues before on the SGEM (Dogma of Wound Care). With regards to abscesses we have discussed packing or not packing. Our bottom line in 2012 was that routine packing of simple cutaneous abscesses might not be necessary (Better Out than In).

Another issue that has been debated is whether or not to routinely prescribe antibiotics. A study by Hankin and Everett. Are Antibiotics Necessary After Incision and Drainage of a Cutaneous Abscess? was published in Ann Emerg Med 2007. We reviewed this paper on SGEM#13. Our conclusion at that time was that the evidence did not support using antibiotics routinely in simple cutaneous abscesses even in the era of MRSA.

A new study looking at Trimethoprim–Sulfamethoxazole versus Placebo for Uncomplicated Skin Abscess by Talan et al was published in NEJM March 2016. We will be reviewing this study soon on the SGEM.

Apparently there is no randomized controlled trial demonstrating the benefit of irrigation in the treatment of simple cutaneous abscesses. Treating these conditions can be painful, takes time and has a financial cost. There is also the risk of contamination to the patient and emergency medicine provider, like the PA doing the irrigation.

Results

Two hundred and nine patients were enrolled with 187 completing the study. The median age was in the late 30's with just over 40% being female.

No difference in need for further intervention at 30 days

- Primary Outcome: 15% irrigation group vs. 13% in the non-irrigation group. There was a 2% non-significant difference (95% CI -8% to 12%)
- Differences Between Groups: Irrigation group was about 5 year younger, had packing more often (89% vs. 75%) and received outpatient antibiotics more often (91% vs. 73%).

TALK NERDY TO ME

Commentary

1. *Single Centre*: This was a single center study with a high rate of MRSA, which can limit its generalizability to other practice settings.
2. *Not Consecutive*: Patients were not recruited consecutively but rather sporadically and most eligible patients were not enrolled. This could have introduced some selection bias into the study. They state; *"However, we do not believe the results were biased because patient were enrolled on all days of the week, both day and night."*
3. *Unbalanced groups*: The groups were not balanced at baseline with the irrigation group being five years younger. While statistically significant it is probably not a clinically important difference.
4. *Treated Differently*: The two groups were not treated equally. The irrigation group was more likely to have packing and receive antibiotics. There is evidence suggesting packing does not make a difference, although it is relatively weak. The issue of outpatient antibiotics after incision and drainage is even more complicated given the recent study by Talan et al. However, that should have biased the study towards irrigation being superior but the key result was no statistical difference. Another problem was the lack of standardization in the irrigation solution used or the amount of irrigation.
5. *Non-Blinded*: Patients and clinicians knew the group allocation. This could potentially explain some of the variation in treatment observed between the two groups. The lack of blinding and differences in treatment make it more difficult to interpret the results.

Clinical Application

Although abscess management varies by location and patient, irrigation of simple cutaneous abscesses may not be needed, as it does not seem to improve treatment success.

CONCLUSION VS COMMENTARY COMPARISON

We agree with the author that based on this data that irrigation does not appear to improve outcomes after incision and drainage of cutaneous abscesses. However, the study does have significant limitations and a future study with standardized treatment protocols would help clarify whether irrigation provides any efficacy.

STUDY QUALITY CHECKLIST

The study population included or focused on those in the ED	
The patients were adequately randomized	
The randomization process was concealed	
The patients were analyzed in the group to which they were randomized	
The study patients were recruited consecutively (ie., no selection bias)	
The patients in both groups were similar with respect to prognostic factors	
All participants (patients, clinicians, outcome assessors) were unaware of group allocation	
All groups were treated equally except for the intervention	
Follow-up was complete (i.e., at least 80% for both groups)	
All patient-important outcomes were considered	
The treatment effect was large enough and precise enough to be clinically significant	

WHAT DO I TELL MY PATIENT?

We know that incision and drainage can be painful and we want to reduce that pain as much as possible. There is new evidence that suggests irrigation of your abscess may not be beneficial and we can skip this painful part of the procedure if you would like.

References

Chinnock B, Hendey GW. Irrigation of cutaneous abscesses does not improve treatment success. Annals of emergency medicine. 2016 Mar 1;67(3):379-83.

GUEST SKEPTIC: Chip Lange, PA-C
EM PA in rural Missouri community hospitals

157 Nebulized Hypertonic Saline for Acute Bronchiolitis

Case Scenario:
You are working in the emergency department when an eight months old presents with nasal congestion, tachypnea, and retractions. You suspect he suffers from an acute bronchiolitis. You wonder about the most accurate and up to date treatment options.

Clinical Question:
Is nebulized hypertonic saline safe and effective for acute bronchiolitis?

Bottom LINE

Routine use of hypertonic saline cannot be recommended at this time for mild to moderate acute bronchiolitis.

Nebulized Hypertonic Saline for Acute Bronchiolitis: A Systematic Review. Zhang et al. Pediatrics 2015.

P

RCTs or quasi-RCTs of infants up to 24 months of age with diagnosis of acute bronchiolitis

✘ Exclusions: Studies that included patients who had had recurrent wheezing or were intubated and ventilated, and studies that assessed pulmonary function alone.

I

Nebulized hypertonic saline (≥ 3%) alone or mixed with bronchodilator

C

Nebulized normal saline alone or mixed with same bronchodilator or standard care.

O

Primary outcomes: Length of stay for hospitalized patients and admission rates for outpatients.

Secondary outcomes: Clinical severity score (CSS), rate of readmission to hospital or emergency department, oxygen saturation, respiratory rate, heart rate, time for the resolution of symptoms/signs, duration of oxygen supplementation, results of pulmonary function tests, radiologic findings, and adverse events.

Authors' Conclusion:

"Nebulized HS is a safe and potentially effective treatment of infants with acute bronchiolitis."

Background

During winter months in Quebec, and I suspect it is the same in many other places, bronchiolitis is one of the most frequent emergency department complaints.

Bronchiolitis is the most common disease of the lower respiratory tract infection seen in children less than one year of age. They tend to present similar to an asthma exacerbation (coughing and wheezing). It is usually a mild illness needing only supportive care. However, it can be a more serious illness requiring hospitalization and rarely causes death.

A good history and physical exam are sufficient to confirm the diagnosis. Treatment usually involves supportive care and supplemental oxygen if oxygen saturations are below 90%.

