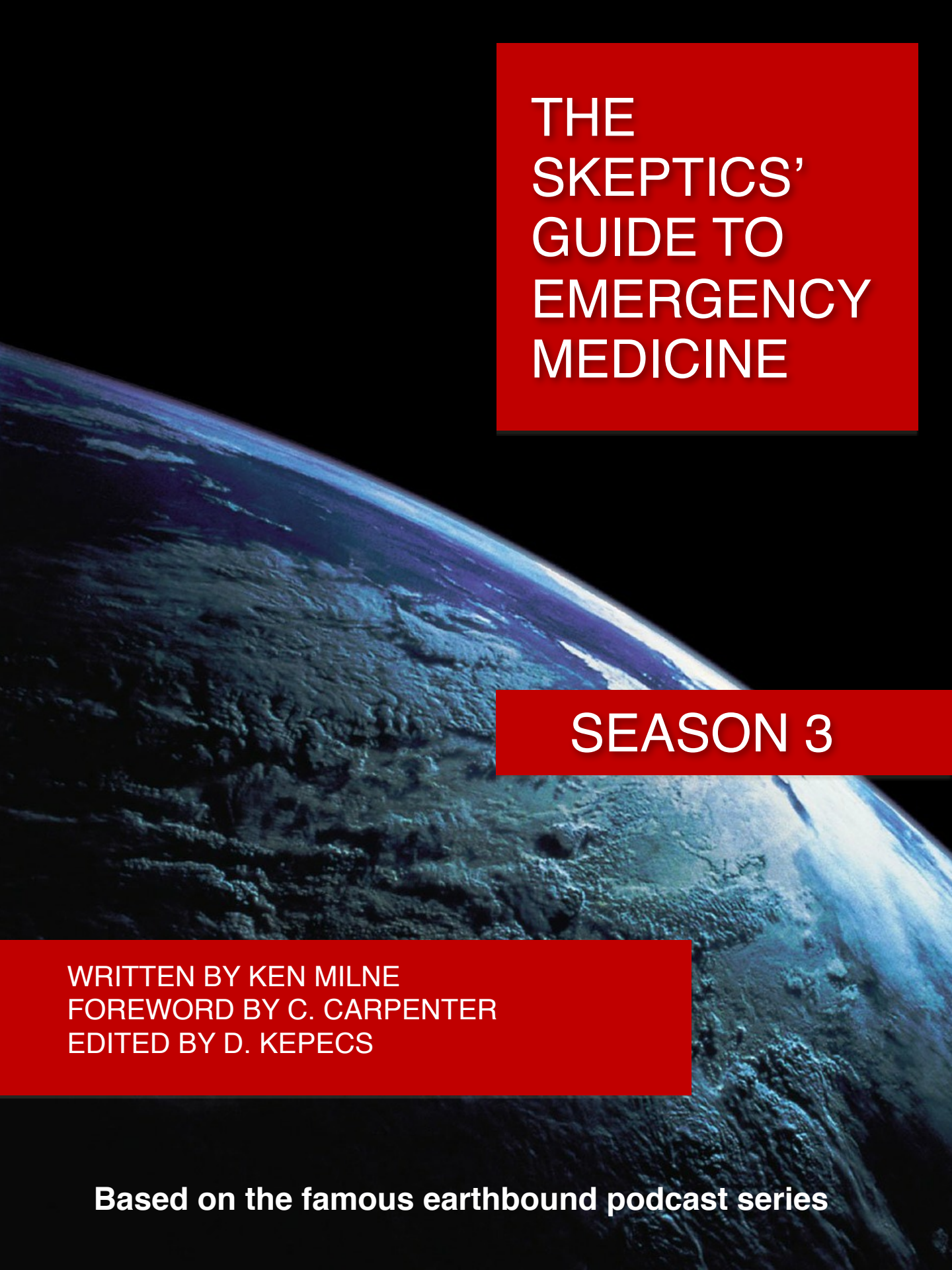

THE SKEPTICS' GUIDE TO EMERGENCY MEDICINE

SEASON 3

WRITTEN BY KEN MILNE
FOREWORD BY C. CARPENTER
EDITED BY D. KEPECS

Based on the famous earthbound podcast series

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:

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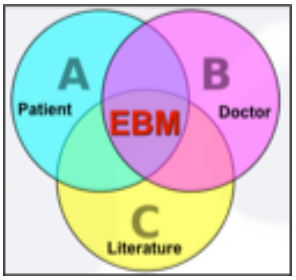
The SGEM makes a reasonable effort to supply accurate information but does not assume any liability for errors or omissions. Because of the nature of the program and its format, it is not recommended that they serve as the sole basis for patient evaluation and treatment.

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

Evidence Based Medicine

Evidence based medicine (EBM) was coined by Dr. Gordon Guyatt and the Evidence Based Medicine Working Group in 1992. It is defined as the overlap between clinician expertise, a patient's unique situation and personal values, and research evidence. It is about increasing patients' choices, not decreasing choices. Unfortunately, a growing body of evidence suggests that clinical experience alone is insufficient to ensure that patients receive contemporary, guideline- based medical care. In fact, half of the patients in the United States do not receive evidence-based management in primary care (1). Since there are over 3,800 biomedical publications that appear every day in PUBMED and since an emergency medicine provider needs to read 26 articles in Annals of Emergency Medicine to find one manuscript that changes their practice (2). It is not surprising that busy clinicians often overlook new innovations and updated guidelines.



It is no wonder that the Institute of Medicine estimates that it takes (on average) 17 years for 14% of research evidence to permeate into everyday bedside practice. One evolving approach to the information overload challenge confronting busy clinicians is the BEEM Rater Instrument, the only validated tool to filter practice-changing medical research from the "noise" of other publications. The BEEM Rater Instrument was designed and validated by SGEM contributors -- and is the methodological backbone of the SGEM evidence selection process. The BEEM process can be used to significantly reduce the "information overload" challenge for busy clinicians.

EBM provides a new approach to incorporating clinical research into bedside practice. The process of EBM provided a template to seek, find, appraise, and apply research findings to individual patients, as opposed to the passive dissemination of research that had been relied upon by investigators, journals, and educators in the past.
EBM offers an approach to help busy clinicians to find, evaluate, and use clinical research in their practice, but it is not a panacea (3). Most clinicians lacked a high-quality exposure to EBM during their medical training (4,5) and there is ample evidence that traditional CME is ineffective (6).

1. McGlynn EA, Asch SM, Adams J, Keesey J, Hicks J, DeCristofaro A, Kerr EA: The quality of health care delivered to adults in the United States. N Engl J Med 2003, 348(26):2635-2645. PMID 12826639
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6. Forsetlund L, Bjorndal A, Rashidan A, Jamtvedt G, O'Brien MA, Wolf F, Davis D, Odgaard-Jensen J, Oxman AD:Continuing education meetings and workshops: effects on professional practice and health care outcomes.Cochrane Database Syst Rev 2009, Issue 2. Art. No.: CD003030. DOI: 10.1002/14651858.CD003030.pub2. PMID 19370580

EBM critics often portray the EBM construct of finding, appraising, and using clinical evidence as an unreal expectation (7,8.9). However, these same critics offer no viable alternatives (10,11). To misquote Winston Churchill, *"EBM is the worst form of medicine, except for all the others that have been tried."*

The stepwise approach to EBM involves starting with a specific clinical question you are looking to answer. You then go through a five-step process in an attempt to answer the question.

Step 1: PICO

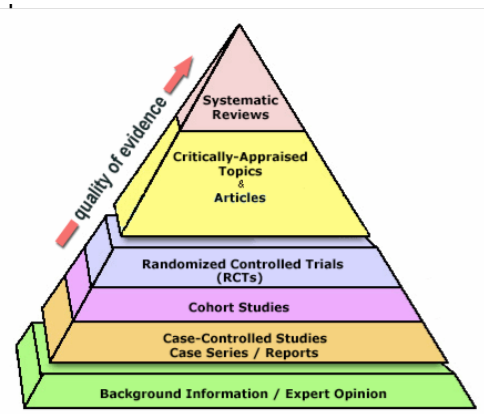
This stands for Population, Intervention, Control and Outcome. You want to find a study population that is similar to your patient. What was the intervention and what were the controls (placebo, sham or other treatment). Finally, were the outcomes patient oriented outcomes and not disease oriented or surrogate markers.

Step 2: Devise a Search Strategy

This could be as broad as a Google or Google scholar search. While capturing many hits, it may be difficult to distinguish the signal from the noise. PubMed is a large database you are probably familiar with already. It has various filters to help refine your search to obtain an answer to your clinical questions. Another search strategy you may want to try is Turning Research Into Practice (TRIP DataBase). It can be very useful to narrow your search. Alternatively, Washington University amazing Journal Cl (www.emjclub.com) may have already asked and answered the same question.

Step 3: Select the Least Biased Information

There is a hierarchy of EBM that is beautifully illustrated in this pyramid. It goes from the lowest form of evidence like an expert opinion, to the highest form of evidence such as systematic reviews. You want to find the highest form of evidence possible when trying to answer your clinical question.



7. Tobin MJ: Counterpoint: evidence-based medicine lacks a sound scientific base. Chest 2008, 133(5):1071-1074. PMID 18460514
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Step 4: Critically Appraise the Study

You need to review the manuscript found in the search. For a randomized clinical trial (RCT) there are eleven questions you need to ask yourself:

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

Step 5: Consider the Limitations

Think about what the limitations were based on your critical appraisal and summarize these thoughts. Consider these broad issues:

- External validity
- Biases
- Randomization
- Blinding
- Patient Oriented Outcomes (POO)
- Clinically Significant

In the end after looking at the evidence, critically appraising it and considering the limitations you will have to decide is the information practice changing? How would you apply this information clinically? What would you tell your patients?

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.

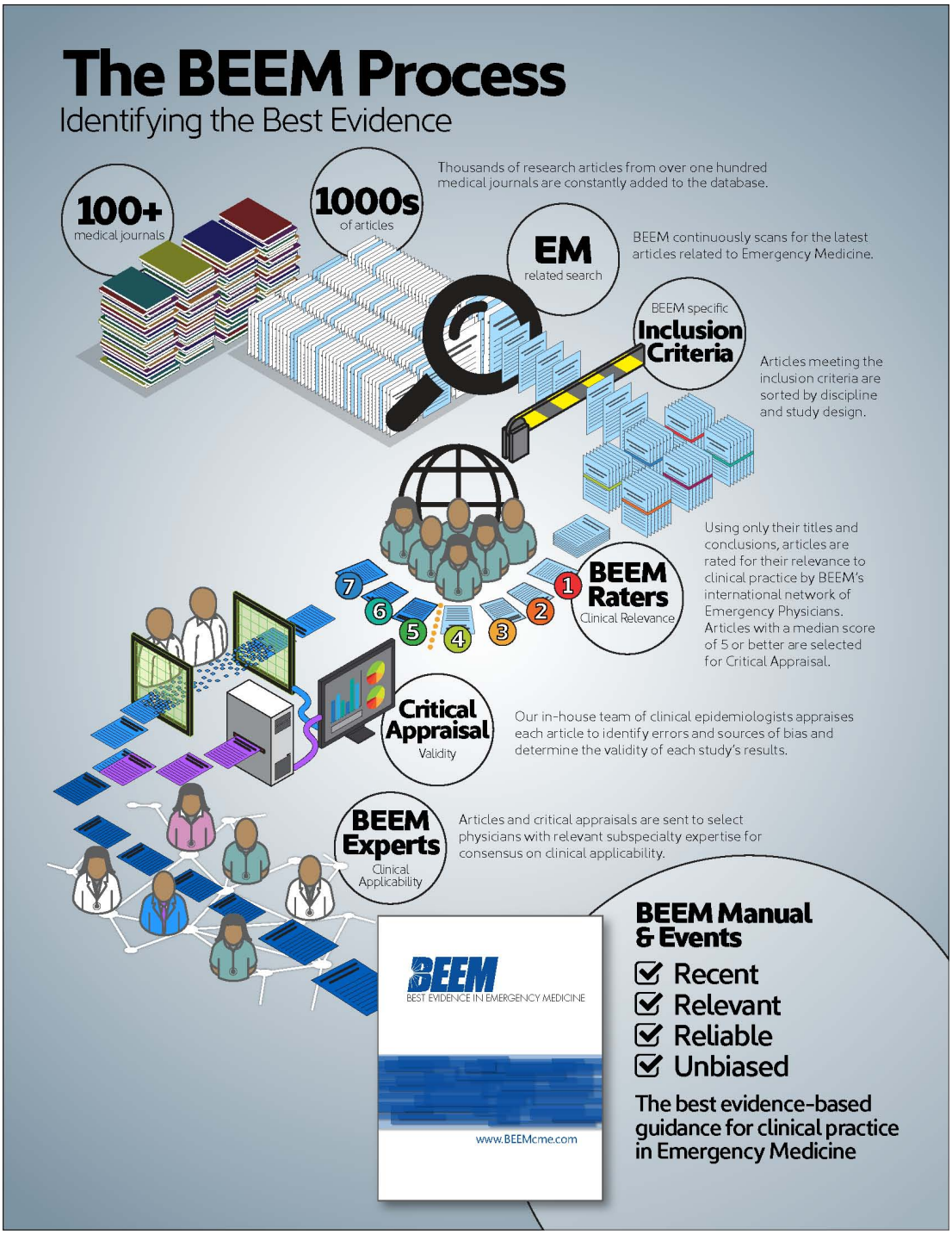
BEEM Vision:
The vision of BEEM is to be the most valid, reliable, and unbiased global source of current clinically-relevant patient-centered research for Emergency Physicians.

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
100+
medical journals
1000s
of articles
Thousands of research articles from over one hundred medical journals are constantly added to the database.
EM
related search
BEEM continuously scans for the latest articles related to Emergency Medicine.
BEEM specific
Inclusion Criteria
Articles meeting the inclusion criteria are sorted by discipline and study design.
BEEM Raters
Clinical Relevance
Using only their titles and conclusions, articles are rated for their relevance to clinical practice by BEEM's international network of Emergency Physicians. Articles with a median score of 5 or better are selected for Critical Appraisal.
Critical Appraisal
Validity
Our in-house team of clinical epidemiologists appraises each article to identify errors and sources of bias and determine the validity of each study's results.
BEEM Experts
Clinical Applicability
Articles and critical appraisals are sent to select physicians with relevant subspecialty expertise for consensus on clinical applicability.
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Won't Get Fooled Again: TPA for CVA

Case Scenario:

78-year-old man presents to emergency department with right leg and arm weakness for the last four hours. He has a history of hypertension and dyslipidemia. His vitals are unremarkable except for a blood pressure of 165/95. A non-contrast CT head is performed that shows no acute intracranial pathology. Your stroke team asks you to administer thrombolysis and admit.

Q:

Is thrombolysis safe and effective treatment in patients who present with signs of an ischemic stroke of less than six hours duration?

BOTTOM LINE

Thrombolysis for acute stroke…I remain skeptical.

Thrombolysis for Acute Ischemic Stroke (Review)

Wardlaw JM et al. Cochrane Database Syst Rev. July 2014

P Seven randomised trials, involving 10,187 patients, with definite ischemic stroke

I Any thrombolytic agent – urokinase, streptokinase, rt-PA, recombinant pro-urokinase or desmoteplase

C Placebo

O Functional independence at long-term follow up, with safety outcomes of spontaneous intracerebral hemorrhage and death

Authors' Conclusion:

"Thrombolytic therapy given up to six hours after stroke reduces the proportion of dead or dependent people. Those treated within the first three hours derive substantially more benefit than with later treatment. This overall benefit was apparent despite an increase in symptomatic intracranial haemorrhage, deaths at seven to 10 days, and deaths at final follow-up (except for trials testing rt-PA, which had no effect on death at final follow-up)". (Wardlaw et al., 2014)

Background

Acute ischemic strokes represent the leading cause of disability in our society and the third most common cause of death. There have been many studies performed looking at thrombolysis for acute CVA.

We have covered the original 1995 NINDS article on SGEM#70.

I presented 12 major trials for thrombolysis in CVA at the Swedish National Emergency conference early this year at SweetBEEM. To summarize there were four trials stopped due to harm or futility, six showing no benefit, and only two showing benefit. This was not enough proof for me to reject the null hypothesis.

Trial	Journal	Time	Primary Benefit	Harm
MAST -Italy (n=622)	Lancet 1995	<6hr	**None**	Increased early death
ECASS-I (n=620)	JAMA 1995	<6hr	**None**	Beneift not outweigh the risk
NINDS-I (n=291)	NEJM 1995	<3hr	**None**	No difference
NINDS -II (n=333)	NEJM 1995	<3hr	~13% absolute benefit mRS at 90d	Increase ICH
MAST - Eu (n=310)	NEJM 1996	<6hr	**None**	**Stopped early due to harm**
ASK (n=340)	JAMA 1996	<4hr	**None**	**Stopped early due to harm**
ECASS-II (n=800)	Lancet 1998	<6hr	**None**	No difference
ATLANTIS-B (n=613)	JAMA 1999	3-4hr	**None**	**Stopped early *"unlikely to prove beneficial"***
ATLANTIS-A (n=142)	Stroke 2000	<6hr	**None**	**Stopped early due to harm**
ECASS-III (n=821)	NEJM 2008	3-4.5hr	7% absolute benefit	Increase ICH
DIAS-2 (n=193)	Lancet 2009	3-9hr	**None**	No difference
IST-3 (n=3035)	Lancet 2012	<6hr	**None**	No difference

Results

In evaluating 27 trials, the authors perform 39 analyses, some with multiple sub-analyses. They also tend to focus primarily on those involving rt-PA, or alteplase, as the approved and guideline-recommended therapy.

Thrombolytic therapy, up to six hours, dead or dependent – 23 trials, 9,318 participants

2679/4891 (54.7%) allocated thrombolysis vs. 2608/4427 (58.9%) allocated control

OR 0.85 (95% CI 0.78 to 0.93), with significant heterogeneity (I^2 = 39%, P = 0.03)

Results

Thrombolytic therapy, up to six hours, risk of symptomatic intracranial hemorrhage – 25 trials, 10,186 participants:

402/5372 (7.4%) allocated thrombolysis vs. 84/4814 (1.7%) allocated control

OR 3.75 (95% CI 3.11 to 4.51), without heterogeneity (I^2 = 7%)

Thrombolytic therapy, up to six hours, risk of death from all causes – 28 trials, 10,187 patients

1043/5372 (19.4%) allocated thrombolysis vs. 856/4815 (17.7%) allocated control

OR 1.18 (95% CI 1.06 to 1.30), with significant heterogeneity (I^2 = 48%, P = 0.003)

These trials included urokinase, streptokinase, and desmoteplase – and modern thrombolytic therapy is typically undertaken with alteplase, or rt-PA. How about the results for just the rt-PA trials?

rt-PA, up to six hours, dead or dependent – 8 trials, 6729 participants

1830/3372 (54.2%) allocated rt-PA vs. 1947/3357 (57.9%) allocated contro

OR 0.85 (95% CI 0.77 to 0.93), with significant heterogeneity (I^2 = 45%, p = 0.04)

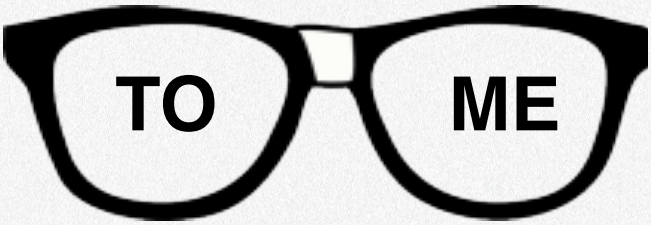
rt-PA, within 3 hours, dead or dependent – 6 trials, 1779 participants

531/896 (59.2%) allocated rt-PA vs. 603/883 (68.3%) allocated control

OR 0.65 (95% CI 0.54 to 0.80), without heterogeneity

The authors therefore lead their published abstract conclusion with the sentence: *"Thrombolytic therapy given up to six hours after stroke reduces the proportion of dead or dependent people."*

TALK NERDY TO ME



Commentary

This Cochrane Review update the 2009 version through the addition of the Third International Stroke Trial (IST-3), the largest stroke trial to date. To remind listeners, IST-3 enrolled patients up to six hours, and specifically enrolled those who were not eligible for tPA under the current European license, but where the treating clinician believed tPA was promising therapy.

A minimal initial number were enrolled double-blind, but following the approval of tPA in Europe, Boehringer Ingelheim ceased supply of the study medication. This resulted in transition to an open-label design, in which both the treating clinician and the patient were aware of treatment allocation.

This introduces several forms of bias, including alteration of the type or intensity of other initial treatment based on allocation, a placebo effect after being given the "promising" therapy, and a nocebo effect if randomized to no additional treatment.

Outcome assessments at 6 months were blinded to allocation, but many occurred via telephone or postal mail, relying on un-blinded patients or family members to report functional status. This trial is subject to substantial limitations to internal validity, and its inclusion in this updated Cochrane Review – comprising over half the total number of patients treated with thrombolytic therapy – diminishes the reliability of the analysis as a result of bias in favour of thrombolytics

The SGEM did a critical review of IST-3 on Episode#29. The bottom line from that review was treatment with tPA harmed (death) 1 in 25 early, the fatal and non-fatal bleed rate when up significantly and there was no benefit seen at 6 months in the primary outcome.

The authors appropriately note many of these threats in their reporting of potential sources of bias. Only 14 of 27 included trials met criteria for high-grade concealment. Other than IST-3, most were double-blind, placebo-controlled trials – although, the authors note saline placebo is not identical in appearance to tPA, and prolonged incidental bleeding from venipuncture or gingiva in tPA patients could serve to un-blind patients or clinicians. Blinding of follow-up assessment was only explicitly declared in seven trials, which may have resulted in clinicians aware of acute phase events performing the follow-up assessment.