Many treatments similar to those given to asthmatic children have been tried (example: beta-agonists, ipratropium, oral and inhaled steroids). These asthma treatments and antibiotics have been shown not to be effective for the treatment of bronchiolitis.

3% hypertonic saline (HS) is a newer treatment option. In theory, it rehydrates the respiratory tract, thins the epithelial edema and enhances secretion clearance.

In 2013, Zhang and colleagues published a meta-analysis on acute bronchiolitis. In this systematic review, there were 1,090 children aged up to 24 months with mild to moderate viral bronchiolitis. According to their analyses, they concluded that even if a tendency to reduce hospital admission was observed, there was no statistical evidence of an effect of nebulized hypertonic saline on hospital admission.

In November 2014, the American Academy of Pediatrics Clinical Practice Guidelines recommended that "*Nebulized hypertonic saline should not be administered to infants with a diagnosis of bronchiolitis in the emergency department*" (*AAP 2014*).

Also in 2014, the Canadian Paediatric Society declared that "*Evidence does not currently support its routine use in the outpatient setting*" (*CPS 2014*) .

In June 2015 the National Institute for Health and Care Excellence (NICE) put out their guidelines for the diagnosis and management of bronchiolitis. They too do not recommend hypertonic saline to treat children with bronchiolitis.

Results

24 trials involving 3,209 patients

Decrease LOS (0.45d) and reduced risk of hospitalization (20%)

Primary Outcomes:

- Length of stay mean reduction of 0.45 days (95% CI: -0.82 to -0.08) 15 trials involving 1956 patients
- Risk of hospitalization reduced by 20% RR 0.80 (95% CI: 0.67 to 0.96) 7 trials involving 951 patients

Secondary Outcomes:

- Post-treatment clinical severity score first three days
  - Day 1: MD -0.99 (95% CI: -1.48 to -0.50)
  - Day 2: MD 21.45 (95% CI: 22.06 to 20.85)
  - Day 3: MD 21.44 (95% CI: 21.78 to 21.11) (5 trials, 404 inpatients);

Adverse Events:

- 21 out of the 24 trials assessed adverse events associated with hypertonic saline.
- Only one significant event occurred in which self-limited desaturation and bradycardia occurred following hypertonic saline treatment. Most studies noted that hypertonic saline treatment was associated with coughing and hoarse voice.

TALK NERDY TO ME

Commentary

1. *Target Population*: Do you think the patients represented the target population?
   - *The assessment of bronchiolitis and its definition were appropriate. However, it is possible that by including infants aged more than 12 months old, asthmatic children were included, thus limiting the effect of hypertonic saline.*
   - *Also, although most studies included infants with mild to moderate acute bronchiolitis, some trials, namely Evergard et al included infants with severe disease presenting saturation rates lower than 92%. Patients with severe bronchiolitis are usually not the ones that are treated to prevent hospital admission.*
   - *It is interesting to note that the authors of one of the included but unpublished study (Silver et al.) pointed out that their study was included in the systematic review, even though they included children who presented with recurrent wheezing. This was supposedly an exclusion criteria for the systematic review.*
2. *Parent Oriented Outcomes:* We usually ask about patient oriented outcomes but what about all *"parent"* oriented outcomes in this study?
   - *I think that all clinically important issues were considered. However, acute bronchiolitis is a disease that lasts a few weeks and is thus associated with parental leave from work. The economic burdens was not studied.*
3. *Treatment Comparisons*: Were the treatments being compared correctly chosen?
   - *There was some heterogeneity in treatments given, for example the presence or absence of a bronchodilator. The inclusion of a bronchodilator in asthmatic infants might induce a bias by treating the asthma exacerbation. This bias might underestimate the real effect of hypertonic saline.*
   - *Also, the comparison of different hypertonic saline concentration has to be taken into account, along with the inclusion of variable control groups, mostly normal saline nebs but some without nebs (Evergard). Normal saline might not be a real placebo, having some potential therapeutic effect. That being said, it is the most appropriate control in our opinion to assure blinding.*
   - *Finally, we noted that one of the outpatients trials, Sarrel et al (2002), included patients treated daily for five days, which is quite different from the usual emergency department setting. Is this really an outpatient trial?*
4. *Quality of Included Studies*: They used the GRADE criteria and found the studies included to be of moderate quality. How do you think that impacted the results and our interpretation of the results?
   - "the quality of evidence could be graded only as moderate, mainly due to inconsistency in the results between studies and risk of bias in some trials, according to the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) criteria."
   - *In my opinion, in view of the amount of small studies with inconsistency in the results, there is still place for a bigger and well-designed randomized control trial to assess the question of hypertonic saline in acute bronchiolitis.*

Commentary

5. *Safety*: They claim safety of nebulized hypertonic saline in their conclusions but there is a difference between safety and adverse events?
   - *This was not a randomized control trial with the primary outcome of safety. A more accurate conclusion would be that there were no increased adverse events or harms observed.*
     - In the results section the state: "Variation in reporting and in outcomes precluded the possibility of conducting meta-analysis of safety data."
     - Their comment about safety was softened in the discussion. "These results suggest that nebulized HS is a safe treatment in infants with bronchiolitis, especially when administered in conjunction with a bronchodilator."

Clinical Application

It is difficult to define a practice guideline for the emergency department due to the great variability in treatment regimens used, namely the different hypertonic saline concentration and the number and recurrence of administered doses.

In light of the results of this new meta-analysis, the exact place of hypertonic saline in the emergency department for treating viral bronchiolitis remains uncertain, as is the exact recipe to be used. A randomized clinical trial with more patients, using repeated 3% hypertonic saline in the first hour of the emergency department visit, compared with nebulizer normal saline, along with a more appropriate selection of patients with viral bronchiolitis (less than 12 months old, no previous wheezing and no history of atopia) would help to clarify the exact place of hypertonic saline in treating viral bronchiolitis.

STUDY QUALITY CHECKLIST

The clinical question is sensible and answerable	👍
The search for studies was detailed and exhaustive	👍
The primary studies were of high methodological quality	👎
The assessment of studies were reproducible	👍
The outcomes were clinically relevant	👍
There was low statistical heterogeneity for the primary outcomes	👍
The treatment effect was large enough and precise enough to be clinically significant.	👍

CONCLUSION VS COMMENTARY COMPARISON

We agree that the data demonstrates a decrease hospital length of stay and lowers the risk of admission. We do not agree with the conclusion of safety but rather no evidence of harm.

WHAT DO I TELL MY PATIENT?

I explain viral bronchiolitis, its symptoms, its risks and its duration. If it's a mild episode, I discharge without treatment but with appropriate documentation explaining when to return to the emergency department. If it's a moderate episode, I decide with the parents if the hypertonic saline treatment might help their child and prevent hospitalization. My impression is that hypertonic saline works mostly in the secretory phase of the disease, when the infant has a lot of crackles. I thus sometimes use it. In the majority of moderate cases, it is useless and standard care, clearing the nose and hydration, is sufficient.

I strongly believe that for most cases of viral bronchiolitis, less is more. The parents leave the emergency department with clear instructions on when to return: signs of dehydration and disease severity. Since viral bronchiolitis lasts a few weeks, it is essential to adequately inform the parents.

References

Zhang L, Mendoza-Sassi RA, Klassen TP, Wainwright C. Nebulized hypertonic saline for acute bronchiolitis: a systematic review. Pediatrics. 2015 Sep 28:peds-2015.

GUEST SKEPTIC: Dr. Chantal Guimont
Family Doctor in a mixed pediatric and adults tertiary care center; Faculty at Laval University, Quebec CIty, Quebec, Canada

158 Tempted by the Fruit of Another – Dilute Apple Juice for Pediatric Dehydration

Case Scenario:
2-year-old girl presents with 2 days of vomiting and diarrhea. She is minimally dehydrated and tolerating oral fluid only. You remember reading about the sodium-glucose co-transporter and electrolyte fluids that were initially developed by the World Health Organization for children with diarrheal diseases. You have heard parents ask about just using watered down juice and debate whether this is a viable option for these children.

Clinical Question:
In children with mild gastroenteritis who are minimally dehydrated, is diluted apple juice and preferred fluids as good (or even better) an oral rehydration fluid compared to an electrolyte rehydration solution?

Bottom LINE

When advising parents with children with mild gastroenteritis and minimal dehydration, offering half-strength apple juice and preferred fluids compared to electrolyte solutions is a better choice.

Effect of dilute apple juice and preferred fluids vs. electrolyte maintenance solution on treatment failure among children with mild gastroenteritis: A randomized clinical trial.

Freedman et al. JAMA. May 2016

P

Children presenting to the emergency department between six months to five years age. They needed to have three or more episodes of vomiting or diarrhoea in past 24 hours and symptoms could not have been going on for more than 96 hours. The children also needed to weigh at least eight kilograms and have minimal dehydration on the Clinical Dehydration Scale (CDS).

- The CDS is a four-item, eight-point scale. Children with a CDS less than five and capillary refill of less than two seconds were classified as minimally dehydrated.

✘ Excluded: Inflammatory bowel disease, celiac disease, diabetes mellitus, inborn errors of metabolism, prematurity with corrected postnatal age less than 30 weeks, bilious vomiting, hematemesis, hemtochezia, clinical concern of an acute abdomen or a need for immediate intravenous rehydration.

I

Half-strength apple juice or preferred fluids once they went home (5ml q2-5min in emergency department, then 10ml/kg for each episode of diarrhoea or 2ml/kg for each episode of vomit).

C

Apple-flavoured, sucralose-sweetened electrolyte maintenance solution

- Those who vomited in either group received oral ondansetron

O

Primary: Treatment failure that consisted of a composite outcome of five things:

- Hospitalization or intravenous rehydration
- Subsequent unscheduled health care visit (emergency department, urgent care clinic, walk-in clinic or office)
- Protracted symptoms (More than 2 episodes of vomiting or diarrhea within a 24-hour period occurring more than 7 days after enrollment)
- Cross over (physician request to administer a solution representing treatment allocation crossover at the index visit)
- Three percent or greater weight loss or Clinical Dehydration Scale score of five or higher at in-person follow-up

Secondary: Frequency of diarrhea and vomiting, percent weight change at 72 to 84 hours, intravenous rehydration at initial visit or a subsequent visit within seven days, hospitalization at initial visit or a subsequent visit

Authors' Conclusion:

"Among children with mild gastroenteritis and minimal dehydration, initial oral hydration with dilute apple juice followed by their preferred fluids, compared with electrolyte maintenance solution, resulted in fewer treatment failures."

Background

Gastroenteritis is a common illness in children and these children are at risk of dehydration from inadequate intake, excessive losses or both together. If children are unable to tolerate oral hydration we often have to use intravenous fluids and sometimes require admission to hospital for ongoing fluids.

Goldman et al Pediatrics in 2008 published a helpful table describing the degree of dehydration in children ranging from mild, moderate to severe.

Degree of dehydration	Mild (5-7% body weight)	Moderate (7-9% body weight)	Severe (>10% body weight)
Fontanelle	Slightly sunken	Very sunken	Very sunken
Mucous membranes	Slightly sticky	Dry	Very dry
Skin turgor	Normal	Slightly decreased	Markedly decreased
Capillary refill time	Normal (<3 seconds)	Normal (<3 seconds)	Delayed (≥3 seconds)
Urine output	Normal	Slightly decreased	Decreased or absent
Mental status	Normal	Slightly fussy	Irritable or lethargic

Most cases of gastroenteritis are mild, self-limiting and can be treated effectively with oral rehydration. For more information on visit this site on Oral Rehydration Therapy. The Canadian Pediatric Society also has an algorithm for oral rehydration (see below).