We mentioned earlier that several trials were stopped prematurely as a result of safety, futility, or enrolment issues. ATLANTIS A was stopped after 142 patients due to an excess of symptomatic intracranial haemorrhage.

ATLANTIS B was stopped after 619 patients due to futility, and the authors note data has only been publicly presented on 547 of them.

ASK, MAST-E, MAST-I, and MELT were stopped early by their data monitoring committees. AUST was discontinued after slow recruitment. The authors do not acknowledge the distorting effect of early termination when weighting results for pooled analysis.

The authors also downplay the potential bias resulted to trial funding and author affiliation. They note "8/27 trials were run by companies that make the clot-dissolving drugs", but go on to state most participants come from trials funded by Government or charity sources. However, this statement is only true based on the inclusion of IST-3. The majority of trials comprising the remaining participants, including most trials evaluating tPA, were funded by Genentech and Boehringer Ingelheim. All tPA trial reports were co-authored by individuals declaring conflict-of-interest with one of the two manufacturers.

All trials were performed in specialized stroke centres, and patients were assessed by expert neurologists prior to enrolment and treatment. The generalizability of any of these findings to many practice settings is limited, and observational studies show mixed results regarding safety and rate of treatment of stroke mimics.

The simple summary of this review boils down to the reliability of the evidence, rather than the analyses of the authors. However, after nearly two decades of tPA, most clinicians' opinions are fully crystalized. Regardless of the conclusions or analyses in this article, few will change practice.

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 assessments of studies were reproducible	
The outcomes were clinically relevant	☑
There was low statistical heterogeneity for the primary outcome	
The treatment effect was large enough and precise enough to be clinically significant	

CONCLUSION VS COMMENTARY

COMPARISON

Those treated with tPA after three hours derived NO benefit, according to their analyses. Analysis 1.19 reports death or dependency at follow-up with an OR of 0.93 (95% CI 0.83 to 1.04) versus control. Therefore, even accepting the data at face value, the authors present a misleading conclusion through inappropriate partitioning of data.

Case Resolution

You reassess the patient and he seems to be improving clinically. You discuss the potential benefits and risk of thrombolysis. By now it is now over 4.5hrs and the treatment window has closed. The patient is not given tPA and admitted for further care.

This is a challenging case and we are clearly in a realm of uncertainty. There are few risk stratification and prognostic tools out there to predict outcome with tPA. But this patient is far from that idea patient population. His age, hypertension and dyslipidemia are clinical features likely increasing his chance of intracranial hemorrhage.

In these trials in a typically younger population the symptomatic intracranial hemorrhage rate was 7.4%. Just roughly estimating his chance of ICH after tPA is probably 10-12% or even higher with a corresponding increase in mortality.

His unilateral weakness is improving. Is this a transient event? It is difficulty to say so close to the onset of symptoms. Stroke mimics and TIAs also do great with tPA but they also do great without treatment. The level of disability is an important consideration. A patient with some weakness might be reasonable to expect to regain some function with rehabilitation, whereas profound hemiparesis is almost certain to be completely disabled for the remained of his life.

Many individuals will actually make the decision to take that substantial risk of bleeding in order to gain an even smaller chance of independent living. Assessment of pre-stroke functional status is also an important consideration. Then as you say this patient's presents near the end of this proposed therapeutic window. In general, and in this specific case, I would say the risks even exceed the theoretical benefits.

Clinical Application

I will continue to offer tPA, as recommended by the American Heart Association guidelines, and tacitly mandated by medicolegal consequences if not offered. The manner in which patients are provided informed consent for this therapy dramatically influences their likelihood of electing to receive treatment.

WHAT DO I TELL MY PATIENT?

Single assay troponins (high sensitivity) cannot be used as a rule out test on initial presentation for patients with symptoms onset of varying timeframes of presentation (0 - > 6 hours).

References

Wardlaw JM, Lindley RI, Lewis S. Thrombolysis for acute ischemic stroke: still a treatment for the few by the few. West J Med. 2002 May;176(3):198-9.

Guest Skeptic: Dr. Ryan Radecki
Ryan (@EMLitofNote) is an Associate Professor, Dept of Medicine, Division of Emergency Medicine at the University of Texas Medical School and founder of Emergency Medicine Literature of Note

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Achy Breaky Heart:
Colchicine for Acute Pericarditis

Case Scenario:

33-year-old woman presents to emergency department with sharp RSCP which is pleuritic in nature. Well's low and PERC negative. ECG consistent with acute pericarditis. Other lab investigations normal.

Q:

Is colchicine more effective in combination than standard anti-inflammatory therapy for acute pericarditis, than standard anti-inflammatory therapy alone?

BOTTOM LINE

Adding colchicine to usual anti-inflammatory management with GI prophylaxis prevents recurrence or refractory pericarditis symptoms with a NNT of 5. The most common side effect being diarrhea. Strict exclusion criteria limits application to uncomplicated pericarditis without systemic manifestations or evidence of elevated cardiac biomarkers (including non-specific troponitis)

A randomized trial of colchicine for acute pericarditis

Imazio et al. NEJM 2013

P 240 adult patients all diagnosed with first episode of acute pericarditis

I Colchicine (0.5– 1.0 mg) daily for 3 months in conjunction with conventional anti-inflammatories

C
1) ASA 800mg or Ibuprofen 600mg q8h for 7-10 days followed by taper for 4 weeks
2) Prednisone (0.2-0.5mg/kg) daily was given to patients with contradictions to ASA

O Incessant or recurrent pericarditis

Authors' Conclusion:

"The use of colchicine in addition to standard anti-inflammatory therapy with GI prophylaxis in the treatment of acute pericarditis reduced the rate of refractory or recurrent episodes and increased the time to recurrence when compared to placebo". (Imazio et al., 2013)

Background

Pericarditis is inflammation of the pericardium, most often from an infectious or idiopathic cause. There are also other less common etiologies like neoplastic, autoimmune, drugs, trauma and radiation.

The classic history is positional, pleuritic chest pain radiating to the trapezius muscles. The pain is worsened by lying flat and relieved sitting forward. Other historical clues would be concurrent or recent infectious symptoms, eg. low grade fever, cough, general weakness.

On exam there are two important diagnostic findings: a pericardial friction rub, and a pericardial effusion on bedside U/S.

Background

For investigations, the ECG is the diagnostic test of choice, which should show widespread ST elevation, and PR depression inferiorly and PR elevation in aVR. However, this is a very simplified description of the pericarditis ECG, and I would highly recommend listeners check out Amal Mattu's pericarditis EKG videos.

For blood tests, the WBC and CRP are insensitive and non-specific. The troponin is used to look for myocardial involvement (myopericarditis), however, with the new high-sensitivity troponins, we may be calling myopericarditis more in the future.

To summarize, there are generally 4 consensus diagnostic criteria:

1. Classic Chest Pain
2. Friction Rub
3. Effusion on Ultrasound
4. ECG Changes

Colchicine is a plant derived alkaloid that functions as a microtubule inhibitor. It comes from the autumn crocus or meadow saffron plant. It is one of the oldest anti-inflammatories and has been used to treat rheumatic diseases for about 2500 years. Traditional uses include treatment of familial Mediterranean fever, Behcet's disease and gout. Unfortunately, colchicine also has a pretty narrow therapeutic window, so you can imagine that there was quite a bit of colchicine toxicity back in the day.

For some good information as background material check out Controversial Issues in the Management of Pericardial Disease. Imazio et al Circulation 2010;121:916-928

Results

Based upon the data presented the NNT for the primary outcome to prevent the one case of recurrent or incessant pericarditis was 4.8 (95% CI 3-11). Figure 2 in the manuscript showed the Kaplan-Meier Survival Curves for freedom from incessant or recurrent pericarditis.

Kaplan-Meier survival curve is the probability of surviving in a given length of time while considering small time intervals. It is a standard way of expressing the number of subjects living for a certain amount of time after treatment from clinical trials.

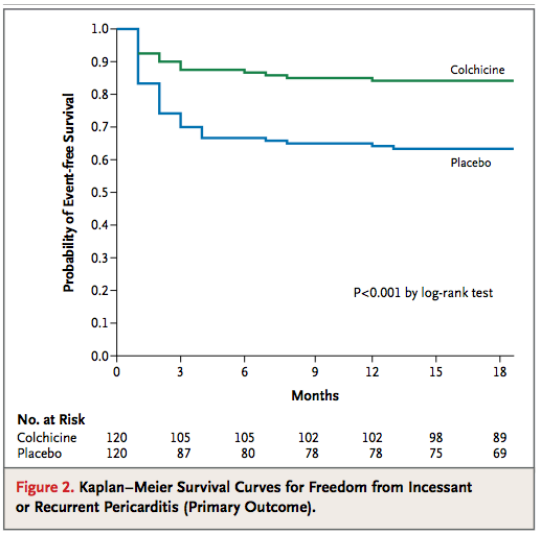


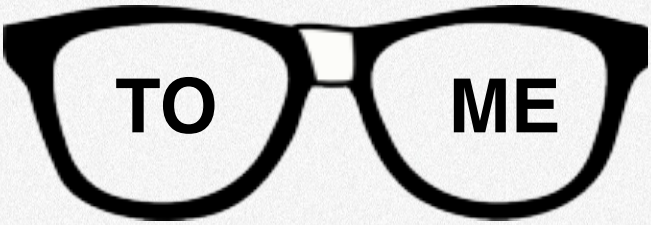
Figure 2. Kaplan–Meier Survival Curves for Freedom from Incessant or Recurrent Pericarditis (Primary Outcome).

Results

Secondary Outcomes:

- Symptom persistence 72hrs (ARR 20.8%, NNT=5)
- Recurrence frequency (ARR 31%, NNT=3)
- Hospitalizations (ARR 9.2%, NNT=11)
- Remission 1 week (ARR 26.7%, NNT=4)
- Prolonged time to first recurrence (24.7 weeks vs. 17.7 weeks)

TALK NERDY TO ME



Comments

This was a well done RCT with excellent adherence to drug regimens (95%) and no losses to follow-up. The effects of colchicine was seen early and the benefits were sustained out to 18 months. Benefits were seen both in the primary and secondary outcomes.

The authors reported a NNT of 4 but recomputed the NNT is 4.8 with 95% CI 3-11, so actual applied NNT is 5.

This paper was funded by the pharmaceutical industry, as disclosed via a non-influence statement in the article As with many RCT the study was powered to show benefit but underpowered to detect rare adverse effects.

The main side effects in both groups were gastrointestinal (GI) disturbances, and were statistically insignificant between groups (9.2% in the colchicine group, compared to 8.3% in the placebo group, P=0.67). It is possible the side effects were caused by the standard therapies (ASA, ibuprofen, corticosteroids) all despite prophylactic GI protection with proton pump inhibitor.

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 groups 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	☑

Case Resolution

This 33 year old woman diagnosed with pericarditis was given a prescription for ibuprofen 600mg TID for 7 days followed by a tapering dose over 1 month, colchicine 0.5mg daily for three months and proton pump inhibitor for 3 months. She was also referred to cardiology for on-going follow-up.

Clinical Application

Colchicine (0.5-1.0mg) daily for three months in conjunction with conventional anti-inflammatories and GI prophylaxis can be used for acute non-suppurative pericarditis to prevent recurrence or refractory symptoms

WHAT DO I TELL MY PATIENT?

You have inflammation around your heart called pericarditis. Anti-inflammatory drugs like ibuprofen and ASA can help treat your symptoms. An additional medicine called colchicine has been shown to prevent prolonged symptoms. Colchicine has also been shown to prevent pericarditis from happening again. These two type of medications can be hard on the stomach so we are going to give you something to protect your gut. The most common side effect to these effective pericarditis treatments is diarrhea.

References

1. Imazio M, Brucato A, Adler Y. A randomized trial of colchicine for acute pericarditis. N Engl J Med. 2014 Feb 20;370(8):781
2. Imazio M, Spodick DH, Brucato A, Trinchero R, Adler Y. Controversial issues in the management of pericardial diseases. Circulation. 2010 Feb 23;121(7):916-28

Guest Skeptic: Dr. Chris Bond

Chris is a Clinical Lecturer at the University of Calgary. Founder of SOCMOB blog. He is also a dogma basher, wine and food super geek.

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Let Your Back Pain Slide:
Paracetamol for Low-Back Pain

Case Scenario:

35-year-old man presents to emergency department with mechanical back pain after doing some heavy lifting on the weekend. He has no "*red flags*".

Q:

Does paracetamol improve time to recovery from pain compared to placebo in patients with low-back pain?

BOTTOM LINE

It appears that paracetamol does not improve time to recovery compared to placebo for out-patients with low-back pain.

Efficacy of paracetamol for acute low-back pain: a double blind, randomized controlled trial

Williams CW et al. Lancet 2014

P 1,652 patients from Australia and New Zealand

I Paracetamol as needed and paracetamol as regimen

C Placebo

O Time to pain free (VAS 0 or 1) maintained for 7 days

Authors' Conclusion:

"Our findings suggest that regular or as-needed dosing with paracetamol does not affect recovery time compared with placebo in low-back pain, and question the universal endorsement of paracetamol in this patient group." (Lancet et al. 2014)

Background

The leading cause of disability worldwide is low-back pain. Guidelines recommend paracetamol (acetaminophen) as the first-line agent. There have been no randomized control trials comparing paracetamol vs. placebo for low-back pain.

Results

- 550 regular paracetamol group
- 549 to the as-needed paracetamol group
- 553 to the placebo group

Was there a difference in their primary outcome of time to recovery from low-back pain? Just to remind everyone that was defined as self-reporting 0-1 on a pain VAS (pain free) for 7 days.

There was no difference in median time to recovery between the three groups. Regular 17 days (95%CI 14-19), As-needed 17 days (95% CI 15-20) and placebo 16 days (95% CI 14-20).

Results

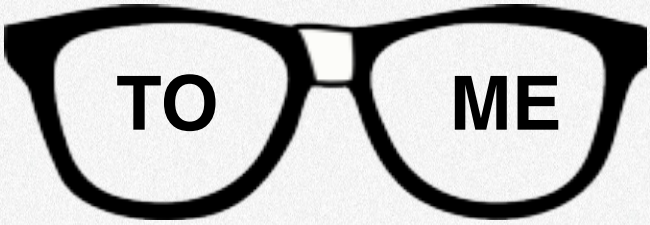
Primary Outcome: There was not a difference in their primary outcome. It took a median time of between two and three weeks for all groups to be *"pain free"* for their low-back pain.

They also expressed this as a hazard ratio (HR):
- Regular vs. Placebo HR 0.99 (95%CI; 0.87-1.14)
- As-Needed vs. Placebo HR 1.05 (95% CI 0.92-1.19)
- Regular vs. As-Needed HR 1.05 (95% CI; 0.92-1.20)

Secondary Outcomes: They looked at pain intensity, disability, function, global rating of symptom change, sleep quality, and quality of life, adherence to drug, concomitant treatment use and work absenteeism, adverse events, treatment satisfaction and patient masking.

There was no difference in these parameters. Table 3 in the manuscript details the change in secondary outcomes. They did longitudinal mixed models and did not demonstrate any differences between groups for any of the secondary outcomes.

TALK NERDY TO ME



Commentary

This is a large and well designed study which aims to see if paracetamol is an efficacious treatment for uncomplicated lower back pain with no red flags. It is important to note that the time to self reported VAS 0-1 for one week was the primary outcomes. Both as needed and a regular dosing of paracetamol does not seem to make for a more speedy recovery.

It was a very well done study but I have some concerns that 1/3 of the patients approached declined to participate. There are also issues with external validity to the ED setting. Are people who mainly present to the General Practitioners office different from those that present to the ED in Australia and New Zealand?

Naproxen was used as a rescue medication, and as this study was industry sponsored this study might later be used as support for naproxen as standard for lower back pain.

So you are not just a skeptic but you are also a cynic. But the drug company that sponsored this trial makes paracetamol so you would think the bias would be towards finding an effect?

Commentary

The lack of effect says more about the complex nature of low back pain in our society than the treatment.

When there are multiple modalities all claiming to have great effect for the same condition I am skeptical that anything really works well (medical, manipulative, non-science based, etc).

I would interpret the data saying the natural history of acute low back pain with no underlying serious pathology is a self-limiting condition. We should not expect acetaminophen to effect time to recovery in this type of situation.

There is a strong placebo effect involved in the treatment of low back pain. If the placebo effect is large and the active treatment effect is small it may be hard to distinguish the signal (treatment) from the noise (placebo).

Patients who believe in the treatment modality will more likely get benefit. So I think when it comes to treating non-serious low back pain, it all depends…

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 groups 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	☑

Clinical Application

This is just one randomized clinical trial looking into the issue and is not strong enough evidence for me to abandon recommending this treatment modality. I would like to see the study replicated in my practice environment.

Specifically, a study looking at consecutive patients presenting to the emergency department with low-back pain

CONCLUSION VS COMMENTARY

COMPARISON

Agree with their conclusions based on the data presented and encourage being skeptical of the universal endorsement of paracetamol for these types of patients.

WHAT DO I TELL MY PATIENT?

You appear to have a mechanical injury to your low-back. There are no "*red flags*" to suggest anything more serious is going on right now. The natural history of this condition is for it to resolve with or without treatment. Has anything worked well for you in the past? Different treatments have different potential benefits and harms. Taking paracetamol has not been shown to speed up how fast you get better. Most people get better within a few weeks. You should try to stay active and see your primary care doctor in a couple of weeks if the pain is not resolving. Please return to the emergency department if your pain is getting worse, you develop any of those red flags we discussed or are otherwise concerned.

References

Williams CM, Maher CG, Latimer J, McLachlan AJ, Hancock MJ, Day RO, et al. Efficacy of paracetamol for acute low-back pain: a double-blind, randomised controlled trial. Lancet. 2014 Nov 1;384(9954):1586-96.

Guest Skeptic: Dr. Pal Ager-Wick
Pal is a consultant at Legevakten in Drammen. He is also has a keen interest in everything evidence based especially ultrasound.

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Shock Through the Heart:
Ottawa Aggressive Atrial Fibrillation Protocol

Case Scenario:

A 35-year-old woman presents to the emergency department with palpitations. She states that she woke up this morning and went for a run and began feeling her heart race. She stopped and rested but her heart rate wouldn't come down and it felt irregular. This all started about 2 hours ago. Her vitals are unremarkable except that her heart rate is 140 bpm and irregular.

Q:

What is the effectiveness and safety of the Ottawa aggressive protocol to perform rapid conversion and discharge of patients with these arrhythmias?

BOTTOM LINE

The Ottawa Aggressive Protocol appears to be highly effective in converting patients with recent onset atrial fibrillation or flutter back to sinus rhythm. In this cohort of 660 patients, there were no thromboembolic events and the relapse rate was 8.6% at 7 days.

Association of the Ottawa Aggressive Protocol with Rapid Discharge of Emergency Department Patients with Recent-Onset Atrial Fibrillation or Flutter

Stiell IG et al. CJEM 2010

P 660 consecutive, retrospective cohort of ED patients presenting with a primary diagnosis of recent-onset atrial fibrillation or flutter between June 2000 – June 2005

I Ottawa Aggressive Protocol

C None

O Conversion to sinus rhythm, discharge from hospital, discharge in atrial fibrillation

Authors' Conclusion:

"The Ottawa Aggressive Protocol is effective, safe and rapid and has the potential to significantly reduce hospital admissions and expedite ED care" (Stiell IG et al. 2010)

Background

Atrial fibrillation is one of the most common dysrhythmias encountered in the ED. Patients with chronic AF often present with increased heart rates, chest pain and weakness among other presentations. There has been a debate going on for a number of years as to which is the best strategy to address these patients, rate or rhythm control. This debate has raged for years with little end in site.

Dr. Ian Stiell and colleagues published an article in 2011 in Annals looking at variation in Recent-Onset atrial fibrillation management in Canada and found a ton of variability. Rhythm control was selected in 42-85% of patients across hospitals and electricity was chosen as the primary strategy for rhythm control in 7-69%. Lots of differing opinions.

Background

In the USA there's a lot of fear of cardioversion. Actually, the fear is of cardioverting and the patient throws a clot. What happens is that a lot of patients are rate controlled, admitted and we let cardiology sort it out. With all this variability in practice, Stiell and colleagues sought to show that their protocol was both effective and safe.

Details of the Ottawa Aggressive Atrial Fibrillation protocol

1. **Assessment**
   - Stable without ischemia, hypotension or acute CHF?
   - Onset clear and less than 48 hours?
   - Severity of symptoms?
   - Previous episodes and treatments?
   - Anticoagulated with warfarin and INR therapeutic?
2. **Rate control**
   - If highly symptomatic or not planning to convert
   - Diltiazem IV (0.25 mg/kg over 10 min; repeat at 0.35 mg/kg)
   - Metoprolol IV (5 mg doses every 15 min)
3. **Pharmacologic cardioversion**
   - Procainamide IV (1 g IV over 60 min; hold if blood pressure < 100 mm Hg)
4. **Electrical cardioversion**
   - Consider keeping patient NPO × 6 h
   - Procedural sedation and analgesia given by emergency physician (propofol IV and fentanyl IV)
   - Start at 150–200 J biphasic synchronized*
   - Use anterior–posterior pads, especially if not responding
5. **Anticoagulation**
   - Usually no heparin or warfarin for most patients if onset clearly < 48 h or if therapeutic INR for > 3 wk
6. **Disposition**
   - Home within 1 h after cardioversion
   - Usually no antiarrhythmic prophylaxis or anticoagulation given
   - Arrange outpatient echocardiography if first episode
   - Cardiology follow-up if first episode or frequent episodes
7. **Patients not treated with cardioversion**
   - Achieve rate control with diltiazem IV (target heart rate < 100 beats/min)
   - Discharge home on diltiazem (or metoprolol)
   - Discharge home on warfarin and arrange INR monitoring
   - Arrange outpatient echocardiography
   - Follow-up with cardiology at 4 wk for elective cardioversion
8. **Recommended additions to protocol**
   - Consider transesophageal echocardiography if onset unclear
   - Alternate rhythm-control drugs: propafenone, vernakalant, amiodarone
   - If TEE-guided cardioversion > 48 h, start warfarin
   - If $CHADS_2$ score ≥ 1, consider warfarin and arrange early follow-up

CHF = congestive heart failure; INR = international normalized ratio; IV = intravenously; NPO = nil per os (nothing by mouth); TEE = transesophageal echocardiography.*Most patients treated with electrical cardioversion in the current study were managed with monophasic cardioversion.

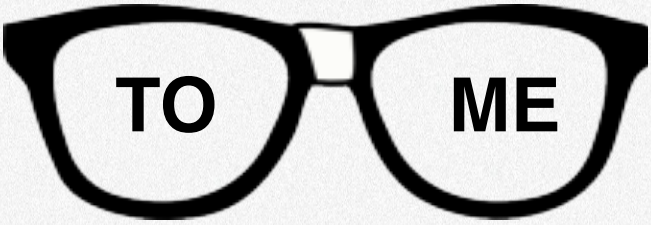
Ottawa Aggressive Atrial Fibrillation Protocol

Once the patient is assessed and it's determined that their symptoms began <48 hours prior to presentation, they were entered into the protocol. Rate control was given if either the patient was highly symptomatic while awaiting cardioversion or if cardioversion was not going to be pursued. Rhythm control was then initiated with an infusion of procainamide 1000 mg over 60 minutes. If procainamide worked, great the protocol was completed. If it didn't work, the patient moved on to electrical cardioversion. Chemical cardioversion was skipped in patients who were unstable or they had a history of AF with failure of procainamide. They then go on to discuss anticoagulation and disposition.

Results

1. 660 patients recruited
2. 95.2% with atrial fibrillation, 4.9% with atrial flutter
3. Procainamide conversion rate was 58.3%
4. Of the 243 patients who underwent electrical cardioversion, 91.7% success rate
5. 96.8% of patients were discharged home and 93.3% of them were in sinus rhythm upon discharge.
6. Adverse events were seen in 7.6% and there were no cases of torsades de pointes or CVA or death.
7. Median LOS: 4.9 hours. 3.9 hours in those converting with procainamide, 6.5 hours in those requiring electrical cardioversion.

TALK NERDY TO ME



Commentary

Does this Change What We Do? It is hard to say. I still think at least in the US, there's a lot of concern about converting someone and throwing an embolism. There was a recent letter in JAMA that questioned whether the cutoff for cardioversion should be 48 hours or 12 hours. They found that the risk of thromboembolic event was 0.3% in the group converted at < 12 hours and 1.1% from 12-48 hours.

Even though this rate is still quite low, it's probably higher than we'd like to see. It is important to note that in patients with 3 weeks of anticoagulation who are then cardioverted, the thromboembolic rate is still up to 0.8%. I know this was plastered all over Social Media when it came out and Ian Stiell himself said that his group is looking into these numbers as this may change recommendations.

Aside from the limitation of thromboembolic phenomena, I think many US EPs would rather defer the procedure, along with the procedural sedation, to the cardiologists and inpatient guys. But I think this is the wrong reason to not cardiovert. The other day, we had a young guy come in with recent onset AF of about 2 hours and we had him sedated and cardioverted within 15 minutes. It just doesn't take that long to do this.

It is these controversial issues in medicine that often teach us the most. When there is no clear answer on what is the best approach it makes us think even harder. New onset rapid atrial fibrillation is one of those areas.

We all want to give the best care to patients based on the best evidence. However, sometimes the best evidence is weak. This is truly a "classic" example of…we need more information. Until we have that more definitive study it motivates us to know both sides of the argument. To understand why some evidence supports rate control and other evidence supports rhythm control as an optimal strategy.

Remember that evidence based medicine is not just about literature. EBM was originally defined as the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients. The literature is just one part of EBM. It also involves clinical expertise and the patient's unique situation and personal values. It is where these three important things over lap that you get the "best" care.

EBM is about increasing patient's choices not decreasing choices. And this is done using shared decision-making. So ultimately, the EBM answer to any clinical question, as my mentor Dr. Anderw Worster taught me so well is…it all depends.

Case Resolution

You discuss the options with your patient and she elects for chemical cardioversion. After the administration of procainamide, she is still in atrial fibrillation. She then elects for electrical cardioversion. You perform procedural sedation and convert the patient with 150J biphasic and she converts to sinus rhythm. 1 hour after the procedure, you discharge home for follow up with your local cardiologist.

References

1. Stiell IG, Clement CM, Brison RJ, Rowe BH, Borgundvaag B, Langhan T, et al. Variation in management of recent-onset atrial fibrillation and flutter among academic hospital emergency departments. Ann Emerg Med. 2011 Jan;57(1):13-21.

2. Stiell IG, Clement CM, Perry JJ, Vaillancourt C, Symington C, Dickinson G, et al. Association of the Ottawa Aggressive Protocol with rapid discharge of emergency department patients with recent-onset atrial fibrillation or flutter. CJEM. 2010 May;12(3):181-91.

Guest Skeptic: Dr. Anand Swaminathan
Anand (@EMSwami) is the Assistant EM program director at NYU/Bellevue Hospital.

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Preventing Falling to Pieces

Case Scenario:

84-year-old woman who lives independently and alone in her own home presents via ambulance with a standing level fall. She was bending over, lost her balance and hurt her left, non-dominant arm. The x-ray of her left shoulder is negative for any fracture. The daughter-in law arrives to take her home, but asks if Mrs. C is at risk for further falls in the future.

Q:

Can healthcare personnel accurately identify subsets of geriatric adults at increased risk of falls or injurious falls in the months following an episode of emergency department care?

BOTTOM LINE

Persons 65 years or older are an increasing percentage of the total population. These people fall, get injured and even die. We do not have good ED evidence to help us predict accurately or reliably who is at risk of falling. High quality research is need for healthcare providers, funders, and guideline developers to use in deriving screening protocols.

Predicting Geriatric Falls Following an Episode of Emergency Department Care: A Systematic Review

Carpenter, CR. Acad Emerg Med 2014

P Community-dwelling, non-critically ill geriatric adults after an episode of ED care

I Fall and injurious falls risk stratification at 1- to 6-months evaluated in ED settings

C None

O Prognostic accuracy (sensitivity, specificity, likelihood ratios) for individual risk factors and prediction instruments to predict falls in the months following an episode of ED care

Authors' Conclusion:

"Our findings suggest that regular or as-needed dosing with paracetamol does not affect recovery time compared with placebo in low-back pain, and question the universal endorsement of paracetamol in this patient group." (Lancet et al. 2014)

Background

In the geriatric population (all those over age 65), standing level falls are the #1 cause of traumatic mortality.

A fall can be defined as an unintentional, sudden descent to a lower level. This can be a fall from a bed or chair to the ground or down some stairs to a lower level of the home. In the vast majority of cases, we are not talking about falls from roofs or ladders.

For community dwelling adults over the age of 65 about 1/3 will suffer a standing-level fall. By the time you people reach 80 years of age that increases to half or 50%. Many of these people who fall end up in the ED.

These falls cause a lot of morbidity. They can cause contusions, lacerations and fractures. Fractures can obviously be any bony structure, but commonly include the spine, hip, pelvis, ankle, wrist and humerus. There are about 300,000 hip fractures every year in the US and by 2014 will probably have doubled.

These injuries must cost a lot of health care dollar. In the USA standing-level falls cost about $19 billion a year.

As mentioned earlier, falls are the leading cause of traumatic mortality in this age group. Older adults who are admitted to the hospital after a fall (the sickest subset) will be readmitted to the hospital within one-year in 44% of cases and 33% will die within one-year.

Results

601 manuscripts with five papers met the inclusion criteria for a full review. Two articles did not include data to do a 2×2 table. This left you three ED-based studies with 767 patients.

Two of the studies were prospective (660 patients) and one was retrospective (107). The two prospective studies contained 29 individual predictors. These predictors included past falls, number of medications used, self-reported dementia or depression, use of canes or walkers, ability to drive, sense of imbalance, and many others, as well as simple objective physical tests like the chair stand, chair sit, ability to raise feet while walking and turn 180º, and visual and auditory acuity.

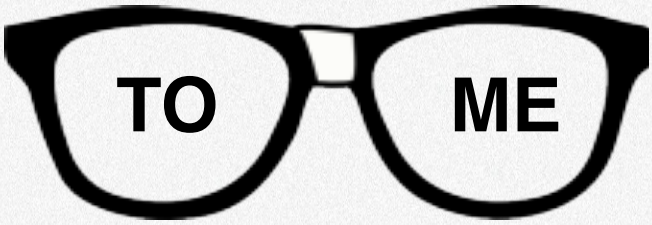
The incidence of falls at 6 months was 31% for those who presented with a chief complaint of falls. The incidence of falls was about half (14%) if the chief complaint was something else.

The best positive likelihood ratio (+LR) was found in one of the two studies and had a result of 6.55 (95% CI 1.41-30.38). However, when that was combined in the meta-analysis gave a +LR of 2.54 (95% CI 1.62-3.98). The best negative likelihood ratio (-LR) was if the patient could cut their own toenails –LR 0.57 (95% CI 0.38-0.86).

We described the Tiedemann and Carpenter fall-risk prediction instruments. Both instruments use a simple scoring system based upon two to four fall-risk factors. A Tiedmann score of three had a +LR 3.76 and a –LR 0.46 In contrast, the Carpenter score of >1 gave a similar +LR score, but proved much more useful to distinguish subsets at lower risk of falls with –LR of 0.11.

We opine that *"although our results fail to provide a definitive fall screening strategy, the quantitative summary estimates of fall incidence and risk factor accuracy and reliability provide an evidence basis on which clinicians, nursing leaders, administrators, educators, policy-makers, and researchers can build."*

TALK NERDY TO ME



Commentary

Clearly there is a need to figure out who is a greater risk in this geriatric population. These types of falls cause significant morbidity/mortality, cost a lot of money, and we simply lack the resources to treat every older adult as high-risk for future falls.

Risk assessment in aging adults is advocated by multiple professional organizations and licensing bodies. Nonetheless, geriatric patients rarely receive guideline directed care for falls following an episode of ED care

Multiple barriers exist between contemporary ED management of community-dwelling senior citizens and optimal injurious falls prevention. The first and most prominent obstacle is the lack of ED-validated risk stratification instruments to distinguish low-risk from non-low-risk for falls. If we cannot identify the "at-risk", how can we efficiently and cost-effectively proactively work to prevent future falls? Funding agencies need to recognize this conundrum, too.

Systematic Review 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 assessments of studies were reproducible	☑
The outcomes were clinically relevant	☑
There was low statistical heterogeneity for the primary outcome	
The treatment effect was large enough and precise enough to be clinically significant	☑

There are some non-EM guidelines committees and prominent funding agencies opine that fall-risk stratification risk factors and instruments from office-based settings, hospital wards, and nursing homes ought to extrapolate to the ED. However, evidence based medicine proponents argue that validation in the ED is essential. The current meta-analysis from the Academic Emergency Medicine Evidence Based Diagnostics series takes an essential first step toward this objective.

One limitation of this study was its English only search. This was due to lack of funding resources. The English search did identified 601 abstracts to review. Dr. Carpenter attended the International Association of Gerontology and Geriatrics meeting in Seoul Korea in June 2013. This meeting brought together the world's medical and non-medical experts in the care of an aging population. He sought expertise in ED-based falls prevention, cognitive assessment, frailty, and functional vulnerability during my week in Korea. Dr. Carpenter also serves as the Chair of the American College of Emergency Physicians Geriatric Section and is the founding member of the International Consortium for Emergency Geriatrics. Based upon these exposures and leadership positions, he is not convinced that there is a novel EMERGENCY DEPARTMENT based fall-risk stratification protocol somewhere else in the world.

Case Resolution

This lovely 84yo woman (who was my grandmother in 1995) is treated conservatively for her minor contusions and is discharged home with her daughter-in law. She is advised to follow- up with her PCP in the next week and return to the ED if she has increasing pain, decreasing function or is otherwise concerned. Of concern, Sirois et al noted that 15% of these patients (community dwelling geriatric standing level fall, discharged home from the ED with minor injuries) will experience significant functional decline at 3-months

Clinical Application

ED-based fall-risk screening for older adults should use the most accurate risk-stratification instruments available until better tools are developed and validated in ED settings. Using other instruments like STRATIFY or HENDRICH II in the ED leaves clinicians, patients, payers, and policy-makers without valid, evidence-based estimates of post-ED fall risk. Funding agencies and researchers should more aggressively pursue more definitive and clinically useful fall-risk stratification.

WHAT DO I TELL MY PATIENT?

Standing level falls are very common and can even cause death in people over age 65. There is about 1/3 chance your mother-in law will fall again in the next 6 months. Unfortunately, there is no single fall risk factor that we know of that can predict who will or will not fall. However, there is some information I can give you to try and prevent another fall

References

1. Carpenter CR, Avidan MS, Wildes T, Stark S, Fowler SA, Lo AX. Predicting geriatric falls following an episode of emergency department care: a systematic review. Acad Emerg Med. 2014 Oct;21(10):1069-82.
2. Sirois MJ, Emond M, Ouellet MC, Perry J, Daoust R, Morin J, et al. Cumulative incidence of functional decline after minor injuries in previously independent older Canadian individuals in the emergency department. J Am Geriatr Soc. 2013 Oct;61(10):1661-8.

Guest Skeptic: Dr. Chris Carpenter
Chris (@SAEMEBM) is an Associate Professor (Emergency Medicine), Washington University and author of the book Diagnostic Testing and Clinical Decision Rules.

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Hunting High and Low:
Best MAP for Sepsis Patients

Case Scenario:

A 74-year-old man is brought by EMS for altered level of consciousness. The ECG shows sinus tachycardia and portable CXR demonstrates right lower lobe infiltrate. You start Early Goal Directed Therapy (EGDT) by rapidly recognized this man is septic, provided IV fluids and appropriate IV antibiotics for pneumonia. Now you are starting to think about more fluids +/- vasopressors to increase his Mean Arterial Pressure (MAP)

Q:

Does a MAP of 80-85mmHg decrease 28 day mortality as compared to a MAP of 65-70mmHg?

BOTTOM LINE

The ideal target MAP in septic shock is still unclear – patient factors play a role and care should likely be individualized.

High versus Low Blood Pressure Target in Patients with Septic Shock

Asfar et al. NEJM 2014

P 776 patients >18y with septic shock refractory to fluids who required vasopressors at >0.1mcg/kg evaluated within 6h of initiation of vasopressors

I Target MAP of 80-85 mmHg for max of 5 days

C Target MAP 60-70 mmHg for max of 5 days

O Death from any cause at 28 days

Authors' Conclusion:

"No significant difference between the two groups in the overall incidence of serious adverse events" (Arsaf et al. 2014)

Background

Sepsis remains a major contributor to ED morbidity, carrying a short-term mortality of approximately 20% (ProCESS). With approximately 750,000 annual cases in the US, recognition and early treatment of severe sepsis and septic shock has become a pillar of Emergency Medicine.

Sepsis can be defined as a "*clinical syndrome complicating severe infection characterized by inflammation remote from the site of infection. Dysregulation of the inflammatory response can lead to multiple organ dysfunction.*"

There is a continuum of sepsis ranging from SIRS (Systemic Inflammatory Response Syndrome) to septic shock.

- SIRS – temperature <36 or >38'C, HR >90 RR >20 (or PaCO2 <32mmHg), WBC <4 or >12, or >10% immature forms
- Sepsis – 2/4 SIRS criteria + infection.
- Severe sepsis – Sepsis + hypotension end organ failure
- Septic shock – Sepsis and hypotension refractory to fluid treatment

Background

Mean Arterial Pressure (MAP) is he average arterial pressure during a cardiac cycle, represents the perfusion pressure seen by the organs/tissues. MAP = (CO x SVR) + CVP, or estimated by MAP = 2/3 Diastolic BP + 1/3 Systolic BP (inaccurate if tachycardic).

Sepsis management involves early recognition with early intervention. Rapid administration of broad spectrum antibiotics (then titrating to pathogen), and a sequential approach to fluid administration to CVP targets, vasopressor administration to MAP targets, and PRBC transfusion to hematocrit and ScvO2 targets has resulted in marked improvements in survival. Recent studies (ProCESS) have indicated that invasive blood pressure monitoring may not be required, as previously thought.

There is a hypothesis that a higher MAP may be better than a lower MAP. Dunser et al (2009) found in a retrospective cohort study that MAP below 75mmHg were associated with increased need for renal replacement therapy. Badin et al (2011) found in a prospective cohort study that in patients presenting with septic shock and renal impairment at baseline, MAP targets of 72-82mmHg resulted in less AKI at 72h.

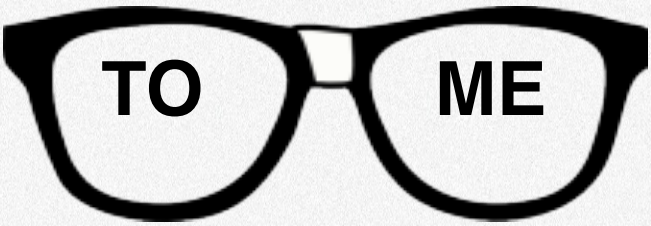
Results

No significant difference in the primary outcome between the groups for mortality at 28 days. The mortality rate for the High MAP was 36.6% vs. 34.0% for the Low MAP target. This gave a Hazard Ratio of 1.07 (95% CI 0.84-1.38; p=0.57)

There were 776 patients enrolled in this study. They determined their sample size of 800 patients assuming a death rate of 45%. This was to provide a power of 80% to show a 10% difference in the primary outcome (death at 28 days) with a two sided alpha level of 0.05.

There were also no differences detected in the secondary outcome of mortality at 90 days. High 43.8% vs. Low 42.3% HR 1.04 (95%CI 0.83-1.3; p=074). No differences were found in serious adverse events. High 19.1% vs. Low 17.8%

TALK NERDY TO ME



Commentary

Overall, this was a high quality study looking at a clinically relevant topic. It was good to try and stratify patients based on hypertension. However, the authors noted the challenge in determining patients' baseline blood pressures. This is important as it may indicate patients who have auto-regulated to a higher baseline MAP, and therefore require a higher MAP in treatment of sepsis to perfuse end-organs.

Commentary

Lack of clinician blinding is a threat to validity, but unfortunately cannot be overcome in this type of study. The MAP values exceeded the targets in both groups, but were still significantly different. A large number of patients excluded were excluded from the study. Many they did not get to in less than six hours. Was there any trend in the excluded patients that could have resulted in study bias?

More than 80% of patients in both groups received steroids. This is different from clinical practice in Canada. In addition, approximately 7% of patients in both groups received Protein C.

Mortality rate was different in this study compared to the ProCESS trial and the original Rivers study. The higher mortalities across groups seen in this French study compared with ProCESS may be because of different infection profiles at inclusion.

The inclusion of ICU patients in this Asfar study (presumably patients who have already identified themselves as "sick") could also contribute to the increased mortality. In addition, ProCESS sample was younger, with a larger female proportion. Unfortunately baseline comorbidity scores differed between studies and cannot be used to compare the samples directly.

	Asfar		Rivers		ProCESS		
Infection Source	Lo BP	Hi BP	Std Tx	EGDT	EGDT	Std Tx	Usual care
Lung	51.5	52.1	39.5	38.5	31.9	34.1	33.1
Abdominal	17.3	16.8	Peritonitis – 4.2 Surgical Intra-abdominal process – 5.9	Peritonitis – 3.4 Surgical Intra-abdominal process – 7.7	15.7	12.8	11.2
Urinary Tract	11.3	11.3	27.7	25.6	22.8	20.2	20.6
Other	18.8	18.6	---	---			
Community Acquired	65.2	67.5	---	---			
Abscess of arms/legs	---	---	0.8	1.7	Skin/soft tissue - 5.7	Skin/soft tissue -7.4	Skin/soft tissue -8.3
Unknown source	---	---	---	---	13.0	10.5	14.5
Catheter-related	---	---	---	---	2.5	3.6	2.4
CNS	---	---	---	---	0.7	0.7	0.9
Endocarditis	---	---	---	---	0.2	0.7	0.7

Commentary

In patients with hypertension, higher MAP resulted in less renal injury and need for renal replacement therapy. Results suggest that other than an increased risk of atrial fibrillation in the high MAP group there is no significant difference.

Considering the clinical picture is important in determining target MAP. Patients with uncontrolled hypertension at baseline will require higher MAPs to maintain end organ perfusion. These results suggest that perhaps there is not an ideal target MAP and support clinical practice of adjusting MAP to target end organ perfusion.

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 groups 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	☑

Case Resolution

The patient receives 4 litres of normal saline in the emergency department. His resuscitation also includes non-invasive positive pressure ventilation, a central line and levophed to support blood pressure. He is then admitted to the ICU for ongoing critical care.

Clinical Application

Reasonable to consider MAP above 65mmHg depending on the case.