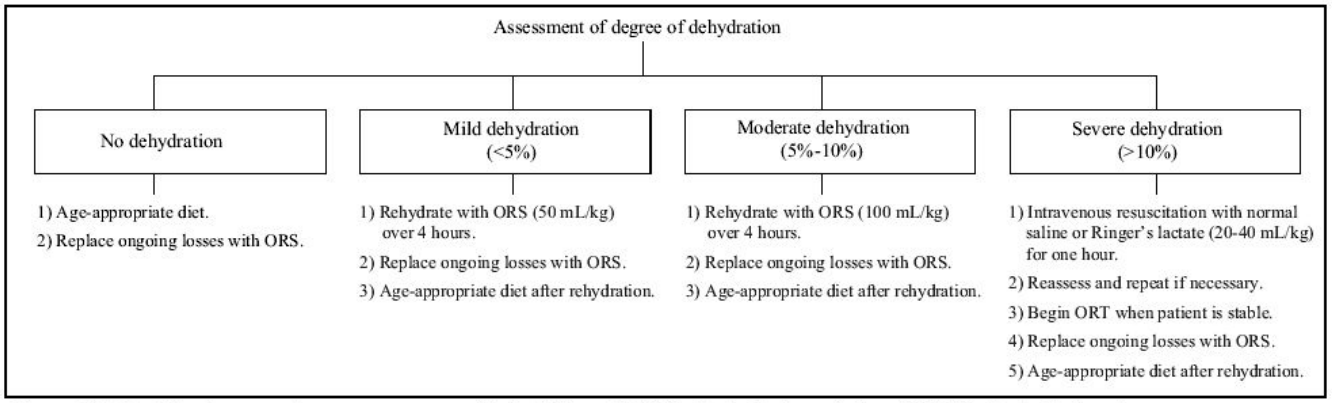


Figure 1) *Algorithm for managing acute gastroenteritis in children. ORS Oral rehydration solution; ORT Oral rehydration therapy*

We covered ondansetron on SGEM#12. Bottom line – Ondansetron is an effective anti-emetic preventing further vomiting, intravenous fluids and admissions for children with gastroenteritis.

NNT of 5 to stop vomiting
NNT of 5 to prevent one intravenous insertion
NNT of 14–17 to prevent one admission

Background

We also talked about ondansetron on SGEM#122. For the centers studied, the rates of ondansetron use increased from 0.1% to 42%. However, there was no significant difference in the rates of intravenous insertion or hospitalization during this time frame.

Children with vomiting from gastroenteritis, and mild-moderate dehydration, should have a trial of oral rehydration therapy. Failing this, ondansetron should be administered. Failing that, intravenous fluid should be considered.

Results

3,668 children presenting to the emergency department were assessed for eligibility. There were 647 children randomized into the study (n=323 for half-strength apple juice/preferred fluids and n=324 for electrolyte solution). The majority of exclusions were because no research personnel were present to enroll the child (1,297). It was about evenly split between boys and girls and the mean age was 28 months. There were not differences between groups at baseline.

There were some other interesting baseline data:

- 90% had history of vomiting and >40% had a history of diarrhea
- Mean time to presentation was around 3:30pm
- Mean time to vomit onset and emergency department visit was 30hrs and for diarrhea around 25hrs
- Ondansetron was used in about two-thirds of cases

Treatment Failure: 16.7% half-strength apple juice and preferred fluid vs. 25.0% electrolyte solution

- Primary Outcome: Treatment failure
  - 16.7% (95%CI 12.8%-21.2%) half-strength apple juice group and preferred fluid vs. 25.0% (95%CI 20.4%-30.1%) electrolyte solution group.
  - NNT of 12 with half-strength apple juice and preferred fluids to prevent one treatment failure.
  - Difference between groups was -8.3% (97.5%CI -infinity to -2.0) showing non-inferiority ($p<0.001$).
  - That is better than the pre-specified non-inferiority margin of +7.5%.
  - The experimental group (half-strength apple juice and preferred fluids) was also shown to be superior to the control group ($p=0.006$).
- Secondary Outcomes:
  - Less intravenous hydration in the half-strength apple juice and preferred fluids group (0.9% vs. 6.8%) at index ED visit ($p<0.001$).

TALK NERDY TO ME

Commentary

Overall this is a very well conducted randomized trial. Listen to the podcast to hear the full discussion with Dr. Crocco on the five issues identified.

1) *Convenience Sample*: They did not recruit patients consecutively. It was a convenience sample (12 hours/day, 6 days/week, October to April). The risk with convenience sampling is that the sample of patients included in the study may not reflective, or cannot be generalized, to the overall population presenting to the emergency department. The number one reason for exclusion was no research personnel present (1,297). We could not find in the manuscript or the supplemental material a clear idea of what time of day the research personnel were available.

2) *Composite Outcome*: They used a composite outcome consisting of a number of clinically relevant measures. There are risks of composite outcomes, specifically that the metrics may not all have the same clinical relevance. In this case, the composite outcome "treatment failure" included hospitalization or intravenous rehydration, unscheduled health care visit, protracted symptoms, cross over and weight loss or dehydration after index case. These individual components may or may not be equal in terms of relevance to the family and patient. In this composite outcome the most statistically significant difference was in intravenous rates.

3) *Concealment*: Allocation was concealed in the emergency department by having identical opaque bottles of rehydration fluid but not at home. Upon discharge, parents were given an opaque envelope with instructions for care at home, which included the revelation of which treatment arm the child was in, thus eliminating concealment at that time. This has the potential to induce bias into the study. It is hard to know in which direction the bias would deviate the results. Would knowing that your child is getting dilute apple juice or electrolyte solution make you more or less likely to seek care? Hard to know.

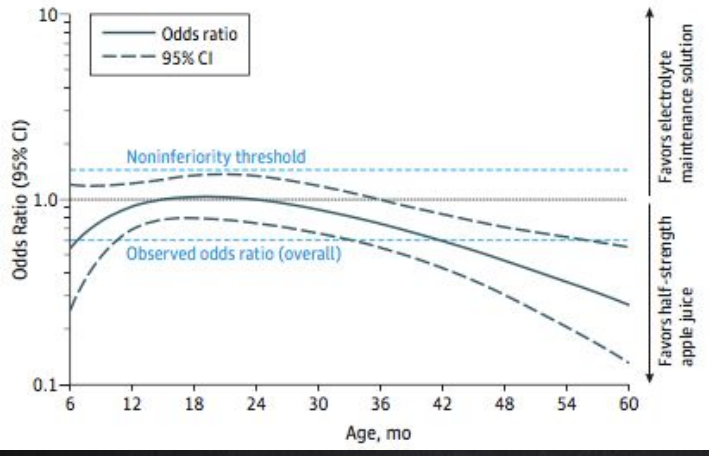
4) *Clinical Dehydration Scale*: They used the CDS in this study. There are a number of dehydration scales and for the purposes of research it is important to use one that is appropriately validated. Dr. Crocco generally uses clinical gestalt assessment, but encourages people to use what they feel is most appropriate for them and their patients given their environment and experience.

5) *Non-Inferiority and Superiority*: This was designed as a non-inferiority study. They demonstrated that dilute apple juice was not only non-inferior but also superior to an electrolyte solution. Watch for a whole SketchyEBM episode coming out on this issue.