WHAT DO I TELL MY PATIENT?

It looks like you have a serious infection. We are going to give you intravenous fluids, increase your blood pressure with medication if needed, provide broad-spectrum antibiotics, monitor your response to treatment and admit you to the hospital for further care.

References

1. Dunser MW, Takala J, Ulmer H, Mayr VD, Luckner G, Jochberger S, et al. Arterial blood pressure during early sepsis and outcome. Intensive Care Med. 2009 Jul;35(7):1225-33.

2. Asfar P, Meziani F, Hamel JF, Grelon F, Megarbane B, Anguel N, et al. High versus low blood-pressure target in patients with septic shock. N Engl J Med. 2014 Apr 24;370(17): 1583-93.

CONCLUSION VS COMMENTARY

COMPARISON

Agree that this study does not demonstrate a 28 day mortality advantage of a higher targeted MAP in patients with septic shock undergoing resuscitation.

Guest Skeptics: Dr. Erin Brennan and Dr. Stuart Douglas
Residents in Emergency Medicine at Queen's University

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CT Angiography:
Cerebrovascular Injury Detection in Trauma Patients

Case Scenario:
21-year-old man loses control of his snowmobile and presents to a small rural hospital with a head and neck injury. His vital signs are stable. Glasgow Coma Scale=7. He is moving all extremities. There is a $C_{3/4}$ fracture identified on xray. He is intubated at the rural hospital and transferred to you at the trauma centre.

Q:

Is CT angiography accurate for detecting blunt cerebrovascular injury?

BOTTOM LINE

Blunt cerebrovascular injury is an uncommon but dangerous injury to miss. Unfortunately, the current best test to confirm the problem remains one that is onerous to perform and not as widely available as CT.

Diagnostic Accuracy of Computed Tomography angiography for Blunt Cerebrovascular Injury Detection in Trauma Patients: A Systematic Review and Meta-analysis

Roberts et al. Ann Surg 2013

P Patients >16 years after blunt trauma with suspected blunt cerebrovascular injury based on risk factors or clinical signs. N = 1426 patients presenting to United States trauma centres

I CT angiography (CTA) of carotid and vertebral arteries

C Digital subtraction angiography (DSA) of carotid and vertebral arteries

O Summary diagnostic accuracy of CTA compared to DSA for blunt cerebrovascular injury

Authors' Conclusion:

"Existing evidence suggests that the diagnostic performance of CTA varies considerably across studies, likely due to an implicit variation in diagnostic threshold across trauma centers. Moreover, although CTA appears to lack sensitivity to adequately rule out BCVI, it may be useful to rule in BCVI among trauma patients with a high pretest probability of injury." (Roberts et al., 2013)

Methods

Eight studies with a total 5704 carotid or vertebral arteries in 1426 trauma patients were included.

Pool results for blunt cerebrovascular injury detection with CTA vs. digital subtraction angiography

Key Results

- Sensitivity 66% (95% CI 49-79%) I2 =80 (lots of heterogeneity)
- Specificity was 97% (95% CI 91-99%) I2=94
- +LR was 20 (95% CI 6.9-58.4) I2=88
- -LR was 0.35 (95% CI 0.22-0.56) I2=75

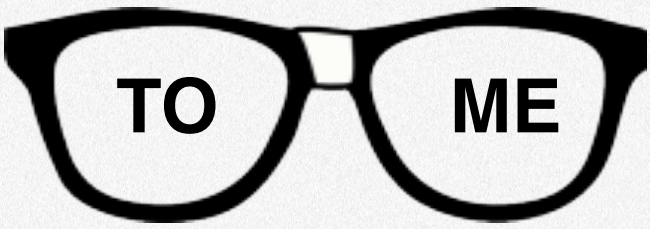
Likelihood Ratios (LRs)

Positive LRs	Negative LRs
>10 = Diagnostic	< 0.1 = Diagnostic
5 – 10 = Strong	0.1 – 0.2 = Strong
2 – 5 = Moderate	0.2 – 0.5 = Moderate
1.1 – 2 = Weak	0.5 – 0.9 = Weak
1 = No Effect	1 = No Effect

LRs assess the value of a diagnostic test

Positive test result (+LR) = sensitivity/(1-specificity)
Negative test result (-LR) = (1-sensitivity)/specificity

TALK NERDY TO ME



Commentary

This was a well-performed SR/MA. However, most of the studies included had unclear blinding. There was also a problem with heterogeneity was in all the measures between studies. Sources of heterogeneity might include who was reading the CTA, CT modality (16 or fewer slices), or diagnostic threshold variability between studies.

This study discussed likelihood ratios for diagnostic value of the test. If you have a LR of 1 it means no effect. However, if you have a +LR of >10 it is highly diagnositic for ruling in the condition. If you have a –LR of <0.1 it is highly diagnostic of ruling out the condition.

Commentary

This review shows diagnostic accuracy of CTA for blunt cerebrovascular injury varies across institutions. While the pooled -LR was inadequate to rule-out blunt cerebrovascular injury at 0.35. This is greater than the <0.10 to feel confident about ruling out a condition.

On the other hand, the +LR of 20 warrants consideration in ruling in the injury for those with high pre-test probability. Further study with a standard diagnostic threshold is required.

If ultimately deemed to be specific enough, CTA will allow testing for an easily missed but devastating injury without resorting to a cumbersome and time- consuming procedure. However, this review will not be the last word on the matter.

Case Resolution

You have a high pre-test probability this man has a blunt cerebrovascular injury. You get a CT angiography which is negative. A digital subtraction angiography is performed and demonstrates a blunt cerebrovascular injury. He is sent to the appropriate referral service to address this rare but critical injury

CONCLUSION VS COMMENTARY

COMPARISON

We agree there is significant variability in the sensitivity of CTA for blunt cerebrovascular injury across institutions, a conclusion that, on its own, warrants further study to confirm why this is the case.

Systematic Review Quality Checklist

The diagnostic question is clinically relevant with an established criterion standard	☑
The search for studies was detailed and exhaustive	☑
The methodological quality of primary studies were assessed for common forms of diagnostic research bias	☑
The assessments of studies were reproducible	☑
There was low heterogeneity for estimates of sensitivity or specificity	
The summary diagnostic accuracy is sufficiently precise to improve upon existing clinical decision making models	

WHAT DO I TELL MY PATIENT?

We are uncertain whether a CT scan of the blood vessels in your head and neck will confidently exclude significant injuries. For the time being, if you've suffered a serious head or neck injury, it's better to be at a trauma centre with an interventional radiologist who can perform the more invasive and time-consuming test to exclude these injuries. However, if an interventional radiologist is unavailable and a CT angiogram demonstrates a significant injury, we will consult the surgeons immediately.

References

Roberts DJ, Chaubey VP, Zygun DA, Lorenzetti D, Faris PD, Ball CG, et al. Diagnostic accuracy of computed tomographic angiography for blunt cerebrovascular injury detection in trauma patients: a systematic review and meta-analysis. Ann Surg. 2013 Apr;257(4):621-32.

Guest Skeptic: Dr. Marcel Emond
Associate Professor, Laval University
Emergency Physician, Level one trauma centre in Quebec City
Research Director of the Canadian Emergency Team Initiative

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ARISE Up, ARISE Up:
EGDT vs. Usual Care for Sepsis

Case Scenario:

62-year-old man sent from a nursing home with a three day history of a productive cough, intermittent fevers and today is a bit confused. The transfer notes include a history of congestive heart failure, COPD, hypertension, type-2 diabetes, and mild dementia. His vital signs are: Temp 39.1C, heart rate 103, blood pressure 115/100, respiratory rate 26, Oxygen saturation Sat 92% and a normal blood sugar.

Q:

Does an emergency department patient with septic shock need aggressive EGDT or "*usual*" resuscitation?

BOTTOM LINE

Invasive EGDT-based sepsis resuscitation is not required compared to early recognition and liberal IV fluid resuscitation and empiric antibiotics in the septic patients.

Goal-Directed Resuscitation for Patients with Early Septic Shock.

The ARISE Trial. NEJM 2014

P Adults <18yo presenting to ED with 6h of suspected/confirmed infection, 2+ SIRS criteria, and evidence of refractory hypotension or hypoperfusion

I Full EGDT provided by a trained study team using a standardized EGDT delivery protocol

C "*Usual*" care as per physician discretion. Use of SCVO2 not allowed.

O All-cause death at 90 days

Authors' Conclusion:

"In critically ill patients presenting to the emergency department with early septic shock, EGDT did no reduce all-cause mortality at 90 days."

Background

Suneel's Five Key Points of Sepsis Care

1. Recognize sepsis early
2. Broad spectrum antibiotics
3. Fluid resuscitation
4. Lactate levels
5. Transfer to appropriate care

Results

All groups were well balanced and similar. In this case the demographic and clinical characteristics nearly identical in both cohorts (EGDT n=796, usual care n=804).

No Significant Differences:

- IV fluid volumes given in both arms (avg 2.5L)
- Randomization times (avg. 2.7hrs after ED arrival),
- Mean time to antibiotics (avg 70min; lungs & urinary most common sites of origin)
- Positive blood culture rates (38% both groups).

Significant Differences:

- More ICU admissions in EGDT group (87%) vs usual care (76.9%),
- More fluid given in first 6hrs in EGDT arm (diff approx 250cc),
- Vasopressors 66.6% EGDT vs usual care (57.8%),
- Blood transfusion (13.6% EGDT vs 7.0% usual),
- Dobutamine (15.4% vs 2.6%),

Primary Outcome

NO SIGNIFICANT DIFFERENCE

90 day all-cause mortality (EGDT 18.6% vs usual 18.8%), nor survival time

Secondary and Tertiary Outcomes:

- ED length of stay shorter in EGDT (1.4hrs) vs. usual care (2.0hrs)
- Vasopressor use EGDT (76.3%) vs. usual (65.8%),
- No difference mean vasopressor infusion times.
- No other significant differences in secondary or tertiary outcomes.
- No difference in adverse event rates (7.1% EGDT vs. 5.3% usual).

Commentary

This was a very well done study with very good methods. They had good randomization, multi-center and multi country. They did intention to treat analysis. There was >99% follow for both groups. Planned safety analysis at 50% enrolment. This was reviewed by a independent data and safety monitoring committee.

Only obvious and unavoidable issue was they were unable to blind physicians and patients due to nature of interventions. However, we feel that this would have favored EGDT and only strengthens the result accepting the null hypothesis of no superiority.

No clinically relevant differences in all primary, secondary or tertiary outcomes (although some are statistically different).

There have been some other great reviews of the ARISE trial:

- Intensive Care Network, The Bottom Line and EMCrit with Scott Weingart

Case Resolution

Having recognized the sepsis potential of this patient and confirming a high lactate, you initiate broad spectrum antibiotics for what is most likely a clinical pneumonia. You give aggressive fluid resuscitation with IV normal saline or ringers lactate. Then call your consultant to arrange admission to the intensive care unit.

CONCLUSION VS COMMENTARY

COMPARISON

We agree there is significant variability in the sensitivity of CTA for blunt cerebrovascular injury across institutions, a conclusion that, on its own, warrants further study to confirm why this is the case.

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 groups 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 lots of IV fluids, broad spectrum antibiotics and admit you to the hospital.

References

Investigators A, Group ACT, Peake SL, Delaney A, Bailey M, Bellomo R, et al. Goal-directed resuscitation for patients with early septic shock. N Engl J Med. 2014 Oct 16;371(16):1496-506.

Guest Skeptic: Dr. Suneel Upadhye
Associate Clinical Professor, McMaster University
Associate Member Department of Clinical Epidemiology and Biostatistics
Chair Canadian Association of Emergency Physicians Standards Committee

93

Ketamine: A Bad Reputation?

Case Scenario:

During the primary survey, you observe that the patient is not protecting his airway with a GCS of 6. You prepare for a rapid sequence intubation prior to the patient getting a CT scan. You ask your ED pharmacist to prepare ketamine 2 mg/kg IV and succinylcholine 1.5 mg/kg for intubation.

Q:

Does ketamine raise intracranial pressure and adversely affect cerebral perfusion pressures, neurologic outcomes, or mortality compared with other intravenous induction agents commonly used to intubate adult patients in the emergency department?

BOTTOM LINE

Ketamine seems to be a reasonable alternative agent for patients requiring RSI in the ED. Evidence to show that ketamine has negative effects on neurologic outcomes is weak and has been extrapolated from non-ED patients. This systematic review found no compelling evidence that ketamine worsens ICP, CPP, or neurologic outcomes as measured.

The Effect of Ketamine on Intracranial and Cerebral Perfusion Pressure and Health Outcomes: A Systematic Review

Cohen et al. Ann Emerg Med. 2014

P 10 studies with 953 patients at least 16 years of age either intubated prior to or at the point of data collection

I Ketamine (either by bolus or infusion)

C Any other sedative drug that might be used for RSI in the ED

O Primary outcomes were measures of ICP/CPP; secondary outcomes included neurologic outcomes, ICU LOS and mortality

Authors' Conclusion:

"The available data suggest that ketamine does not adversely affect intracranial or cerebral perfusion pressures, neurologic outcomes, or mortality compared with other intravenous induction agents commonly used to intubate adult patients in the ED" (Cohen et al., 2014)

Background

Ketamine is an NMDA receptor antagonist that exerts sedative, amnestic, and analgesic effects as a dissociative anesthetic. It can be used as an induction agent for rapid sequence intubation in the ED, and has relatively stable hemodynamic effects, especially when compared with other agents such as midazolam, propofol, or the ultra-short acting barbiturates. Despite this, the use of ketamine for RSI among ED physicians is low.

ED physicians have been reluctant to use Ketamine. We have been warned not to use it in certain situations. One concern is that it could raise intracranial pressure.

Ketamine's *bad reputation* comes from several small case-control series from approximately 30-40 years ago that suggested that ketamine increases ICP through sympathetic stimulation. These case-control series evaluated patients with intracranial pathology including space-occupying lesions or obstructive hydrocephalus, and were not necessarily representative of the majority of ED patients.

Up until just recently, etomidate may have been regarded by emergency physicians to be the induction agent of choice in RSI. However, it too now has a *bad reputation*. There are concerns about adrenal suppression (in the setting of sepsis) and acute lung injury (in the setting of trauma).

Results

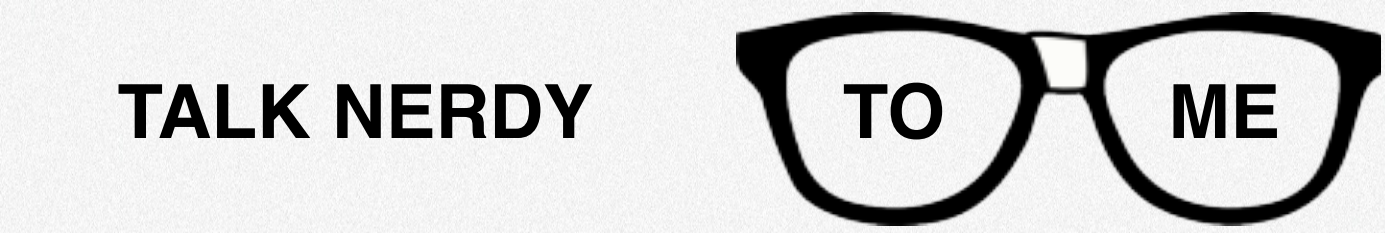
Data was available on 168 of the included 953 patients regarding ICP and/or CPP. The populations and designs in these studies were too heterogeneous to pool the results; however examination of many of these studies showed that there were no differences in ICP or CPP between ketamine and the control group.

Two studies showed a small decrease in ICP in the ketamine group compared to the control group immediately post-dose, but that turned into an increased ICP at 30 minutes in one of the studies. One study reported an increase in ICP measurements after prolonged infusions of ketamine, and another reported an increase in ICP after bolus doses of ketamine, but statistical significance was not reported-this study evaluated patients with space-occupying intracranial lesions or obstructive hydrocephalus..

Four of the five clinical trials included in this analysis had a measurement of neurologic outcome. All measurements were too heterogeneous to perform any pooled analysis.

The largest study (n=655), by Jabre and colleagues, used GCS as a primary outcome and found no differences between the ketamine and control groups.

Other smaller studies found no differences with respect to GCS at ICU discharge or scores on neuropsychometric testing. Two trials reported mortality data (total of 680 patients) as a secondary outcome and found no significant differences between groups.



Commentary

The authors in this study set out to evaluate whether or not there was definitive evidence that ketamine had detrimental effects on ICP, CPP, and neurologic outcomes when compared to other induction agents. However, only 168 of the 953 patients had the primary outcome of interest evaluated. In fact, the largest study included in this analysis (Jabre, et al.), which included 655 patients, never measured an ICP or CPP. So it's difficult to say that this analysis conclusively shows a lack of effect of ketamine on the ICP.

Secondary outcomes in this analysis included some LOS and mortality measures, as well as markers of neurologic function such as the GCS and some neuropsychometric tests. Unfortunately, markers such as the GCS and neuropsychometric testing are subject to interobserver variability, and in the included studies were only used as secondary outcomes (thus, were not powered to find a difference in most cases).

They did to a reasonable job of searching the literature using internet databases and the gray literature. However, studies were excluded if they were not printed in English, which may have missed research conducted in non-English speaking centers.

The authors of this analysis used a Jadad score to determine the methodological quality of the RCTs included. The Jadad score is a procedure intended to independently assess the methodologic quality of a clinical trial, and is based on three aspects of the design (1) randomization, (2) blinding, and (3) a full account of all patients randomized, included those who withdrew or dropped out. Scores on the scale range from zero (very poor quality) to five (rigorous).

Dimensions of Trial Quality Measured by Assessment Tools

	Jadad	Delphi*	CONSORT*	Cochrane
Randomization	J1, J2, J6	D1a	C1, C8, C10	A
Masking	J3, J4, J7	D4, D5, D6	C11	D, E, F
Allocation Concealment		D1b	C9	B
Handling of Withdrawals and Dropouts	J5	D8	C13, C16	H, I, K
Measures of Variability		D7		
Pre-specified Analyses			C6	
Stopping rules			C7	
Statistical methods			C12, C17	
Baseline data		D2	C15	C
Address Multiplicity			C18, C20	

The Jadad score was widely used in the past. New scoring systems with more dimensions have been developed over time. Berger and Alperson published an article called *A General Framework for the Evaluation of Clinical Trial Quality* discussing the various aspects of four different scoring systems.

Two of the clinical controlled trials included in this analysis had a Jadad score of 2, two trials had a score of 3, and only one trial had a score of 5. The authors also used the Cochrane Risk of Bias Tool to rate the likelihood of selection, performance, attrition and detection bias. This is Table 2 of the manuscript.
All of the outcomes that the authors set out to evaluate in this study were not able to be pooled due to heterogeneity of the populations, interventions, and outcome measures. This is what differentiates a systematic review from a meta-analysis.

Systematic reviews are a qualitative analysis intended to simply describe the existing data, where meta-analyses are quantitative in nature and try to combine evidence from the populations of smaller studies to make assumptions about the group as a whole.

Unfortunately, it's difficult to draw larger conclusions about the effects of ketamine on ICP with the collection of studies in this systematic review because each of them are relatively different.
What we can see is the lack of demonstrable harm that ketamine has on our neurologic parameters of interest when compared to the control arm in each of the papers.

Case Resolution

You discuss with your trauma surgery and neurosurgery teams that in undifferentiated patients requiring RSI in the ED, there is no good evidence to say that ketamine has an appreciable negative effect on ICP, CPP, or neurologic outcomes. Ketamine represents a reasonable induction agent for RSI in this patient. The patient is intubated after receiving the drugs you ordered during the initial resuscitation (above) and remains hemodynamically stable throughout the procedure. After undergoing the appropriate diagnostic testing, the patient is diagnosed with a traumatic subarachnoid hemorrhage and is transferred to the trauma-surgery intensive care unit for further management.

Clinical Application

In patients who require RSI in the ED, ketamine is a reasonable alternative to other available induction agents, especially if patients have normal or low blood pressure. Other agents would be preferred in the setting of hypertension, as ketamine can increase blood pressure through sympathetic stimulation.

CONCLUSION VS COMMENTARY

COMPARISON

The authors conclude that ketamine does not adversely affect ICP, CPP, neurologic outcomes, or mortality compared with other induction agents., Given the questionable original evidence suggesting that ketamine has detrimental effects on ICP, it seems that the best available evidence we have at this point does not demonstrate an appreciable negative effect on ICP, CPP, or neurologic outcomes.

WHAT DO I TELL MY PATIENT?

I would tell them in undifferentiated patients requiring RSI in the ED, there is no good evidence to say that ketamine has an appreciable negative effect on ICP, CPP, or neurologic outcomes. In my opinion, ketamine is a reasonable induction agent for RSI in this patient.

References

Cohen L, Athaide V, Wickham ME, Doyle-Waters MM, Rose NG, Hohl CM. The effect of ketamine on intracranial and cerebral perfusion pressure and health outcomes: a systematic review. Ann Emerg Med. 2015 Jan;65(1):43-51 e2.

Guest Skeptic: Dr. Meghan Groth
Meghan (@EMPharmGirl) is an emergency medicine pharmacy specialist at Fletcher Allen Health Care in Burlington, Vermont and Professor of pharmacy at the Albany College of Pharmacy and Health Sciences.

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You Better Think Ultrasound for Acute Abdominal Aneurysm

Case Scenario:

66-year-old man develops sudden onset back/flank pain. He has a history of hypertension and smokes cigarettes. You are concerned about a potential acute abdominal aneurysm. A CT abdomen has been ordered and is pending.

Q:

How reliable is a bedside emergency department ultrasound for detecting acute abdominal aneurysm?

BOTTOM LINE

Emergency department US, when applied by "*trained*" emergency physicians, is an excellent accurate diagnostic modality to detect triple A's in symptomatic adult patients. When in doubt, go on to more definitive imaging

Key Results

Sensitivity = 0.99 (0.95-1.00); heterogeneity (I2) = 13.2%
Specificity = 0.99 (0.97-0.99); heterogeneity (I2) = 46.8%
LR+: 10.8-infinity
LR-: 0.00-0.025

Commentary

They had well described methods in this study. They used the MOOSE (Meta-Analyses and Systematic Reviews of Observational Studies) reporting guidelines. They also used QUADAS (Quality Assessment of Diagnostic Accuracy Studies) tool to evaluate the quality of the studies included.

Overall prevalence of triple A in various studies: 4.8-60.6%. This could potentially influence diagnostic test performance for negative (NPV) and positive predictive value (PPV) in studies with variable prevalence of triple A.
While disease prevalence impacts PPV and NPV it does not affect positive and negative likelihood ratios.
The search was limited to published English language manuscripts. We do like to see a more exhaustive search. There may be great papers in other languages. But if we never search those other languages we will never find them.

This can also be one of the leaks in the knowledge translation pipe. That is why the SGEM is starting to podcast in French as well as English to reach a greater audience and cut the KT window down to <1yr.
There was a moderate heterogeneity detected between studies (up to 50%), necessitating use of random-effects
analyses; attributed to operator training and experience.

Random effect model we cannot assume that the true effect size is identical between the studies. We suspect that there are other reasons influencing the effect size besides sampling error. Therefore, when heterogeneity is high we must use the random effect model to analyze the data.
There was little commentary on inter-rater reliability in any of the included studies.

Studies were at risk of verification bias. This is when the treating physician aware of test result, influences ordering of reference standard test. This can lead to a risk of overestimating sensitivity.

The studies included were also at risk of test review bias. This is where the interpreter of reference standard result influences the interpretation of the emergency department ultrasound result.

There are many forms of bias unique to diagnostic research. One of the best papers is by Kohn et al called Understanding the direction of bias in studies of diagnostic test accuracy

Commentary

Another issue was "indeterminate scans" were coded as false positives as they triggered a need for further imaging/investigations to avoid missed symptomatic triple A's. This would maximize specificity at the expense of sensitivity.

The authors suggest that it may be more conservative to code indeterminate scans as false negative. This would optimize sensitivity and recalculate new Sensitivity/Specificity and Likelihood Ratios which they did not do. However, with this coding system, both Sensitivity and Specificity were very high, suggesting that coding treating indeterminate scans as potential positives does not lead to increased patient harm.

Systematic Review 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 assessments of studies were reproducible	☑
The outcomes were clinically relevant	☑
There was low statistical heterogeneity for the primary outcome	
The treatment effect was large enough and precise enough to be clinically significant	☑

Another thing is the issue of emergency department ultrasound training. There seems to be little evidence-based consensus on what constitutes adequate training for competence in emergency department ultrasound for various diagnostic entities.

All Canadian Emergency Medicine training programs now incorporate emergency department training.

American College of Graduate Medical Education requires emergency ultrasound training for all Emergency Medicine residents. Abdominal aortic aneurysm is one of those modalities that is required

Clinical Application

Another issue was "*indeterminate scans*" were coded as false positives as they triggered a need for further imaging/investigations to avoid missed symptomatic triple A's. This would

You have a blood clot in your lung. We have blood thinners to treat this problem. Most people in the USA are admitted for this condition. In Canada about half of patients are treated at home. There is some research that supports home treatment for low risk patients if they have good follow-up. Do you want to be admitted to hospital or be treated at home?

References

1. Cosford PA, Leng GC. Screening for abdominal aortic aneurysm. Cochrane Database Syst Rev. 2007 Apr 18(2):CD002945.
2. Rubano E, Mehta N, Caputo W, Paladino L, Sinert R. Systematic review: emergency department bedside ultrasonography for diagnosing suspected abdominal aortic aneurysm. Acad Emerg Med. 2013 Feb;20(2):128-38.

CONCLUSION VS COMMENTARY

COMPARISON

Overall agreement with authors' conclusion, with caveat of training requirements, and limitations in search strategy.

Guest Skeptics:

Dr. Matt Dawson

Director of Point of Care Ultrasound at the University of Kentucky
Co-creator of Ultrasound Podcast, Introduction to Bedside Ultrasound Volumes 1 and 2 digital textbooks, One Minute Ultrasound smartphone app, Sonocloud, and other random ventures.

Dr. Mike Mallin

Director of Emergency Ultrasound and the Emergency Ultrasound Fellowship at the University of Utah. He is particularly interested in echocardiography and has sat for and passed the Echo Boards. He is published in multiple journals that can be found in your trash can.

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Paediatric Fever

Q1:

1) Should parents combine/alternate acetaminophen and ibuprofen?

Q2:

2) Will treating the fever make her sicker, longer?

Q3:

3) Will treating with antipyretics prevent a febrile seizure?

Combined and alternating paracetamol and ibuprofen therapy for febrile children

Wong et al. Cochrane Database of Systemic Interviews 2013

P Randomized controlled trial examining children (<18yrs) with new fever

I Combined or alternating therapy of paracetamol and ibuprofen

C Isolated therapy of either paracetamol or ibuprofen. Alternating therapy as a comparison to combined therapy

O **Primary:** Child discomfort, number of doses of meds given, absences from daycare/school, proportion of febrile children at 1/4/6 hrs post treatment**. Secondary**: Adverse events

Authors' Conclusion:

"There is some evidence that both alternating and combined antipyretic therapy may be more effective at reducing temperatures than monotherapy alone. However, the evidence for improvements in measures of child discomfort remains inconclusive. There is insufficient evidence to know which of combined or alternating therapy might be more beneficial. (Wont et al., 2013)

Background

Parent's are often very concerned about fever in their children. They can develop a real *"fever fear"* and come into the emergency department for evaluation and reassurance. However, we need to help educate them that fever alone is not dangerous.

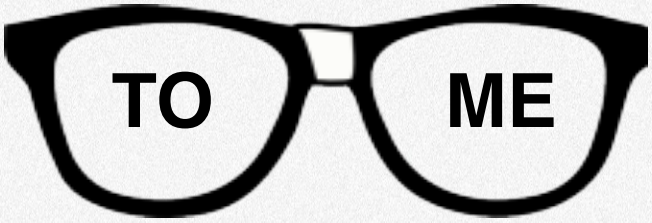
Here is what the American Academy of Pediatrics Guides say about fever *"…fever, in and of itself, is not known to endanger a generally healthy child. In contrast, fever may actually be of benefit; thus, the real goal of antipyretic therapy is not simply to normalize body temperature but to improve the overall comfort and well-being of the child."*

Key Results

Temperature was lower after combined treatment.
1 hour (MD -0.27, 95%CI -0.45 to -0.08)
4 hours (MD -0.70, 95%CI -1.05 to -0.35)
6 hours (MD -1.30, 95%CI -2.01 to -0.59)

Alternating therapy improved comfort compared to single therapy (Analysis 2.1) as well as decreased absent days from daycare by -0.88 (95%CI -1.02 to -0.74).

TALK NERDY TO ME



Commentary

This is a reasonably well-performed systematic review and meta-analysis. Cochrane usually does a good job. There were no restrictions on language/publication type and the authors did a reasonable search of the grey literature. A few issues arise:

1) Why was the unpublished research on this topic discovered through ClinicalTrials.gov not included in the meta-analysis?

2) Why did the authors insist on having several primary outcomes? (Just like in the movie Highlander – there can be only ONE!)

3) Why did the authors not present the data on a research paper that addressed fever-associated symptoms at 24/48/120 hours? (Hay 2008).

It is not surprising that using more antipyretic medications results in tighter control of fever in febrile children. The greater question is “who cares?” There has been a progressive shift away from focusing on normalization of temperature in febrile children towards focusing on patient comfort. This is in keeping with the AAP guidelines we mentioned previously.

The limited data presented in this paper suggests that combined/alternating therapy can be beneficial for comfort, but more studies on this outcome measure are required.

Clinical Application

In febrile children, alternating or combining antipyretics may be helpful in controlling temperature, but this is of limited usefulness. Comfort may also benefit, but this requires more research.

WHAT DO I TELL MY PATIENT?

Treat comfort not fever. If one medication is not working try the other. Be careful if using both as not to accidentally overdose on one or the other

Systematic Review 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 assessments of studies were reproducible	☑
The outcomes were clinically relevant	
There was low statistical heterogeneity for the primary outcome	☑
The treatment effect was large enough and precise enough to be clinically significant	☑

CONCLUSION VS COMMENTARY

COMPARISON

Agree that further research is required and that parents should focus on patient comfort instead of normalizing a temperature. There is, in fact, some evidence from this systematic review that alternating therapy has a benefit on comfort.

BOTTOM LINE

Parents and caregivers should focus on patient comfort instead of normalizing a temperature in febrile children. Alternating therapy may be beneficial for comfort, but more research is required to address this specific question.

Does the use of antipyretics in children who have acute infections prolong febrile illness? A systematic review and meta-analysis

Purssel et al. J Pediatr 2013

P RCT or quasi-randomized trials including children with febrile illness

I Use of antipyretics

C No antipyretics

O Time to recovery

Authors' Conclusion:

"There is no evidence from these studies that the use of antipyretics slows the resolution of fever in children." (Purssel et al., 2013)

Key Results Pooled mean difference in fever clearance was -4.16 hours in favour of antipyretics (95%CI -6.35 to -1.96hrs; P=0.002)

Commentary

This is certainly an interesting question to ask. Will treating a febrile child with antipyretics prolong their illness. This data suggests that treating the fever will NOT prolong their illness.

This study also had significant limitations. Specifically:

There was only a limited attempt at finding data from the 'grey literature'. The authors should have done more than check reference lists from the published papers. They should have studied conference proceedings, and spoken with experts in the field.

Commentary

Of the six studies included, three dealt with patients with malaria and one dealt with patients with varicella. None of those studies are generalizable to the patient population and infectious diseases we are likely to encounter.

Two of the six studies did not have blinding.

The primary outcome examined by this study was time to resolution of fever, a surrogate for more important outcomes. In one study (Brandts 1997) there was a significant increase in malaria clearance time in the antipyretic group. In another study (Kramer 1991) less than 50% of parents were able to correctly identify that their child had received antipyretic/placebo.

Overall, the ongoing recommendation is that parents focus on treating patient comfort and not treat a specific temperature number. This study does not support the regular use of antipyretics to control temperature.

Clinical Application

In children with fever due to illness, the current recommendation is that antipyretics are used to improve comfort and less attention should be paid to actual temperature.

Systematic Review 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 assessments of studies were reproducible	☑
The outcomes were clinically relevant	
There was low statistical heterogeneity for the primary outcome	☑
The treatment effect was large enough and precise enough to be clinically significant	

CONCLUSION VS COMMENTARY

COMPARISON

The search yielded studies that are difficult to generalize to our population and the outcome measure is only a surrogate for clinical improvement

BOTTOM LINE

Antipyretics should be used to improve comfort during an illness

Do Antipyretics prevent the recurrence of febrile seizures in children? A systematic review of randomized controlled trials and meta-analysis

Rosenbloom et al. Eur J Paediatr Neurol 2013

P Randomized controlled trials including children <18 years old

I Antipyretic medications

C Placebo

O Rates of febrile seizure recurrence

Authors' Conclusion:

"Antipyretics were ineffective in reducing the recurrence of febrile seizures (Rosenbloom et al., 2013)

Key Results

Odds Ratio for recurrence of febrile seizures in the antipyretic group was 0.9 (95% CI: 0.57-1.43).

Commentary

So treating the fever did not seem to prevent children from having a febrile seizure. This has been a longstanding myth that febrile seizures can be prevented with antipyretics. This study identified three randomized controlled trials and combined their data to show that there is no significant effect in preventing the recurrence of febrile seizures.

Again, there were some major limitations:

There was no attempt to search the grey literature. The authors should have contacted experts in the field to find unpublished data. They should have searched for conference abstracts or commented on searching the reference lists of included articles.

No language restrictions were applied, but English abstracts required." This sounds like a language restriction to me – we included all languages, as long as they were English.

There was no risk of bias tool used. We see commonly in Cochrane Systematic Reviews a presentation of the included articles risks of bias. Commonly many of the included articles are found to have significant risks of bias, which then undermines the validity of any conclusion made from the study. Without a similar tool applied, we can only guess as to the risks of bias from the included studies.

The authors use the word "ineffective" to describe the usefulness of antipyretics in preventing febrile seizures. It is a common mistake to equate "no evidence of effect" and ineffective. Failing to prove that one thing is significantly better than another does not prove that they are the same.

Clinical Application

In children with febrile seizures, the regular use of antipyretics appears to have no significant effect on reducing the rates of seizure recurrence.

CONCLUSION VS COMMENTARY

COMPARISON

I would clarify that there is no significant difference in recurrence of febrile seizures when children are treated with antipyretics

Systematic Review 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 assessments of studies were reproducible	☑
The outcomes were clinically relevant	☑
There was low statistical heterogeneity for the primary outcome	☑
The treatment effect was large enough and precise enough to be clinically significant	☑

WHAT DO I TELL MY PATIENT?

Treating your child's fever will not likely have any effect on recurrence rates of febrile seizures.

BOTTOM LINE

Antipyretics appears to offer no significant improvement in the recurrence rates of febrile seizures in children

Summary of all three papers

1. Antipyretics don't appear to lengthen duration of fever in ill children
2. Antipyretics an be combined for effect, but to what end?
3. Antipyretics don't appear to decrease risk of febrile seizure recurrence

Fever: Not your enemy!

References

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Guest Skeptic: Dr. Anthony Crocco
Associate Professor, McMaster University, Medical Hospital Emergency Department. Director and Division Head McMaster Children's

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NIPPV: For Out-of-Hospital Respiratory Distress

Case Scenario:

55-year-old man with a history of chronic obstructive pulmonary disease, asthma and congestive heart failure calls 911 complaining of shortness of breath. His respiratory rate is 40, heart rate is 110, O_2 saturation 88%.The paramedics decide to use non-invasive positive pressure ventilation on-route to support this man's respiratory distress

Q:

Does out-of-hospital non-invasive positive pressure ventilation improve in-hospital mortality compared to standard treatment in patients with grossly undifferentiated respiratory distress?

BOTTOM LINE

Non-invasive positive pressure ventilation is a reasonable out of hospital treatment option for adult patients with grossly undifferentiated severe respiratory distress

Effect of Out-of-Hospital Noninvasive Positive-Pressure Ventilation in Adult Patients with Severe Respiratory Distress: A Systematic Review and Meta-analysis.

Mal et al. Annals of Emergency Medicine 2014

P Seven randomized control trials of adult patients (n=632) with out-of-hospital severe respiratory distress

I Non-invasive positive pressure ventilation

C Standard Therapy

O **Primary Outcome**: In-hospital mortality**. Secondary Outcomes:** Need for invasive ventilation, hospital and intensive care length of stay and complications

Authors' Conclusion:

"Out-of-hospital administration of NIPPV appears to be an effective therapy for adult patients with severe respiratory distress".

Background

Acute dyspnea is a common emergency department complaint, in 2003 this chief complaint comprised about 3.5% of more than 115 million emergency department visits nationwide.

A subset of these patients will present in respiratory distress, which is associated with increased morbidity and mortality. Often it can be hard to determine the exact etiology of the shortness of breath in a timely fashion, and therapeutic interventions need to begin before the exact diagnosis is known.

Luckily the most common culprits of respiratory distress share a common treatment modality, and that treatment is non-invasive positive pressure ventilation.

Studies have shown that acute cardiogenic pulmonary edema, chronic obstructive pulmonary disease and asthma exacerbations all benefit from non-invasive positive pressure ventilation.

Cochrane did a SR which included 32 studies (n=2,916) looking at non-invasive positive pressure ventilation for cardiogenic pulmonary edema. Compared to standard medical care non-invasive positive pressure ventilation significantly reduced hospital mortality (RR 0.66, 95% CI 0.48-0.89). This was a study done by Vital et al in 2013.

There was an older Cochrane SR from 2004 by Ram et al. They looked at non-invasive positive pressure ventilation for admitted patients with acute chronic obstructive pulmonary disease exacerbations. There 14 studies in the systematic review (n=758). It too showed a decrease in mortality (RR 0.52, 95% CI 0.35 to 0.76)

Non-invasive positive pressure ventilation has also shown to benefit asthma exacerbations. The Cochrane SR by Lim et al identified six trials for inclusion. Their primary outcome was endotracheal intubation. This is because it is very rare for asthmatics to die and there were no deaths in any of these studies.

There was only two studies in this SR looking at their primary outcome of intubations. These were small studies with a total of 86 patients and only 2 intubations. With such small numbers they could not find a difference between the non-invasive positive pressure ventilation group and standard care.
However, with limited data they were able to show reduced hospitalizations, increased the number of patients discharged from the emergency department and improvement in some surrogate non-patient oriented outcomes like reparatory rate and lung function measurements.

Results

Seven studies were included in the analysis (n=632).
Six of the seven studies used CPAP and one trial used BiPAP.

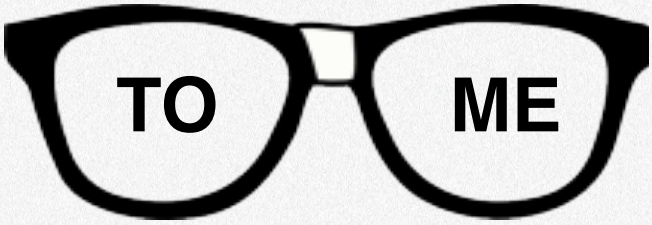
The vast majority of patients (>80%) were suspected to be of acute cardiogenic pulmonary edema.

Commentary

Patients with undifferentiated respiratory distress present to the emergency department regularly. As mentioned earlier, NIPPV has been shown to be effective in reduction mortality in pulmonary edema and chronic obstructive pulmonary disease exacerbations. It is also been shown to be helpful in asthmatics. So the authors ask a reasonable question on whether or not pre-hospital treatment with NIPPV could also be of benefit.

The authors did an extensive literature search including all the standard electronic databases. They also tried to identify any grey or unpublished literature. However, as with many studies they did restrict their search to English language studies.

TALK NERDY TO ME



Commentary

It is hard to determine if the primary studies were of high methological quality. From the data provided they do appear to be reasonable but there was insufficient information for a definitive answer. Five of the studies were judged to be low risk of bias using the Cochrane Collaboration tool for assessing risk of bias. Allocation was concealed in five of the studies. There was no blinding in any of the studies. It would be hard to blind patients or providers if they had non-invasive positive pressure ventilation on their face. When it comes to follow-up it was very good. We look for less than 20% loss to follow-up and they only had 8 out 632 patients not accounted for in the study.

The primary outcome demonstrated significant patient oriented benefit. There was decrease of in-hospital mortality. The number needed to treat was 18 (NNT=18). So only 18 people needed non-invasive positive pressure ventilation to prevent one death. The secondary outcome of need for invasive ventilation was also very good with a number needed to treat of eight (NNT=8).

We must be cautious when applying these results to our practice situation. Six out of the seven studies were done in Europe. Their pre-hospital system is much different than those in North America. They often have emergency physicians or anesthesiologist in the ambulance. This difference could limit the external validity of their conclusions.

Another limitation would be the definition of "standard" therapy. What was "standard" therapy? They used a very broad definition in the manuscript. It included providing simple supplemental oxygen, bronchodilators and a variety of drugs (nitroglycerine, calcium channel blockers, ionotropes, morphine, and steroids). How would this *"standard"* therapy compare to your local therapy for patients in severe respiratory distress?

There were a variety of commercial non-invasive positive pressure products used in the different randomized control trials. Given the overall positive effects demonstrated this would give strength to the conclusion that the intervention works. In addition, there was no accepted standard dose for starting the therapy or the length of therapy.

Under reporting of harm is well know limitation of randomized control trials. It is unfortunate that only five of the studies commented on complications. Three of the studies said there were no harms while two studies reported three patients in the non-invasive positive pressure ventilation group experienced emesis.

Traditionally we have been somewhat cautious in using non-invasive positive pressure ventilation for asthmatics for fear of barotrauma. Only one trial in this review with a total of ten patients were included in this systematic review. In this small sample size there were no report of complications.

Commentary

The authors conclude that pre-hospital non-invasive positive pressure ventilation appears safe and beneficial for patients with respiratory distress. We add to this sweeping conclusion the caveat that non-invasive positive pressure ventilation is safe and beneficial in the appropriate clinical setting, and have yet to clearly and overwhelmingly show that ability for all-comer EMS providers to recognize these appropriate clinical scenarios. Further study with broader inclusion criteria of truly undifferentiated dyspnea using a more clear spectrum of EMS providers may shed light on this and help bring to light any unseen adverse events which previous studies had not been powered to do.

Systematic Review 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 assessments of studies were reproducible	☑
The outcomes were clinically relevant	☑
There was low statistical heterogeneity for the primary outcome	☑
The treatment effect was large enough and precise enough to be clinically significant	

Case Resolution

The 55 year old man with acute respiratory distress arrives with non-invasive positive pressure ventilation in place and doing better. His reparatory rate is normal, HR<100 and O2 saturation is 97%. You start working him up to differentiate what the cause of his decompensation and are optimistic you will not need to intubate him

Clinical Application

Non-invasive positive pressure ventilation can and should have a huge role in pre-hospital care. Non-invasive positive pressure ventilation would likely lead to fewer suboptimal in-field intubations, in addition to fewer patients arriving to the ED in extremis. We should be working with Emergency Medical Service coordinators to enable Emergency Medical Service providers to use non-invasive ventilation, implement clear protocols for appropriate use, and enhancing physician-Emergency Medical Service communication to help make these decisions and manage potential complications.