Anything else you want to say about this study Dr. Crocco? This study is a game-changer. The longstanding paradigm of managing children with gastroenteritis and minimal dehydration has been to use electrolyte solutions, such as developed by the W.H.O. in the 1960-70s. These fluids were originally developed for use in children in low-income countries with cholera outbreaks. Anecdotally these electrolyte fluids are poorly tolerated in kids due to poor taste. This study shows that, in a population of children from a high-resource country, half-strength apple juice and preferred fluids is better than electrolyte solutions for rehydration. Of interest, further analysis of the results showed that there was an interaction between age and effect with a greater effect noted in children over 24 months of age. (See Figure 2.)

Commentary

Figure 2. Treatment Failure Comparing Half-Strength Apple Juice/ Preferred Fluids Therapy and Electrolyte Maintenance Solution Groups as a Function of Age



Clinical Application

In children with mild gastroenteritis and minimal dehydration, half-strength apple juice and preferred fluids is a better choice for rehydration.

CONCLUSION VS COMMENTARY COMPARISON

We agree with authors' conclusions. Half-strength apple juice and preferred fluids is a better choice for rehydrating children with mild gastroenteritis and minimal dehydration compared to electrolyte solutions.

Study Quality Checklist

The study population included or focused on those in the ED	👍
The patients were adequately randomized	👍
The randomization process was concealed	👍
The patients were analyzed in the group to which they were randomized	👍
The study patients were recruited consecutively (ie., no selection bias)	👎
The patients in both groups were similar with respect to prognostic factors	👍
All participants (patients, clinicians, outcome assessors) were unaware of group allocation	👎
All groups were treated equally except for the intervention	👍
Follow-up was complete (i.e., at least 80% for both groups)	👍
All patient-important outcomes were considered	👍
The treatment effect was large enough and precise enough to be clinically significant	👍

WHAT DO I TELL MY PATIENT?

I AM GOING TO GET YOU SOME WATERED-DOWN APPLE JUICE AND SEE HOW WELL YOU ARE ABLE TO DRINK IT. IF YOU ARE ABLE TO KEEP IT DOWN WITHOUT VOMITING, WE ARE GOING TO SEND YOU HOME AND YOUR PARENTS ARE GOING TO CONTINUE TO GIVE YOU THIS FLUID AT HOME AND PREFERRED FLUIDS.

REFERENCES

Freedman SB, Willan AR, Boutis K, Schuh S. Effect of dilute apple juice and preferred fluids vs electrolyte maintenance solution on treatment failure among children with mild gastroenteritis: a randomized clinical trial. Jama. 2016 May 10;315(18):1966-74.

GUEST SKEPTIC: Dr. Anthony Crocco
Medical Director & Division Head of the Division of Pediatric Emergency at McMaster's Children's Hospital, Hamilton, ON, Canada

159 Computer Games – Computer Provider Order Entry (CPOE)

Clinical Question:
What impact will CPOE have on emergency department patient throughput?

Case Scenario:
None

Bottom LINE

Implementation of CPOE may initially be met with some difficulties, worsen emergency department patient flow and contribute to emergency department over-crowding. The long-term impact on patient oriented outcome and physician satisfaction remains to be seen.

The impact of computerized provider order entry on emergency department flow.

Gray A et al. CJEM 2016.

P

Emergency department patients 18 years and older presenting to two quaternary hospitals in July and August of 2013 and 2014.

✘ Excluded: Patients with negative wait times or extreme outliers that exceeded 24 hours (presumed to represent an erroneously wrong day recorded). Also excluded any patients missing vital statistics (eg. Gender, age or CTAS score).

I

Computerized provider order entry (CPOE)

C

Non-computerized order entry

O

Primary Outcome: Emergency department throughput

- Wait Time (WT): Time to first physician assessment after triage (minutes)
- Length of Stay (LOS): Time to disposition after triage (minutes)
- Left Without Being Seen (LWBS): Proportion of patients that LWBS/total patients for a given time period (%)

Secondary Outcome: Subgroup analysis
CTAS 1–5 (WT, LOS and LWBS) and admitted patients (WT and LOS)

Canadian Triage and Acuity Scale (CTAS): This was a national program started in (1999) to standardize emergency department triage in Canada.

Authors' Conclusion:

"CPOE implementation detrimentally impacted all patient flow throughput measures that we examined. The most striking clinically relevant result was the increase in LOS of 63 minutes for admitted patients. This raises the question as to whether the potential detrimental effects to patient safety of CPOE implementation outweigh its benefits."

Background

Emergency department crowding is a growing issue across Canada. As more tertiary care EDs implement computerized provider order entry (CPOE), it is important to analyze emergency department metrics to see how CPOE may impact throughput.

Previous studies have shown that CPOE has no impact on mortality, and may in fact improve pain treatment and adherence to certain common presenting complaint medication protocols (such as stroke and renal colic) [1–4].

Some studies have shown there may be an impact on throughput in a number of possible areas such as decreased physician productivity, increased LOS for admitted patients, or increased time to order labs and imaging [5–7].

Other studies have shown that CPOE fixes some errors, creates new ones and frustrates physicians [8]. There is no consistent or comprehensive evidence in favor of CPOE [9].
A study looking at productivity in a community hospital emergency department showed the mean percentage of time spent on data entry was more than 40% and less than 30% spent on direct patient care. They calculated in a busy 10hr shift the number of mouse clicks was almost 4,000 [10].

To our knowledge there have been no studies to directly evaluate the impact of CPOE on emergency department wait times, a key variable in throughput and crowding.

References:

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4. Blankenship et al. Prospective evaluation of the treatment of pain in the ED using computerized physician order entry. Am J Emerg Med 2012
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9. Georgiou A et al. The effect of CPOE systems on clinical care and work processes in emergency departments: a systematic review of the quantitative literature. Ann Emerg Med 2013
10. Hill RG Jr, Sears LM, Melanson SW. 4000 clicks: a productivity analysis of electronic medical records in a community hospital. Am J Emerg Med 2013

Results

- Median WT increased by 5 minutes (78 vs. 83)
- Median LOS increased by 10 minutes (254 vs. 264)
- Proportion of LWBS increased by 0.9% (7.2% vs. 8.1%)
- Median LOS for admitted patients increased by 63 minutes (713 vs. 776)
- Proportion of LWBS increased significantly for CTAS 3, 4 and 5 patients (CTAS 5 patients 24% vs. 42%)

	Before (2013)	After (2014)	p value
Median WT (min [IQR])	78 (33-165)	83 (33-166)	0.036
Median LOS (min [IQR])	254 (147-417)	264 (153-422)	0.001
LWBS All Patients	1,364 (7.2%)	1,448 (8.1%)	0.002
Admitted LOS (min [IQR])	713 (443.5-1,204.5)	776 (486-1,260)	<0.001
LWBS CTAS 5 Patients	42 (24.3%)	81 (42.0%)	<0.001

Commentary

Listen to the podcast to hear the lead author's responses to our questions.