CONCLUSION VS COMMENTARY

COMPARISON

The authors conclude that pre-hospital non-invasive positive pressure ventilation appears safe and beneficial for patients with respiratory distress. We add to this sweeping conclusion the caveat that non-invasive positive pressure ventilation is safe and beneficial in the appropriate clinical setting, and have yet to clearly and overwhelmingly show that ability for all-comer EMS providers to recognize these appropriate clinical scenarios.

WHAT DO I TELL MY PATIENT?

It would be paramedics telling the patients that they appear in acute respiratory distress. We have a device that can help you breath, been shown to save lives and may prevent you from having a large tube put down your throat

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Guest Skeptics:
Dr. Amy Pazebeck
Amy is a PGY4 emergency medicine resident at NYU-Bellevue.

Dr. Kara Otterness
Kara is a senior EM. Her academic interests include ultrasound, simulation, and resident education.

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Hippy Hippy Shake:
Ultrasound vs. CT Scan for Diagnosing Renal Colic

Case Scenario:
A 36-year-old previously healthy white male is attending his families thanksgiving supper. He develops waves of right flank pain associated with vomiting. A relative who is a nurse suggests it could be renal colic and suggests he goes to the emergency department for assessment.

Q:

In emergency department patients with suspected renal colic, is ultrasound as effective as CT as a diagnostic tool?

BOTTOM LINE

Bedside emergency department ultrasound is safe and has several advantages over CT for the diagnosis of kidney stones

Ultrasound versus Computed Tomography for Suspected Nephrolithiasis

Smith-Bindman et al. NEJM 2014

P 2,759 patients 18-76 years of age in emergency department setting from 15 geographically diverse academic emergency departments

I Ultrasonography

C Computed tomography

O 30-day incidence of high-risk diagnosis with complications related to missed or delayed diagnosis and 6-month cumulative radiation exposure

Authors' Conclusion:

"Initial ultrasonography was associated with lower cumulative radiation exposure than initial computed tomography without significant differences in high-risk diagnosis with complications, serious adverse events, pain scores, return ED visits, or hospitalizations." (Smith-Bindman et al., 2014)

Background

We have covered renal colic a number of times on the Skeptics' Guide to Emergency Medicine.. This included a randomized clinical trial done in France looking at the use of tansulosin for the expulsion of distal ureteral stones (SGEM#4: Getting Unstoned). This small study of only 129 patients did not show superiority of tansulosin over placebo.

SGEM#32: Stone Me was a Cochrane Systematic Review looking at fluids and diuretics for rental colic. It was done by my evidence based medicine mentor Dr. Andrew Worster. The genius that started BEEM and taught me the EBM answer could always be…*"it all depends"*. His SR had only two small studies which met inclusion criteria. The conclusion was no reliable evidence was available to support the use of fluids or diuretics to treat renal colic.

The last time we reviewed renal colic was another Cochrane Systematic Review from Zue et al. The Bottom Line was tamsulosin was useless in most emergency department patients with ureteral colic unless their stone size exceeds at least 4mm. (SGEM#71: Like a Rolling Kidney Stone).

This time we are not going to be talking about renal colic treatment but rather diagnostic strategies.

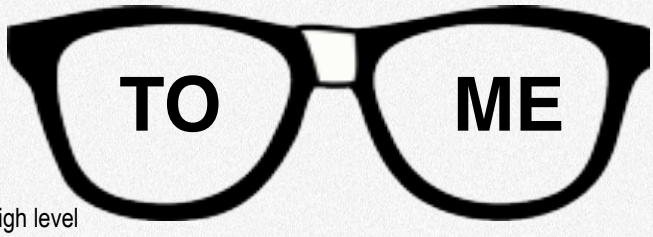
Results

Table 3. Primary and Secondary Study Outcomes According to Study Group.*

Outcome	Point-of-Care Ultrasonography (N=908)	Radiology Ultrasonography (N=893)	Computed Tomography (N=958)	P Value
Primary Outcomes				
High-risk diagnosis with complication — no. of patients (%)	6 (0.7)	3 (0.3)	2 (0.2)	0.30
Radiation exposure — mSv	10.1±14.1	9.3±13.4	17.2±13.4	<0.001
During emergency department enrollment visit	6.5±9.4	4.7±8.4	14.1±9.6	<0.001
From enrollment to 30 days	1.2±4.4	1.8±5.4	1.0±3.9	0.19
30–180 days	1.5±5.5	2.1±6.8	1.2±4.8	0.08
Secondary Outcomes				
Serious adverse events — no. of patients (%)	113 (12.4)	96 (10.8)	107 (11.2)	0.50
Related serious adverse events — no. of patients (%)†	3 (0.3)	4 (0.4)	5 (0.5)	0.88
Emergency department length of stay — hr‡				
Median	6.3	7.0	6.4	<0.001
Interquartile range	4.5–9.0	5.4–9.9	4.7–9.0	
Return emergency department visit — no. of patients/total no. (%)§				
Within 1 wk	86/835 (10.3)	77/816 (9.4)	99/872 (11.4)	0.43
Within 1 mo	136/835 (16.3)	121/816 (14.8)	143/872 (16.4)	0.62
Within 6 mo	231/835 (27.7)	231/816 (28.3)	255/872 (29.2)	0.77
Hospital admission after emergency department discharge — no. of patients (%)§				
Within 1 wk	27/835 (3.2)	25/816 (3.1)	17/872 (1.9)	0.21
Within 1 mo	44/835 (5.3)	48/816 (5.9)	34/872 (3.9)	0.16
Within 6 mo	87/835 (10.4)	84/816 (10.3)	83/872 (9.5)	0.80
Self-reported pain score¶				
At discharge from the emergency department	3.2±2.9	3.0±2.9	3.3±2.9	0.05
At 3-day follow-up	3.0±3.1	2.8±2.9	3.0±3.0	0.42
At 7-day follow-up	2.0±2.9	2.0±2.8	2.0±2.8	0.84
Accuracy for diagnosis of nephrolithiasis‖				
Sensitivity — % (95% CI)	85 (80–89)	84 (79– 89)	86 (82–90)	0.74
Specificity — % (95% CI)	50 (45–54)	53 (49–57)	53 (49–58)	0.38

High-risk diagnosis with complications: No Difference about 0.3%
Radiation exposure (mSv): Difference (more with CT)
Serious adverse events: No Difference about 11%
Emergency Department Length of Stay (hr): Difference in LOS with the longest time having radiology do a US
Return ED visits: No Difference at 1 week, 1 month or 6 months
Hospital admission after ED discharge: No Difference at 1 week, 1 month or 6 months
Accuracy for diagnosis of nephrolithiasis: No Difference
- Sensitivity ~85%
- Specificity ~50%

TALK NERDY TO ME



Commentary

The trial was a well done RCT with a high level of validity. It is unlikely that this trial will be repeated and supports what many EM physicians suspected in the diagnosis of kidney stones in an ED population.

The study did not comment on whether groups were treated differently with regards to disposition, treatment, and follow-up, based on results from different imagine modalities. It should be noted that there were exclusions for obesity in both men and women which could significantly effect the test characteristics of US patients.

This study provides strong enough evidence that there is no harm to implementing ultrasonography for suspected nephrolithiasis, and is benefit in reducing radiation exposure. This evidence should and will impact clinical care, as physicians should stay away from CT in favor of US to reduce radiation exposure, without added risk by performing US.

RCT 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 groups to which they were randomized	☑
The study patients were recruited consecutively (i.e. 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	☑

Case Resolution

The 36 year old man who presented looking like renal colic gets an ultrasound. This confirms a 4mm stone in the distal ureter. His pain and vomiting has settled in the department with intravenous ketorolac and ondansetron.

You write him prescription for an analgesia and antiemetics. You also arrange a follow up with a urologist and provide him with strict return precautions. He thanks you and you leave the room.

CONCLUSION VS COMMENTARY

COMPARISON

Authors' conclusions are similar to our conclusion, in that ultrasonography for suspected nephrolithiasis reduces cumulative radiation exposure without significant differences in bad outcomes as compared to computed tomography

Clinical Application

Emergency medicine physicians should consider ultrasound for suspected nephrolithiasis when appropriate. We could be doing a favor for our patients in reducing radiation exposure, and are not putting the patient at increased risk or harm.

WHAT DO I TELL MY PATIENT?

I would tell my patients that it looks like you have a kidney stone because you are doing the hippy hippy shake. We should start with ultrasound to lessen your exposure to radiation. Radiation increases the chance of developing cancer later in life. If further concerns arise, we can always get a CT scan. The ultrasound is just as good at diagnosing kidney stones and we may be able to get you out of the emergency department faster.

References

Smith-Bindman R, Aubin C, Bailitz J, Bengiamin RN, Camargo CA, Jr., Corbo J, et al. Ultrasonography versus computed tomography for suspected nephrolithiasis. N Engl J Med. 2014 Sep 18;371(12):1100-10

Guest Skeptics:
Dr. Tony Seupaul
Chairman of the Department of Emergency Medicine, University of Arkansas

Dr. Spencer Wright
Spencer is a PGY-3 resident in the Emergency Medicine program at the University of Arkansas

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Don't Stand So Close To Me: You Have the Flu

Case Scenario:

25-year-old nurse with no significant past medical history presents to the ED with a 48 hour history of aching all over, fever and cough. He did not get a flu shot this year. You diagnose him with a flu like illness and provide him advice on management. Before leaving the ED he wants to know if taking one of those flu drugs he sees on the television will help?

Q:

Do neuraminidase inhibitors benefit patients with influenza?

BOTTOM LINE

When balancing possible risks and benefits, the evidence does not support routine use of neuraminidase inhibitors for the treatment or prevention of influenza in any individuals.

Neuraminidase Inhibitors for Preventing and Treating Influenza in Healthy Adults and Children

Jefferson et al. Cochrane Database Syst Rev. 2014

P 20 Oseltamivir trials with 9,623 participants and 26 Zanamavir trials with 14,628 participants

I Neurmanidase inhibitors (Oseltamivir or Zanamivir)

C Note that placebos might contain active substance

O Treatment (symptom relief, pneumonia and hospitalization), Prophylaxis (Influenza or ILI, household transmission and hospitalizations), Harms (Nausea, vomiting, cardiac)

Authors' Conclusion:

"Oseltamivir and zanamivir have small, non-specific effects on reducing the time to alleviation of influenza symptoms in adults, but not in asthmatic children. Using either drug as prophylaxis reduces the risk of developing symptomatic influenza. Treatment trials with oseltamivir or zanamivir do not settle the question of whether the complications of influenza (such as pneumonia) are reduced, because of a lack of definitions. The use of oseltamivir increases the risk of adverse effects, such as nausea, vomiting, psychiatric effects and renal events in adults and vomiting in children. The lower bioavailability may explain the lower toxicity of zanamivir compared to oseltamivir. The balance between benefits and harms should be considered when making decisions about use of both NIs for either the prophylaxis or treatment of influenza. The influenza virus-specific mechanism of action proposed by the producers does not fit the clinical evidence." (Jefferson et al., 2014)

Background

Influenza is a seasonal phenomenon and we have covered the flu before on SGEM#20 *Hit Me with Your Best Shot* when we discussed mandatory immunization for healthcare workers.

Immunization has been on of the most significant advances in modern medicine. Some vaccines have been highly successful (Haemophilus Influenzae B, small pox, polio) while others have been not as successful (HIV). Some vaccines work well but are their effectiveness decreases with time (whooping cough).

The flu vaccine is one that is not highly effective. There are a number of reasons it is not as effective. However, there was a Cochrane review showed that vaccinating healthcare workers, in addition to other preventative interventions, might protect the elderly in long-term care facilities.

The evidence contained in the Cochrane review was not great and had high risk of bias. Evidence based medicine has limitations and sometimes the BEST evidence is not great. Despite the limited data it is still recommended healthcare workers get a flu shot.

This podcast is going to focus on a treatment option after you have been diagnosed with the flu rather than preventing it in the first place. Neuraminidase inhibitors are influenza antiviral drugs often used to treat patients with the flu. Many governments stockpiled these drugs with the H5N1 scare in 2005 and increased their supplies after the 2009 H1N1 pandemic.

There were concerns these drugs were not as effective as promoted by their pharmaceutical companies. Much of this skepticism came from all the data not being available to analyze.

Results

Time to first symptom alleviation: Less than one day

Oseltamivir:

In adults reduced by 16.8 hours, from 7 to 6.3 days (-16.8 hours, 95% CI -25.10 to -8.42)
In healthy children reduced by 29 hours, based on one trial (-29 hours, 95% CI -12 to -47)
No significant effect in asthmatic children (+5.2 hours, 95% CI -11.1 to +21.4)

Zanamivir:

In adults reduced by 14.4 hours, from 6.6 to 6.0 days (-0.60 days, 95% CI -0.81 to -0.39)
No significant effect in children (-1.08 days, 95% CI -2.32 to + 0.15)
Use of relief medication in the placebo-group showed a non-significant 0.41 day decrease
No significant difference in the influenza-infected and the non-influenza-infected subgroups (P = 0.53)

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Hospitalizations: No difference

Oseltamivir:

No significant effect in treatment of adults (RR 0.92, 95% CI 0.57 – 1.50) or children (RR 1.92, 95% CI 0.70 to 5.23)
No significant effect in prophylaxis (RR 1.114, 95% CI 0.66 to 1.94)

Zanamivir:

Hospitalizations were not reported in the trials

Pneumonia: No real difference

Oseltamivir:

Significantly reduced self reported, investigator mediated, unverified pneumonia (RR 0.55, 95% CI 0.33-0.90, NNTB = 100)
Not significant in trials with detailed diagnostic criteria or radiological confirmation of pneumonia. (RR 0.69, 95% CI 0.33 – 1.44)
No significant effect in children (RR 1.06, 95% CI 0.62-1.83)

Zanamivir:

Not significant in X-ray confirmed pneumonia (RR 1.02, 95% CI 0.35 – 3.02)
Not significant when including self reported, investigator-mediated, unverified outcome (RR 0.90, 95% CI 0.58-1.40) In meta-regression of “pneumonia”, treatment effects were not statistically different by age (P = 0.22), drug (P = 0.89) or indication (P = 0.14), but by method of diagnosis (P = 0.025)

Results

Bronchitis, sinusitis and otitis media: No difference

Oseltamivir:

No significant effect on bronchitis (RR 0.75, 95% CI 0.56 – 1.01), sinusitis (RR 1.03, 95% CI 0.76 – 1.40) or otitis media (RR 1.11, 95% CI 0.57 – 2.15) in adults
No significant effect on bronchitis (RR 0.65, 95% CI 0.27 – 1.55), sinusitis RR 1.00, 95% CI 0.58 – 1.72) or otitis media (RR 0.80, 95% CI 0.62 – 1.02) in children

Zanamivir:

Significantly reduced risk of bronchitis in adults (RR 0.75, 95% CI 0.61 – 0.91, NNTB = 56).
No significant effect on sinusitis (RR 1.12, 95% CI 0.84 – 1.48) or otitis media (RR 0.81, 95% CI 0.54 – 1.20) in adults.
No significant effect on bronchitis (RR 0.86, 95% CI 0.26 – 2.80), sinusitis (RR 0.87, 95% CI 0.12 – 6.45) or otitis (RR 1.00, 95% CI 0.59 – 1.72) in children.

Serious complications and study withdrawals: No difference

Oseltamivir:

No significant effect in adults (RR 0.91, 95% CI 0.40 – 2.06)
Could not be assed in prophylaxis due to lack of events
Could not be assessed in children due to lack of events

Zanamivir:

No significant effect in adults (RR 1.10, 95% CI 0.46 – 2.63)
No significant effect in prophylaxis (RR 1.09, 95% CI 0.36 – 3.26)
Could not be assessed in children due to lack of events

Prophylaxis:

Oseltamivir:

Significant effect on symptomatic influenza in individuals (RR 0.45, 95% CI 0.30 to 0.67, NNTB = 33).
No significant effect for all other influenza outcomes
Significant effect on symptomatic influenza in household (RR 0.20, 95% CI 0.09 to 0.44, NNTB = 7), but no significant effect on asymptomatic influenza (RR 1.14, 95% CI 0.39 to 3.33) Post-exposure prophylaxis could not be assessed because of poor trial methodology

Zanamivir:

Significant effect on symptomatic influenza for individuals (RR 0.39, 95% CI 0.22 to 0.70, NNTB = 51))
Significant effect on symptomatic influenza in households (RR 0.33, 95% CI0.18 to 0.58, NNTB = 7)
No significant effect on asymptomatic influenza (RR 0.97, 95% CI 0.76 to 1.24)
No significant effect on asymptomatic individuals in post-exposure prophylaxis of households (RR 0.88, 95% CI 0.65 to 1.20)

Harms of Treatment:
Zanamivir: No significant increase in adverse events were reported

Harms of Treatment:
Oseltamivir:
Nausea, Vomiting and Diarrhea: More

Significantly increased risk of nausea (RR 1.57, 95% CI 1.14 to 2.15, NNTH = 28) and vomiting (RR 2.43, 95% CI 1.75 to 3.38, NNTH = 22) in adults
Significantly decreased risk of diarrhea (RR 0.67, 95% CI 0.46 to 0.98, NNTB = 43) in adults (though placebos might contain active ingredient that induces diarrhea)
Significantly increased risk of vomiting in children (RR 1.70, 95% CI 1.23 to 2.35, NNTH = 19).

Cardiac Effects: Unsure

May reduce cardiac events (RR 0.49, 95% CI 0.25 to 0.97, NNTB = 148), but may increase QTc-prolongation (RD 4.0%, 95% CI 0,71 to 7.30, NNTH = 25)

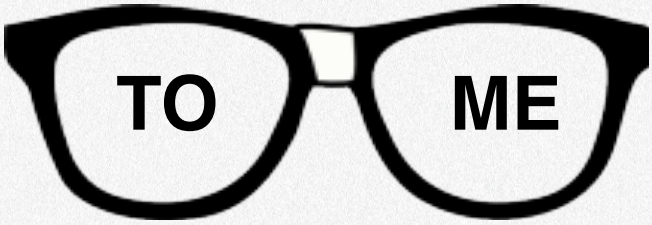
Psychiatric Effects: Perhaps (dose related)

No significant effect in treatment trials, but there was a dose response effect in two “pivotal” treatment trials between daily dosage of 150mg and 300mg (P = 0.038)
Significant effect in prophylaxis trials (RR 1.80, CI 1.05 to 3.08, NNTH 94)

Renal Effects: Perhaps

No significant effect (RR 3.17, CI 0.96 to 10.49, NNTH 150).
Sensitivity analysis with Peto´s method gives significant result (P = 0.02)

TALK NERDY TO ME



Commentary

Rather than reviewing only easily accessible and published data, the reviewers managed to get a hold of the full clinical study reports (CSRs) from regulators and industry. This allows for full statistical re-analysis and assessment of bias. In turn it gives a more complete and accurate picture of the evidence.

CSRs are the intermediate stage between the full raw data collected from a clinical trial and the summarised articles published in the journals. They contain all the information needed to conduct data analysis on data, review bias and make conclusions. These do not include confidential patient information, except in certain easily redacted appendices. Though they should be public property, they are often withheld.

Oseltamivir and Zanamivir were licensed for marketing by the FDA and EMA around the turn of the millennium. Though they at first did not sell well, the H5N1 avian influenza outbreaks quickly brought the drug to blockbuster levels. Since their licensing, the governments of the world have accumulated stockpiles for over 9 billion dollars.

The stockpiling was based on the earlier claims that NIs might reduce the time to alleviation of symptoms somewhat, and more importantly reduce the risk of complications such as pneumonia or death

The 2006 version of this review (Jefferson et al 2006) supported these claims, showing limited effects on time to first alleviation of symptoms and complications. The authors advised against use in regular seasonal influenza, but supported use in endemic or pandemic settings.

During the Influenza A H1N1 p2009 outbreak governments commissioned an updated review from the Cochrane Collaboration. While working on this a comment on the Cochrane-website Japanese paediatrician pointed out that the results were based on only one industry run meta-analysis of ten studies, of which only two were published. Further investigation into trial registries, ethical review boards and regulatory documents showed several missing trials, trial programs and missing data.

Inquiries by the Cochrane team were made to access the missing data, but for several years both industry and the relevant regulators continued to withhold the data. When they finally relented the Cochrane team reviewed the 2.2 GBs of data and regulatory comments to arrive at the review published in April 2014.

As seen in the main results here presented, they differed significantly from what was seen in the published data.

The effects of neuraminidase inhibitors in the treatment or prevention of influenza is in part difficult to assess because of major possible sources of bias in the trials.

There was generally incomplete outcome data for symptoms, complications and safety data; and a high degree of selective reporting. Many studies lacked random sequence generation. Blinding of participants and personnel was inadequate in most trials. The reviewers also report a high risk of other bias. Only allocation concealment and blinding of outcome assessment can be considered generally adequate.

Case Resolution

The nurse was told to stay home from work, drink plenty of fluids, take over the counter medications for aches and pains as needed, wash their hands well, cover their mouth when they cough, consider getting a flu shot next year and *don't stand so close to me*

Clinical Application

The evidence does not support the routine use of neuraminidase inhibitors in the treatment of influenza. The benefit of prophylactic use is debatable when balanced against the risk of adverse events. Exceptions might exist in compassionate cases.

Systematic Review 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 assessments of studies were reproducible	
The outcomes were clinically relevant	☑
There was low statistical heterogeneity for the primary outcome	☑
The treatment effect was large enough and precise enough to be clinically significant	

CONCLUSION VS COMMENTARY

COMPARISON

These are reasonable conclusions giving all the difficulties, limitations and data provided.

WHAT DO I TELL MY PATIENT?

This drug might reduce the length of time you are sick with the flu by about one day, but it might also make those days worse with more nausea and vomiting.

References

Jefferson T, Jones MA, Doshi P, Del Mar CB, Hama R, Thompson MJ, et al. Neuraminidase inhibitors for preventing and treating inf*luenza in healthy adults and children. Cochrane Database Syst Rev. 2014 Apr 10(4):CD008965.*

Guest Skeptic: Marcus Prescott

Marcus is a nurse from Norway. He works at the Trondheim University Hospital. His college thesis was called *"Barriers and Facilitators to the implementation of evidence based practice among RNs in specialist health care"*. Marcus is also a proud member of the Norwegian Skeptics' Society and runs their Skeptics in the Pub events.

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Special Edition

I Flip My Classroom Back and Forth

Dr. Stella Yiu
Stella is an Associated Professor at the Department of Emergency Medicine and a Distinguished Teacher at the University of Ottawa. Stella is an Associated Professor at the Department of Emergency Medicine and a Distinguished Teacher at the University of Ottawa.

Dr. Rob Rogers
otherwise known as Darth Educator, runs the iTeachEM blog and podcast and director of the Teaching Course. Along with a good friend, Dr. Salim Rezaie, started an educational think tank called the Teaching Institute.

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Special Edition

Why Can't this Be Love? Early Goal Directed Dating

Guest Skeptics:

Dr. Chris Bond
Chris is a clinical lecturer and emergency physician at the University of Calgary.

Dr. Teresa Chan
Teresa is an Assistant Professor at McMaster University

Usually we are trying to cut the knowledge translation window down from over ten years to less than one year. The SGEM-HOP cuts that KT window down to less than one week. This is done by getting copies of an important Emergency Medicine manuscript prior to publication. Then we do a structured critical review using a method that has been shown to be validated and reliable.

The first SGEM-HOP on geriatric falls with Dr. Chris Carpenter was a huge success. One interesting finding from that systematic review was that the inability to cut one's own toenails had the best negative likelihood ratio for 6-month fall risk. This second SGEM-HOP is going to be a special one given the holiday season.

Dating in the Treatment of Singledom and Severe Loneliness for Physicians .

Chanet al. The New Pun-land Journal of Medicine. 2014

P Medical students/trainees defined as "*single*" or "*in a successful relationship*". Only those with a Facebook status "*It's complicated*" were excluded from the study

I Derivation of the EGDD protocol and then applied in a post hoc retrospective manor

C Those that were or were not in a relationship

O Marriage or cohabitation

Authors' Conclusion:

We conclude that the use of goal-directed dating at the earliest stages of a nascent interpersonal romantic relationship may result in more clarity and results with regards to the outcome measures of marriage or cohabitation. A prospective study on this algorithm compared to standard dating practices is needed in order to determine the veracity of our claims." (Chan et al., 2014)

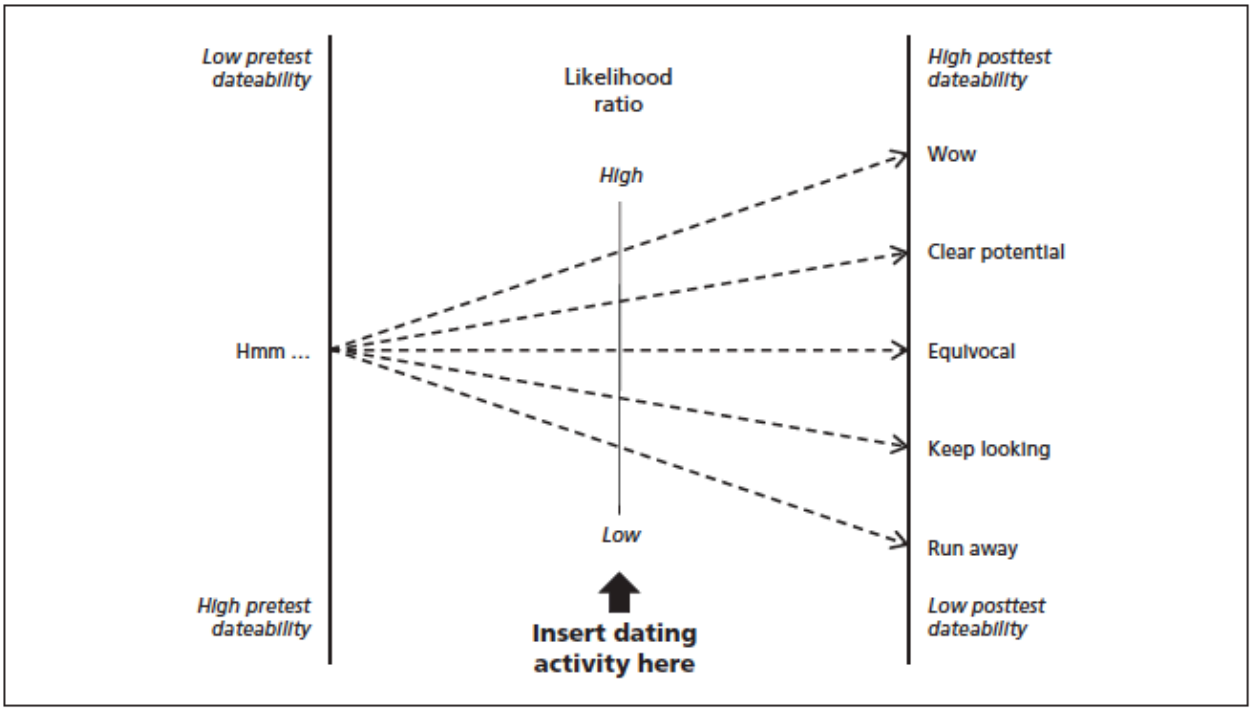
Background

The systemic assumption that one must be in a relationship in order to be fulfilled is rampant in Western culture but the many hours that young physicians spend in intensive care units, emergency departments and hospital wards often result in missing out on key milestones and skill development that are necessary for successful relationships.

A recent article by Purdy and Johnson in the CMAJ 2014 Holiday Edition raised the concept of evidence-based dating. They created a Johnson-Purdy nomogram similar to the Fagan nomogram.

Background

The Fagan nomogram was proposed in 1975 as a graphical tool for estimating the probability a patient has a disease. It requires the physician to estimate the pre-test probability. Then you perform a diagnostic test and draw a line for the post-test probability. The Johnson-Purdy nomogram was a fun way to illustrate an EBM concept and maybe even predict the likelihood of a romantic relationship.



A second article in a series Eve Purdy calls an Evidence-Based Approaches to Life was posted on her Manu et Corde in December. This involved the creation of the Canadian ITAD (Is this a Date) Decision Tool. There are high probability factors and moderate probability factors which raise your ITAD score. There are also factors that will decrease your ITAD score. A total ITAD score >100 predicts you are on a date while an ITAD score of <70 can exclude that you are on a date.

The SGEM has covered two major trials on Early Goal Directed Therapy (EGDT) this year. There was the ProCESS Trial featured on SGEM#69 and the ARISE Trial on SGEM#92. The bottom line from both of these trials was that Invasive EGDT-based sepsis resuscitation was not superior to usual care. The key elements were early recognition of sepsis. liberal IV fluid resuscitation, get a lactate level, empiric antibiotics and admit to an appropriate care setting.

The SGEM was able to get a pre-publication copy of a new protocol called Early Goal Directed Dating (EGDD). This EGDD protocol may support physicians as they navigate the complicated relationship waters and ultimately improve relationship outcomes. This mixed-methods paper first used qualitative methods to develop the algorithm, which was then validated against retrospective recollections of physicians with respect to their current relationship statuses.

Canadian ITAD Decision Tool

You are on a date with a total score ≥ 100; date can be excluded with a total score ≤ 70; gold standard testing required if total score 70-100

High Probability of Date: +40 points
- Brings flowers
- More than usual effort in clothes and scent selection
- One party pays the bill
- Physical contact

Moderate Probability of Date: +10 points
- Venue is one party's house
- One party picks the other up
- Pre-selected time and location
- Post-activity follow up planned
- Unusually complimentary

Unlikely to Be Date: -20 points
- Constant checking of cell-phone
- Picks teeth

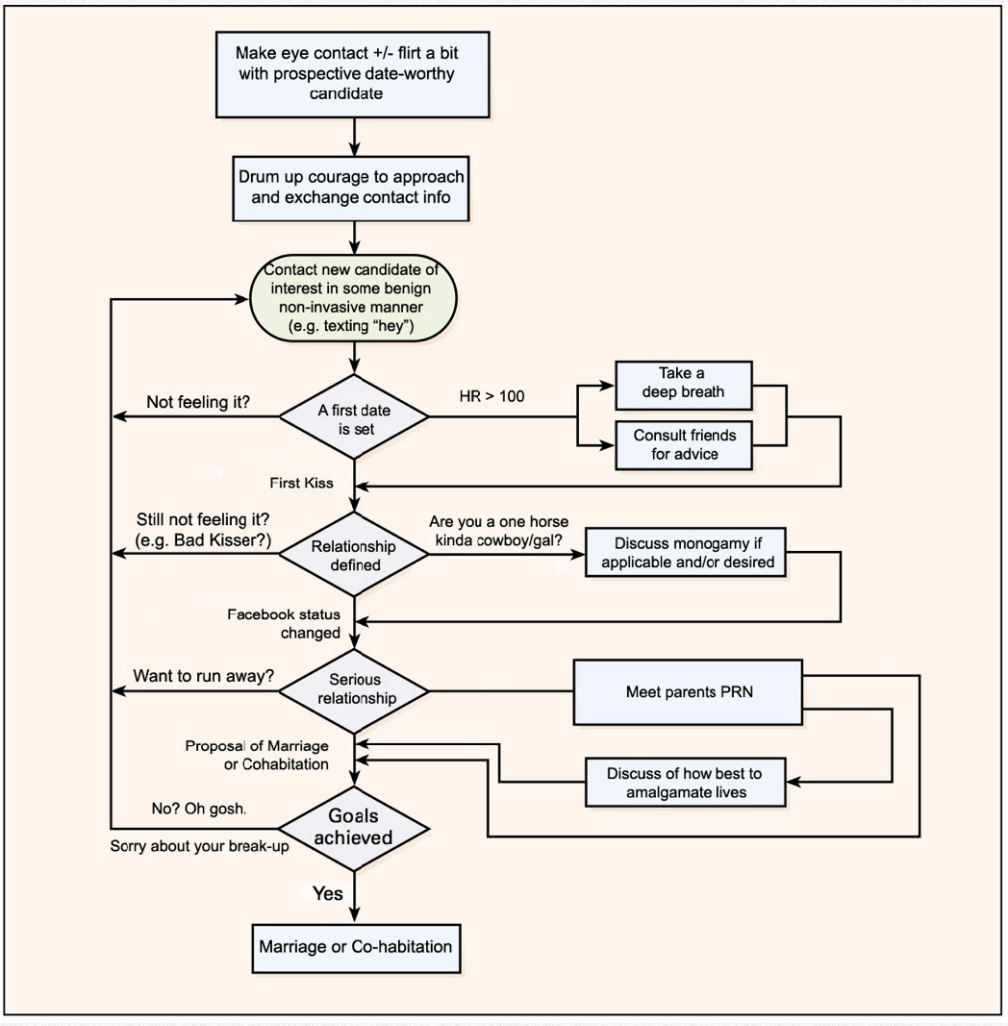
Not a date: -50 points
- Discusses other crushes
- Ends with handshake

Inclusions
- One-on-one social encounter
- At least one Canadian medical student participating
- Ambiguity related to the nature of the activity
- Age 20-35

Exclusions
- Activities planned through an online dating website
- One or more parties already in a relationship
- More than two people present
- Previously expressed romantic intent by one party
- Ends with a kiss

Results

The Early Goal Directed Dating (EGDD) algorithm when applied early in a relationship may result in more clarity and results with respect to outcome measures of marriage or co-habitation.



TALK NERDY TO ME

Commentary

This was a small study but asked a very important question. What are the key components/milestones that increase the likelihood of marriage/co-habitation? However, there were many limits to this study. So many in fact the authors say the limitations were…limitless.

It is important to note that no persons were harmed in the making of this joke article, and hence, the data is completely and utterly the result of the authors' speculations. Secondly, a retrospective cohort study is not truly an optimal study design to derive or test such an algorithm.

here were budgetary limitations which precluded a more robust study, but admittedly, a more robust study with a randomized, controlled, prospectively gathered design would require a substantial population, akin to the subject enrollment of the CRASH-2 study (SGEM#80).

Finally, a longitudinal study with more robust follow-up is required to know if, in the end, there is any mortality or morbidity (e.g. heartbreak, separation or divorce) differences between groups, since there is still a possibility that a resultant relationship may only bet temporary, and upon ending might yield further complications down the road.

BOTTOM LINE

Need to pick appropriate outcomes – Is relationship status just a surrogate outcome and should the primary outcome really be happiness.
Need to pick appropriate study design – This study design may help you derive and algorithm it may not be sufficient to prove effectiveness of an algorithm.
Need to be skeptical of the evidence – Even parody studies.

Case Resolution

Jason, being up to date on the evidence based dating literature (Johsnon-Purdy nomogram and Canadian ITAD Decision Tool) and decided to apply the EGDD algorithm. He realized that the next best step was to communicate clearly the person of interest about the status of their relationship. Together they decided that they would change their Facebook statuses and they have been progressing down the EGDD algorithm since. The authors expect an invite to their wedding.

CONCLUSION VS COMMENTARY

COMPARISON

We agree with the authors' conclusion but we eagerly anticipate the results of the ProCESS EGDD Trial and ARISE EGDD Trial that will compare EGDD to usual dating practices in a head-to-head prospective trial.

WHAT DO I TELL MY PATIENT?

Don't stress and have fun! Remember that all the steps are part of the journey.

101 Puke: Antiemetics in Adult ED Patients

Case Scenario:

You are working in the ED when you pick up the chart for an otherwise healthy 35-year-old male with the chief complaint of abdominal pain and nausea. He has had crampy generalized abdominal pain for the past 24 hours associated with one episode of emesis. He hasn't had any surgeries, he hasn't been traveling, but is a grade 3 teacher and many of the kids in his class have had "gastro". In the department he vomits while you are taking a history. How will you treat his symptoms?

Q:

What anti-emetic is most effective for emergency department patients with undifferentiated nausea?

BOTTOM LINE

Intravenous ondansetron and metoclopramide are not superior than placebo at improving patient perceptions of nausea and vomiting along a visual analogue scale 30 minutes after administration but all three provide a clinically significant improvement in symptoms.

Antiemetic Use for Nausea and Vomiting in Adult Emergency Department Patients: Randomized Controlled Clinical Trial Comparing Ondansetron, Metoclopramide, and Placebo.

Egerton-Warburton *et al.* Annals of Emerg Med. 2014

P Adult patients with nausea and vomiting during ED care for which the physician prescribed intravenous anti-emetics

I Metoclopramide 20mg IV or Ondansetron 4mg IV

C 0.9% Saline

O Mean change in severity rating on the visual analog scale 30 minutes after administration of study drug

Authors' Conclusion:

In summary, this study found that although 20 mg intravenous metoclopramide and 4 mg intravenous ondansetron resulted in slightly greater VAS score reductions than saline solution placebo, differences did not reach significance. Comparable majorities in each group also reported symptom improvement and satisfaction with treatment. This supports the findings of the other placebo- and non placebo-controlled studies, which also suggest that all antiemetic drugs, with the possible exception of droperidol, are similar….This adds weight to a recommendation that drug use not be routine and that condition-specific treatments, where possible, and other supportive measures, such as provision of intravenous fluids, be undertaken in the first instance (Egerton-Warburton et al., 2014)

Background

Nausea and/or vomiting are common emergency department presentations. While investigating underlying cause and establishing a diagnosis are important, so too is the goal of relieving the patient's symptoms. The success of pharmacologic anti-emetic strategies in oncology and post-operative patients (1, 2) has been extrapolated to support their use in patients with un-differentiated nausea and vomiting in the ED. Four studies (3, 4, 5, 6) have shown success of metoclopramide and/or ondansetron in reducing the severity of nausea in the ED but the only two placebo controlled studies showed no benefit of these medications over placebo (3, 4). Severity of nausea and vomiting is frequently measured using a visual analogue scale (VAS) and a minimally significant change has previously been defined as 15mm.

Results

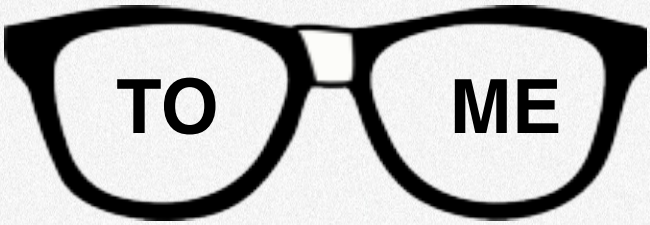
The differences in mean VAS score change for ondansetron, metoclopramide, and placebo of 27 mm (95% CI 22 to 33 mm), 28 mm (95% CI 22 to 34 mm), and 23 mm (95% CI 16 to 30 mm), respectively, were not statistically significant between the 3 groups.

Less need for rescue medication in the metoclopramide group (18%) compared to ondansetron (35%) and placebo (36%). No statistically significant differences in the other secondary outcomes.

Nine adverse events were reported (3.5%) with six were in the metoclopramide group. Of those, two had akathisia, two had restlessness, one had muscle twitching, and one was diaphoretic.

There were also two minor adverse events with ondansetron and one with placebo

TALK NERDY TO ME



Commentary

Sampling: all physicians and nurses were trained in recruiting but a "convenience sample" of patients was recruited based on how busy the department was at a given time. There is no data provided to support that this sample was overall representative of patients coming through the ED. It sounds as though patients were unlikely to be recruited during busy ED times, which likely created some degree of sampling bias.

Differential Co-Treatment: unknown whether groups were treated the same as we have no data on whether opioids/steroids/other medications were given differently to each group. Since there is no guarantee in the protocol that groups remained similar throughout ED stay, we are left to hope that proper blinding prevented against any systematic confounding bias towards or against a specific treatment.

Patient Important Outcomes: The study endpoint was symptoms at 30 minutes, however, nausea often comes in waves rather than being a persistent phenomenon. As such, it would have been helpful to see comparison at a number of different evaluation time points (ie. 60 minutes, 120 minutes) to account for more realistic symptomatology and provide information that may be relevant when considering patient discharge.

Medication Dosing and Type: The dosing of medications must be considered. The recommended dose of ondansetron is 0.15mg/kg so it could be argued that patients were actually under dosed in this trial by receiving 4mg. Conversely, metoclopramide is most often dosed at 10mg (rather than 20mg) so the increased number of side effects may have been attributable to that. Unfortunately this trial did not include anti-emetics delivered PO. IM or SL. We often administer medications this way to avoid an IV. We can't extrapolate the results from this study for those alternate antiemetic strategies.

Case Resolution

You return to the 35 year old. You discuss with him that based on his current symptoms you are not worried that something dangerous is causing his vomiting. You let him know that there are options for IV medications to treat nausea but that they are no better than placebo for patients like him. He opts not to get poked. You highlight that the main key is that he needs to stay hydrated and encourage him to take small sips of electrolyte rich beverage and discharge him home with specific instructions about when to return.

Clinical Application

This study is a reminder that identifying a cause for nausea and vomiting then targeting treatment to that cause is likely more effective than a shotgun approach to all undifferentiated nausea and vomiting.

RCT 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 groups to which they were randomized	☑
The study patients were recruited consecutively (i.e. 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

This is a sample of 270 ED patients that may have been selected with some degree of selection bias and the medications may not have been optimally dosed. It does not provide convincing evidence that anti-emetics have no effect in ED patients with nausea and vomiting but it certainly does question routine use of these medications.

The author's conclusions are actually fairly balanced and agree that this paper simply adds to a growing body of evidence. The authors' conclusions were that it "adds weight to a recommendation that drug use not be routine and that condition-specific treatments, where possible, and other supportive measures, such as provision of intravenous fluids, be undertaken in the first instance"

WHAT DO I TELL MY PATIENT?

We will rule out worrisome/dangerous causes of nausea and vomiting. Most people improve with hydration and we are unsure if medications help. If you get worse, your symptoms change (fever, GI bleeding, pain, etc) or you are otherwise worried we are happy to see you again.

References

1.Carlisle JB, Stevenson CA. Drugs for preventing postoperative nausea and vomiting. Cochrane Database Syst Rev. 2006 Jul 19(3):CD004125.

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Guest Skeptic: Eve Purdy

4th year medical student from Queen's University

Creative for behind the excellent medical student blog Manu et Corde

She is also an editor for BoringEM

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Text Me for Emergency Department Follow-Up

Case Scenario:

37-year-old right-handed attorney presents with right wrist pain after diving for a racquetball. X-rays of the wrist reveal no scaphoid fracture or other injury. He nonetheless decides that a splint and follow-up with Orthopaedic Hand Clinic follow-up is the best option for him. You schedule an appointment 11-days from today. Given his busy schedule, you offer an ED-based reminder that he will receive via his cell phone and he inquires about the need for such a reminder.