1. *Excluded Patients:* You excluded 466 patients before CPOE and 1,235 after CPOE. Why did you have three times as many patients excluded after CPOE and do you think that impacted the results?
2. *Interquartile Range*: You represented wait times and length of stay as medians with interquartile ranges. Why did you use these statistics to describe your data and do you think this gives you a precise estimate of the results?
3. *Statistical vs. Clinical Significance*: You demonstrated statistically significant changes (a few minutes for WT and LOS, ~1% increases LWBS and ~1hr increase LOS for admitted patients who were waiting a median of 12hrs already) but do you think these represent clinically significant changes?
4. *Two Months of the Year*: You only looked at two months (July and August) in 2013 before CPOE and 2014 after CPOE. These are summer months when you have new residents starting and lots of people taking holidays. Do you think these two months are representative of the whole year?
5. *Start Up Phase*: The CPOE was introduced to the entire hospital system as part of a program called HUGO (Healthcare Undergoing Optimization) in April 2014. There is a learning curve with new systems. Perhaps more training or better training was needed. In other words, could the impact on emergency department flow be related to CPOE difficulties in the start-up phase of the HUGO project?
6. *External Validity*: This study took place at the London Health Science Centre (LHSC) that included two quaternary care emergency departments in London, Ontario. Do you think your study has external validity to other emergency departments (Non-Teaching, Community, Rural, Non-Canadian)?
7. *Before/After*: One of the problems with before and after studies is other changes over time could have been responsible for the differences observed. Do you think any other factors could have played a role besides CPOE?

Commentary

8. *Patient Oriented Outcomes*: You measured WT, LOS and LWBS but did you consider and measure other patient oriented outcomes like medication errors, adherence to evidence based medicine protocols, time to pain medications and overall patient satisfaction? These are other quality indicators that have been investigated in other CPOE studies.
9. *Lack of In-Patient Beds*: Many Canadian hospitals, including yours, have occupancy above 80% and sometimes as high as 125%. This can lead to overcrowding in the emergency departments. What impact if any do you think this had on your study?
10. *Physician Satisfaction*: A new study came out in the Mayo Clinic Proceedings showing that physicians' satisfaction with electronic health records (EHRs) and CPOE was generally low and those using EHRs and CPOE were at higher risk for professional burnout (Shanafelt et al 2016). Did you see any issues with physician satisfaction due to the introduction of CPOE?

Clinical Application

None listed

CONCLUSION VS COMMENTARY COMPARISON

We agree that this implementation of CPOE at this quaternary hospital system had a detrimental impact on emergency department patient flow. It is unsure if these increased WT, LOS and LWBS rates are clinically important. We also question whether the potential benefits of CPOE outweigh the potential detrimental effects of CPOE on patient safety.

Study Quality Checklist

The study addressed a clearly focused issue	
The authors used an appropriate method to answer their question	
The cohort was recruited in an acceptable way	
The exposure was accurately measured to minimize bias	
The outcome was accurately measured to minimize bias	
The authors identified all important confounding factors	
The results were precise and estimated risk well	
The results are believable	
The results can be applied to the local population	
The results of this study fit with other available evidence	**

** Yes/No. THere is conflicting evidence with respect to the effect of CPOE on LOS and other patient flow parameters.

WHAT DO I TELL MY PATIENT?

NOT APPLICABLE

REFERENCES

Gray A, Fernandes CM, Van Aarsen K, Columbus M. The impact of computerized provider order entry on emergency department flow. Canadian Journal of Emergency Medicine. 2016 Jul;18(4):264–9.

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Evidence based medicine is easy

A simplified guide to approaching the medical literature

First10EM

Evidence based medicine is easy.

I know that evidence based medicine scares people. That stats seem complicated. Papers are often full of obtuse language. People are constantly debating small details at journal clubs, which can leave many physicians feeling inadequate.

But I can assure you, evidence based medicine is easy. If I can do it, anyone can. The only difficult part is getting into the habit of actually picking up a paper and starting to read.

I am a community emergency doctor with no special training in quantitative research methodology or epidemiology. Everything I learned about evidence based medicine I learned by picking up papers and reading them for myself (with some important insights from people like Jerry Hoffman and Rick Bukata on the Emergency Medical Abstracts). This post runs through the simplified approach I take when reading the medical literature, with the hope that I can convince you that you are also capable of taking an active role in critiquing the medical literature.

Step 1: How do I find a paper to read?

When you are just starting out, I would suggest picking a paper that other people are also reviewing. This could be a paper that was chosen for your group's journal club, that was featured on a program like the Skeptics' Guide to Emergency Medicine, or one that you found in my Articles of the Month. Read the paper yourself, write down your conclusions, and then compare your thoughts to the conclusions of other experts who have read the same paper.

Eventually, you will probably find it limiting to only read papers chosen by others. Having access to a list of newly published research allows you to pick the topics that are most interesting to you. I currently get all of the abstracts from 47 different journals, but that is simply way too much for most people. Just pick one or two high impact journals in your field to scan each month. You can opt to receive notifications of new publications by e-mail, or you can subscribe to the journal's RSS feed.

If you are interested in a specific topic, another great option is to set up a pubmed email alert. It does require that you create a (free) NCBI account, but is easy and ensures that you will never miss an important paper on a topic that interests you (such as "sexual intercourse for the treatment of nephrolithiasis").

Step 2: Is this paper worth reading?

I use the title and abstract to decide whether a paper is worth reading. However, to save time, I don't read the entire abstract. First, I skip directly to the conclusions. If a paper's conclusions are not interesting, or don't seem relevant to my practice or my patients, I can throw the paper away and not waste any more time. If the conclusions seem interesting, I will look at the methods described in the abstract. If the methods are clearly poor or irrelevant to my current clinical practice (such as animal studies), I will not read the paper. If the conclusions are interesting and the methods seem reasonable I will download the paper to read.

Step 3: Read the paper

At first glance, papers seem long and dense. They are intimidating. simply scanning through a 16-page pdf is often enough to kill one's desire to read. Luckily, many of those pages are superfluous. Most of the time, we can be much more efficient in our reading if we understand the structure of a paper:
Title: Helpful (sometimes) for finding the paper in your original search, but basically useless after that.
Abstract: This quick summary of the paper helps you decide if a paper is worth your while. However, the details are far too scant to help us make clinical decisions, so we can skip the abstract when we actually sit down to read a paper.

Introduction: This section provides background information on the topic. However, the data presented is not the result of a systematic review. There is a lot of room for bias in the introduction section. In a lot of ways, the introduction section is just a summary of the authors' opinions on the topic. If the topic is completely new to you, you might find this background information helpful. Most of the time, though, I just skip the introduction section.

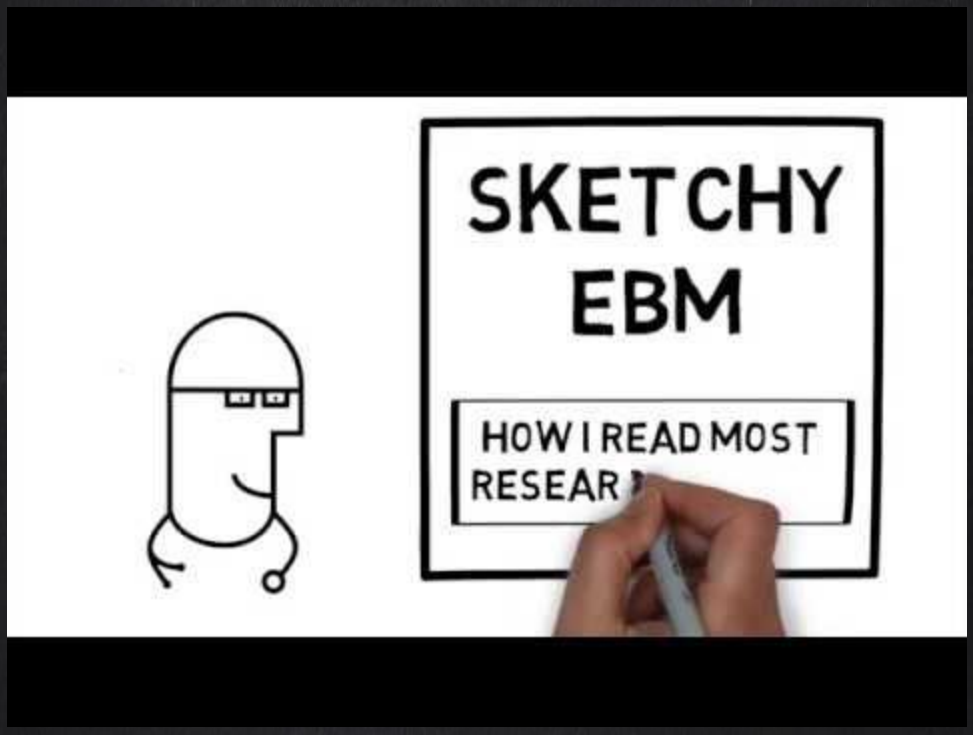
Methods: This is the most important part of any research paper. Good results are meaningless without high quality research methods. Expect to spend most of your time here. The methods section is often the most confusing section, with esoteric language or jargon, but a simplified approach is possible. I will get back to that in a minute. If the methods are very poor, you can save yourself time by stopping now, because with poor methodology you are unlikely to be convinced to change your practice, no matter what you find in the following results section.

Results: This is the real reason you picked up the paper in the first place. You want to know what the study showed, so you are going to have to read through the results section. There are often many different results presented. If you are feeling overwhelmed, focus on the primary outcome of the study (which should have been clearly stated in the methods section).

Discussion: This is another non-systematic review the literature. The authors compare their results to prior studies. Like this introduction, this section represents the opinions of the authors'. Usually, I skip the discussion section.

Conclusion: This is the author's opinion of what their results show. At this point you have already read the methods and results and so should have already drawn your own conclusions about the paper. You don't need to read the authors' conclusions unless you want a taste of the subjectivity present in scientific publication. Therefore, although papers often seem overwhelming long, we can cut down on the amount of time we spend reading by sticking to the most important sections. All of the study's objective science is found in the methods and results sections. The remaining sections add the authors' subjective interpretations, which can be safely skipped most of the time.

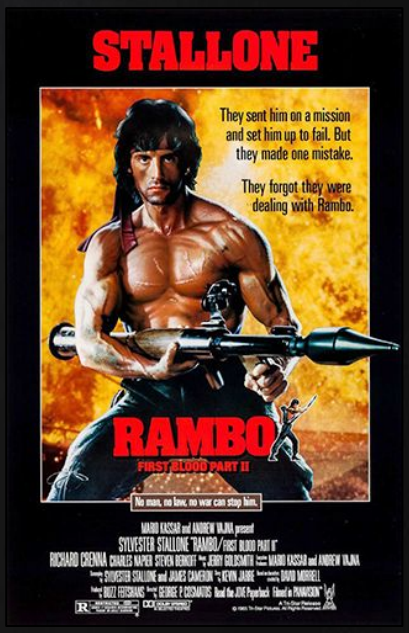
Apparently I am not the only one who skips large chunks of research papers. A very similar approach to reading papers is outlined on Sketchy EBM:



Step 4: Interpret the paper (stats are less important than you think)

Medical research can certainly get very complex. Papers often include language understandable only if you have a PhD in statistics. However, the vast majority of the time a quality critical appraisal is possible by simply asking a few common sense questions as you read.

You can think of a trial like a race. We want the race to be fair. In order to be fair, the race has to have a fair start (all patients start the trial at the same spot), everyone needs to run the same course (all trial participants are treated similarly except for the intervention), and there needs to be a fair finish (the outcome is measured the same for everyone, without bias).



One framework I keep in mind when reading papers is the RAMMBO approach:

- **R**ecruitment
- **A**llocation
- **M**aintenance
- **M**easurement: **B**lind or **O**bjective

Recruitment

- Who was included in this study? Do the study patients look like my patients?
- Is the study size appropriate? (Ideally, this should be easy to tell, because the researchers will describe their sample size calculation).
- Were there important exclusions that could affect the results?

Allocation

- Were the groups similar at the beginning of the trial?
- Was assignment to treatment groups randomized? If assignment wasn't randomized, it is worth considering what factors might have made the groups systematically different (confounders), but keep in mind that it is not possible to identify all confounders.

Maintenance

- Were the groups treated similarly throughout the trial (aside from the intervention of interest)?
- Were the outcomes of interest measured for all (or at least most) of the patients in the trial? (In other words, were patients lost to follow up, which could affect the reliability of the results?)

Measurement

- Were patients, clinicians and researchers all blinded to the treatment? (Bias is much more likely when people are aware of the groups patients were assigned to).
- Or, were the outcomes objective and standardized? (In an unblinded trial, bias is less likely with an objective outcome like mortality than it is with a subjective outcome like satisfaction with treatment).
- Were harms adequately measured?

These simplified RAMMBO questions help me distill the methods section down into common sense questions that I can understand. They are primarily aimed at assessing the validity of the trial's results. After I finish reading a paper, I like to pause and ask myself a few other questions to help place the trial in its appropriate context:

1. Why was the study done?
    a. Is the question important?
    b. Does anyone have a vested interest in the outcome?
2. Is the benefit big enough?
    a. To answer this question, you have to consider both how the benefits weighs against harms, but also the cost that any new intervention might have.
3. How does this study fit with previous research?

In my opinion, the answers to these questions are far more important than any of the statistics or p values you might struggle with while reading. I always consider these questions before I even look at the statistics presented. Although comfort with critical appraisal does require some practice, these questions are relatively straightforward and, I think, make basic critical appraisal easy for any practicing clinician.

Step 4: Use a checklist

Most of the time, the basic questions above are all you need when appraising an article. However, sometimes if a paper is more complex or if I am tackling a more important question, I want to be more thorough with my critical appraisal. In those situations, I recommend using a checklist to help assess all the possible sources of bias in a paper. There are many checklists available. I generally use the Best Evidence in Emergency Medicine (BEEM) checklists:

1. Randomized Clinical Trials
2. Systematic Reviews
3. Diagnostic Studies
4. Clinical Practice Guidelines
5. Clinical Decision Instruments
6. Prognostic Studies

More checklists and EBM tools can be found here.

Step 5: Ask for help

Although I think evidence based medicine is easy, I will admit that there are some aspects that can get very complex. As practicing physicians, it doesn't make a lot of sense for us to learn everything about epidemiology. We need to be expert clinicians, not statisticians. The solution is simple: know when to ask for help.

Start by reading the paper, but when you come across topics that you don't fully understand, reach out for some help. There are many incredible resources when it comes to evidence based medicine. Obviously, we have the #FOAMed community, with many excellent podcasts and blogs that can help with critical appraisal. I plan on updating this blog with a number of EBM resources in the coming year, so keep an eye on https://first10em.com/EBM for added resources. Reaching out to experts directly can also be helpful. As I struggled to learn critical appraisal, I have emailed experts like Jerry Hoffman, Ken Milne, and Andrew Worster on multiple occasions, and each time have been rewarded with friendly and brilliant responses. Local experts like medical librarians and university research methodologists are also excellent resources. Finally, don't underestimate the value of a simple search on Google or YouTube.

Step 6: Apply the research

This is where evidence based medicine can get complex. Reading and appraising papers is easy, but real evidence based medicine requires that clinicians interpret the evidence through a lens of clinical expertise and with patient values in mind. Evidence based medicine is not just about the literature. "Evidence-based medicine is the integration of best research evidence with clinical expertise and patient values." (Sackett 2000)

This is why you are already an evidence based medicine expert. This is why it is better for practicing clinicians to read the literature than expert methodologists. Although a statistician will have incredible insight into the mathematics of the paper, it is only the practicing clinician who can adequately filter the information through their clinical expertise, explain it in simple terms to their patients, and make decisions that mesh the best available evidence with the values of the patient. That is evidence based medicine. These discussions (which we all have every shift) are complex. In comparison, reading the literature is simple, so why not give it a try?

References

Sackett D et al. Evidence-Based Medicine: How to Practice and Teach EBM, 2nd edition. Churchill Livingstone, Edinburgh, 2000, p.1.

Cite this article as: Justin Morgenstern, "Evidence Based Medicine is Easy", First10EM blog, January 8, 2018. Available at: https://first10em.com/ebmiseasy/.
Thank you to Dr. Ken Milne and Dr. Andrew Worster for providing feedback on this blog post.

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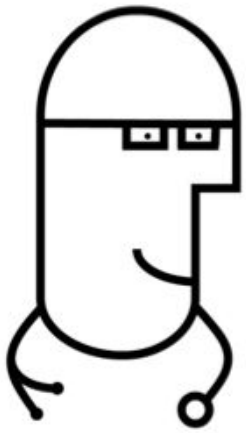

Sketchy EBM

Always draw your own conclusions!

Do you find EBM and clinical epidemiology:

a) Annoying

b) Boring

c) Complicated

d) Useless

e) All of the above

Then Sketchy EBM is for YOU!

Sketchy EBM has distilled some important EBM and clinical epidemiology topics down to bite-sized, completely digestible, short videos.

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Are you a risk-taker? You'll learn about RISK!

Are you odd? You'll learn just how ODD you might be! Knowing about odds can make you a better gambler!

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If EBM videos are not your thing – Sketchy EBM also has a few helpful clinical and quality of care videos. And if that's still not your thing, but you like watching angry people rant, then have a look at the fine collection of RANThonys! Uncorked rage can be fun and educational!

No matter what you do, remember to always draw your own conclusions!

SKETCHY EBM

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Dr. Milne is the Chief of Staff at South Huron Hospital in Exeter, Ontario, Canada. He has been doing research for over 30 years publishing on a variety of topics. He is passionate about skepticism, critical thinking and medical education. He is the creator of the knowledge translation project, The Skeptics' Guide to Emergency Medicine. When not working he is trying hard to be an endurance athlete. Dr. Milne is married to Barb and has three amazing children.

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Lucas is a second year medical student at Case Western Reserve University School of Medicine. Helping with this e-book was the ideal combination of his interests in Emergency Medicine and FOAM. When not studying, he enjoys cycling and running to explore the city and parks of Cleveland.