Q:

Can an automated text message to remind emergency department patients of follow-up appointments improve adherence to follow-up?

BOTTOM LINE

Under-powered single-center randomized controlled trial with per-protocol analysis suggesting that English- or Spanish language text messaging improves post-ED appointment compliance with NNT 10, although the effect is not apparent in Spanish speaking patients

Improved Attendance at Post-Emergency Department Follow-up Via Automated Text Message Appointment Reminders: A Randomized Controlled Trial

Arora *et al.* Acad Emerg Med. 2015

P Urban ED patients >18 years of age who own a cellphone, are capable of reading text messages, and have a follow up appointment scheduled within3 to 30 days following ED.

I English or Spanish personalized mobile phone text message appointment reminders at 7, 3 and 1 day before their first scheduled follow up appointment

C Usual care with written follow-up instructions

O Proportion of subjects who attended their first (closest to discharge date) scheduled follow-up appointment

Authors' Conclusion:

Automated text message appointment reminders resulted in improvement in attendance at scheduled post-ED discharge outpatient follow-up visits, and represent a low-cost and highly scalable solution to increase attendance at post-ED follow-up appointments, which should be further explored in larger sample sizes and diverse patient populations. (Arora et al., 2015)

Background: Follow-up appointments in the ED, primary care or specialty clinics are often required after emergency department visits. However, patients often do not show up for these appointments.

The reasons for missing appointments are complex but the most common reason provided is that they just forgot. It is known that these follow-ups can prevent bounce-backs to the ED, improve patient outcomes and reduce malpractice risk. People have tried using case management, sending something in the mail or phone calls. These methods are labor intensive and costly.

Text messaging has surpassed the number of phone calls made on mobile devices. That is why we thought this might be a effective, low cost and acceptable way of addressing the problem of missed follow-up appointments.

Results

Amongst 374/2365 who met eligibility criteria, 70.4% were Hispanic with a median time to ED follow-up appointment of one week.

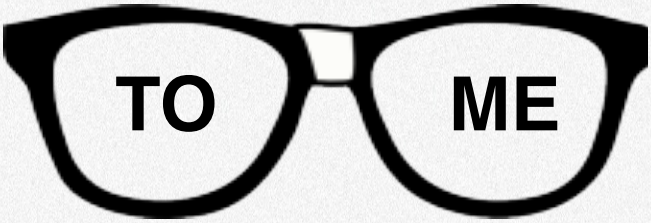
In the Intention to Treat analysis, appointment attendance was 70.2% in the intervention group vs. 62.1% in the control group, a 8.1% absolute risk reduction (95% CI -1.6% to 17.7%, p = 0.100).

In the per-protocol analysis 46 patients from the intervention arm were excluded because they did not receive the text messages and the appointment attendance rate was 72.6% in the intervention group vs. 62.1% in the control group (ARR = 10.5%, 95% CI 0.3% to 20.8%, p = 0.045)

That give you a NNT: Number Needed to Treat (or number needed to text) of 10 (95% CI 5 to infinity).

In multivariate logistic regression, text message reminders significantly increased appointment adherence in English language for both primary care and specialty care appointment types, but had no significant effect on Spanish speakers regardless of appointment type.

TALK NERDY TO ME



Commentary

Fascinating trial using readily available technology to remove one common barrier to post-ED follow-up: forgetfulness.

The randomization process was not concealed from patients who knew whether they were receiving text message reminders or not, but future trials could remove this methodological criticism by using sham texts in the control group.

Commentary

In addition, future investigators could evaluate unintended consequences of this intervention. Although patients without text plans would be charged a maximum of $0.80 for the four text messages sent using this study protocol, other text messaging plans may result in larger costs incurred by patients who cannot afford the expense.

Other unintended consequences might include accidents related to distractions of text messages received at inopportune times (while driving or involved in other high-concentration activities).

Although the concurrent reporting of intention-to-treat (ITT) and per-protocol results may be viewed by evidence based medicine advocates as flawed because only the ITT analysis retains the equal distribution of measured and unmeasured prognostic factors between the intervention and control groups, the approach of reporting both provides the best of both worlds: the purist researcher minimally biased ITT result and the real-world pragmatist per-protocol result.

They report forgetting appointments is the most commonly reported barrier to more efficient post-ED follow-up, but all four of their supporting references are from the United Kingdom with universal access to health care. The situation may be more complex in the United States where indigent urban populations are largely uninsured and those that are insured are most often underinsured with limited access to high quality outpatient follow-up.

Other unmeasured barriers to post-ED follow-up include access to transportation, limited health literacy, job status and ability to miss work for appointments, and ability to afford clinic co-pays.

The pre-study sample size calculation (80% power, two-sided alpha 0.05) included a sample size of 626, but they only enrolled 374. This probably explains the wide confidence intervals on the NNT.

Future studies could look at two-way messaging between patient and the follow-up provider, texting the elderly or impaired patients' caregivers and looking at sub-populations (dialysis patients, chronic pain patients, frequent flyers, frail older adults, and those with high co-morbid disease burdens).

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RCT 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 groups to which they were randomized	☑
The study patients were recruited consecutively (i.e. 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	☑

Case Resolution

The 37 year-old lawyer with the wrist injury receives the text reminder on the day before his appointment, remembers to follow-up with Orthopaedic Hand Clinic, and is able to discontinue his thumb-spica splint with a painless wrist without any further imaging.

Clinical Application

None yet, since this is a single-center exploratory trial and the results merit replication before investing in the infrastructure needed for EDs to provide specific post-discharge follow-up appointment dates/times/locations with text messaging to reinforce later patient recall of the appointment. Nonetheless, this approach is cheap, readily available, and appears promising for future widespread use if the results can be reproduced in other settings.

CONCLUSION VS COMMENTARY

COMPARISON

The current single-center study provides proof-of-concept that text messaging reminders can be initiated from busy urban multilingual ED settings, but additional research is required to understand barriers to efficient follow-up care in North America and the role that text messaging serves to improve this efficiency.

Future studies need to assess unintended adverse consequences and target sub-populations most likely to benefit from text messaging reminders.

WHAT DO I TELL MY PATIENT?

Complete assessment of your medical condition often requires follow-up with another healthcare provider so prior to being discharged from the ED today you have been provided an appointment with another physician. Because you probably do not feel well today and because ED providers gave you a lot of information to think about today, remembering when and where your appointment is can be challenging. Recent research suggests that a text reminder written by you and to you 7-, 3-, and 1-day before your appointment can help you to make it to that office visit with 10 patients like you requiring a text for one to make it to their appointment who otherwise would not.

References

Arora S, Burner E, Terp S, et al. Improved Attendance at Post-Emergency Department Follow-up Via Automated Text Message Appointment Reminders: A Randomized Controlled Trial, Acad Emerg Med 2015

Guest Skeptic: Dr. Chris Carpenter

Chris is an Associate Professor, Emergency Medicine. Director, Evidence Based Medicine, Washington University. Chris also wrote the book on EMB Co-Author of Evidence Based Emergency Care-Diagnostic, Testing and Clinical Decision Rules.

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Just Breathe: Inhaled Corticosteroids for Asthma Exacerbations

Case Scenario:

25-year-old smoker is seen in emergency department for acute respiratory distress. He has a diagnosis of asthma and is an occasional user of salbutamol. He has about two asthma exacerbations/year, one previous hospital admission and no intensive care unit admissions. You are preparing to discharge him home and wonder if inhaled steroids would benefit the systemic steroids you are prescribing.

Q:

Is there a benefit for inhaled corticosteroid use in the emergency department in acute asthma presentations?

BOTTOM LINE

Adding some form of inhaled corticosteroid to acute asthma presentations (either low or high dose) is likely to benefit your patient (adult or paediatric) on multiple levels, but mainly admission requirements. The use of inhaled corticosteroids will not circumvent the requirement for systemic corticosteroid use.

Early Use of Inhaled Corticosteroids in the Emergency Department Treatment of Acute Asthma

Edmonds et al. CDSR 2012

P 1,403 patients from 27 randomized and quasi-randomized clinical trials. The population included adults and children (13 paediatric and 7 adult clinical trials) who presented to the ED in acute respiratory distress thought to be due to acute asthma exacerbation.

I Inhaled corticosteroid therapy (ICS) used in multi-modal therapy for acute presentations for asthma exacerbations.

C Standard treatments for acute asthma exacerbations; beta 2-agonists and systemic corticosteroids

O Primary: Admission to hospital via the emergency department

Authors' Conclusion:

"This review found that inhaled corticosteroids used alone or in combination with systemic corticosteroids helped to relieve asthma attacks, were well tolerated, and had few side effects. The authors conclude that at this time there is insufficient evidence to support using ICS alone as a replacement for systemic corticosteroid therapy in acute asthma attacks" (Edmonds et al. 2012)

Background

300 million diagnosed worldwide
1 in 250 deaths worldwide is attributed to asthma
27 million people in the USA have at some time received a diagnosis of asthma
2 million emergency department visits/year (USA)
Up to 20% admission & bounce-back in two weeks
Steroid therapy is central to asthma management
There are several potential advantages to ICS use such as less systemic side effects, direct delivery to the airway, greater efficacy in reducing airway reactivity and edema

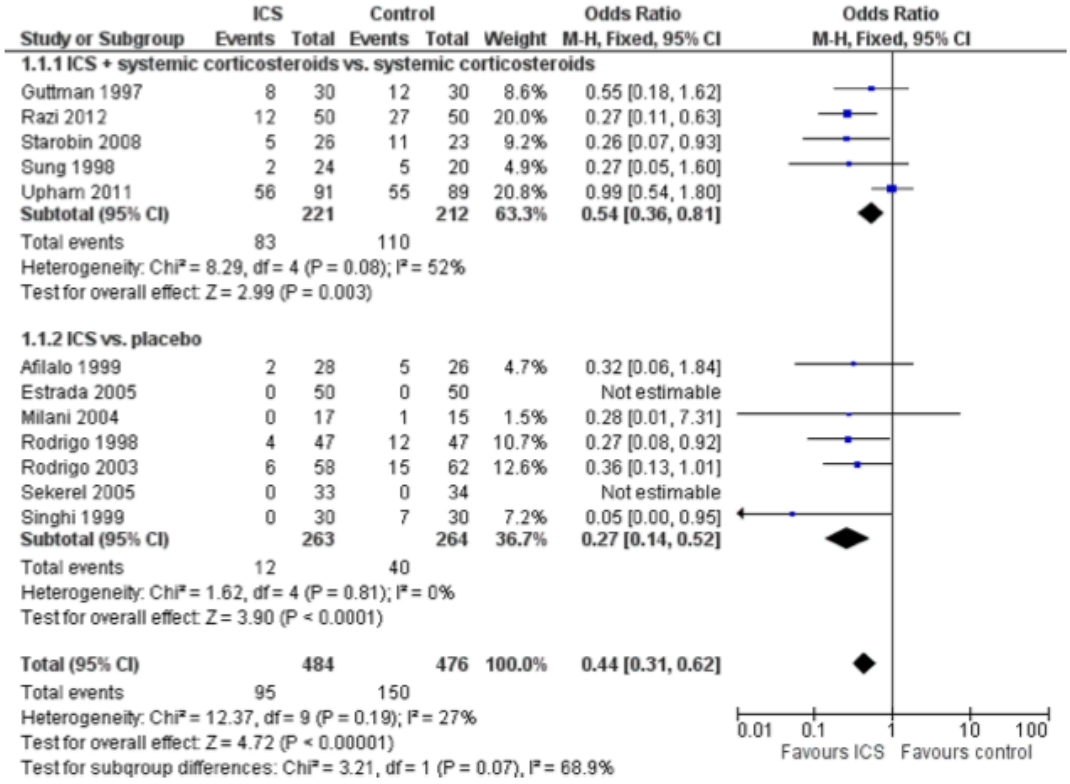
Results

Inhaled corticosteroid use in acute asthma in conjunction with systemic corticosteroids resulted in reduced hospital admissions while not increasing adverse effects or demising the other measures of successful asthma treatment in the emergency department.

Objective parameters of asthma severity also demonstrated improvements with ICS treatment such as; improvements in peak expiratory flow and forced expiratory volume in one second. There were no significant adverse affects noted with ICS treatment (tremor or nausea and vomiting).

ICS reduced admissions OR 0.44, 95% CI 0.31-0.62

Figure 4. Forest plot of comparison: 1 ICS versus placebo, outcome: 1.1 Admission to hospital.



TALK NERDY TO ME

Commentary

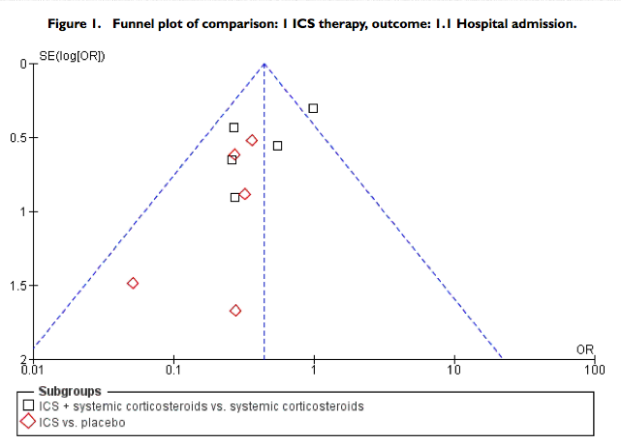
This was a well done Cochrane Review on the subject of inhaled corticosteroids for the treatment of acute asthma. I am going to talk a little EBM nerdy here just to reinforce what a good systematic reviewers did.

They did an exhaustive search looking for information on this subject. They went thought all the reference lists, contacted the authors asking about unpunished studies, hand searched abstracts from international conferences, contacted scientific advisors of various pharmaceutical companies who manufacture ICS products and personally reached out to other trialists working in the filed of asthma…now that is what I call exhaustive.

They assess for heterogeneity visually and calculated the I2 statistics which can be seen in the included forrest plot.

0% to 40%: might not be important
30% to 60%: may represent moderate heterogeneity
50% to 90%: may represent substantial heterogeneity
75% to 100%: considerable heterogeneity

They also looked for publication bias using a funnel plot. This helps you visualize the various studies to see if there is any asymmetry. Some EBM people feel that visual inspection of funnel plots is not useful due to the subjective nature of the assessment.



Systematic Review 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 assessments of studies were reproducible	☑
The outcomes were clinically relevant	☑
There was low statistical heterogeneity for the primary outcome	☑
The treatment effect was large enough and precise enough to be clinically significant	☑

Case Resolution

The 25 year-old man with an asthma exacerbation is discharged home with a short course of oral steroids and inhaled corticosteroids. He is also encouraged to quit smoking cigarettes.

Clinical Application

Inhaled corticosteroid is an option to be considered for acute asthma presentations in children and adults in the emergency department but only when used in conjunction with systemic corticosteroids.

References

Edmonds et al. Early use of inhaled corticosteroids in the emergency department treatment of acute asthma (Review). CDSR Dec 2012.

CONCLUSION VS COMMENTARY

COMPARISON

The main outcomes of focus was hospitalization. This is a very important patient oriented outcome and emergency physician oriented outcome; especially with all the current emergency department over-crowding issues as admitted patients are being boarded in the department.

The secondary outcomes were parameters of asthma severity such as peak flow and forced expiratory peak flow in one second. These often predict hospitalization in the emergency department but in isolation are not as useful to the emergency provider. This because these assessments of peak flow and FEV1 are often not used across all emergency departments

WHAT DO I TELL MY PATIENT?

Early use of steroid puffers with with oral steroids will improve your chances of not needing to be admitted to hospital with your asthma flair.

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Let's Talk About Sex Baby
Let's Talk About STDs

Case Scenario:

28-year-old male who presents to your emergency department with a three-day history of urethral discharge and moderate to severe dysuria. On physical exam, you note the presence of a yellowish urethral discharge and bilateral inguinal adenopathy, which is moderately tender to palpation. You note that his chart states that he has an allergy to ceftriaxone, and when you question him further regarding the type of reaction that occurred, he states to you that the last time he was treated for this, he developed an anaphylactic reaction to the drug. You would like to empirically treat him for gonorrhea and chlamydia.

Q:

What viable options do we have in the empiric treatment of gonorrhea in the patient who has a cephalosporin allergy or if there are concerns related to cephalosporin-resistant infections?

BOTTOM LINE

Azithromycin in combination with either gentamicin or gemifloxacin administered as one-time dose are highly effective and generally tolerable in managing otherwise healthy patients with suspected uncomplicated gonococcal infection.

The Efficacy and Safety of Gentamicin Plus Azithromycin and Gemifloxacin Plus Azithromycin as Treatment of Uncomplicated Gonorrhea

Kirkcaldy et al. Clinical Infectious Diseases 2014

P Patients between the ages of 15 to 60 years of age seen at outpatient STD clinics within the United States with "suspected infection" of Neisseria gonorrhoeae of the urethra or cervix

I Single dose combination of gentamicin (240mg IM) and azithromycin (2g PO) OR
Single dose combination of gemifloxcacin (320mg PO) and azithromycin 2g PO

C None

O Microbiological cure: defined as negative follow-up culture for urogenital N. gonorrhoaeae at 10 to 17 days after receipt of study medication

Exclusion Criteria:

- *Patients <15 years of age*
- *History of renal insufficiency, hepatic insufficiency, cardiac arrhythmia, rheumatoid arthritis, tendon disorder*
- *Recipient of kidney, lung or heart transplant*
- *Allergy to macrolides, aminoglycosides or fluoroquinolones*
- *Concomitant infection requiring systemic antibiotics*
- *Recipient of systemic /intravaginal antimicrobials within 30 days of study*
- *Current use of corticosteroids, immunosuppressives or medications for cardiac arrhythmias*
- *PID, testicular pain, disseminated gonococcal infection, genital ulcer disease*
- *Bacterial vaginosis*

Authors' Conclusion:

"The results of this trial indicate that the combinations of azithromycin plus gentamicin or gemifloxacin exhibit excellent efficacy for treatment of uncomplicated urogenital gonorrhea. Cephalosporin resistance in N. gonorrhoeae is expected to emerge, and these combinations may be helpful for patients infected with ceftriaxone-resistant gonococci or patients with severe cephalosporin allergy. This trial provides much-needed data in the short term, but additional treatment options for gonorrhea are urgently needed." (Kirkcaldy et al., 2014)

Background

For any clinician who really wants to get a good handle and better appreciation of how antimicrobial resistance has really affected the way we treat infections, look no further than the history and evolution of how we have managed gonococcal infections over the past century.

The evolution of treatment strategies for the management of gonorrhea over the past century is rather fascinating and disheartening. We have exhausted the use of penicllins, sulfonamides, tetracyclines, and fluoroquinolones for the treatment of this condition.

In 2011, due to treatment failures, decreased in vitro susceptibility, and greater demonstrated efficacy for pharyngeal infection, the Centers for Disease Control and Prevention (CDC) recommended higher doses of ceftriaxone to be used for gonococcal infection (250 mg from 125 mg administered parenterally as a one-time dose).

Concerns related to an increase in the number of isolates of gonorrhea that exhibited elevated minimum inhibitory concentrations (MICs) to cefixime prompted the CDC to no longer recommend the use of oral cephalosporins for the treatment of gonorrhoea. And just in 2013, the CDC named gonorrhoea as one of the top three diseases considered to be an urgent threat to the United States.

Actions recommended to address the increase in cephalosporin-resistant gonococcal infection included increased public awareness and preparedness by public health agencies and studies to be conducted related to alternative treatment regimens and combinations of therapy as well as the clinical development of novel agents to manage this condition.

Results

Primary Outcome:

100% microbiological cure achieved in those patients treated with gentamicin and azithromycin (lower 1-sided exact 95% CI bound, 98.5%) of 202 patients in per protocol analysis.

99.5% microbiological cure achieved in those patients treated with gemifloxacin and azithromycin (per protocol analysis, lower 1-sided exact 95% CI bound, 97.6%) of 199 patients in per protocol analysis.

Secondary Outcome:

All patients included in the study with pharyngeal gonorrhea and rectal gonorrhea were microbiologically cured.

	Pharyngeal Gonorrhea (n =25)	Rectal Gonorrhea (n =6)
Gentamicin + Azithromycin	10	1
Gemifloxacin + Azithromycin	15	5

Mild to moderate nausea: 25.9% gentamicin/azithromycin versus 40.3% gemifloxacin/azithromycin

Diarrhea: 17.4% gentamicin/azithromycin versus 22.1% gemifloxacin/azithromycin

Vomiting within 1 hour: 3.3% gentamicin/azithromycin versus 7.7% gemifloxacin/azithromycin

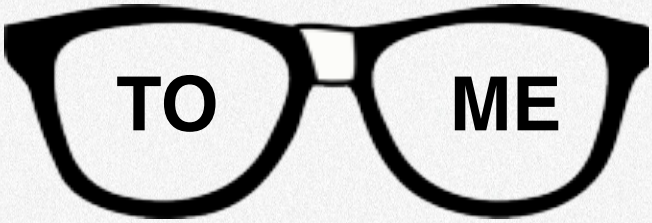
Antimicrobial susceptibility: Percentage of isolates with elevated minimum inhibitory concentrations at or above breakpoint prior to treatment for N. gonorrhoea.

Azithromycin: 0.5%

Gentamicin: 0%

Gemifloxacin: 17.1%

TALK NERDY TO ME



Commentary

Male to Female Ratio: Compared to the male population, a large proportion of females who were randomized and treated were excluded from analysis in the study due to negative bacterial cultures upon enrollment (48.7% female versus 11.8%). However, this may be representative of the fact that gram-stain may not be as reliable for diagnosis of gonorrhea in females compared to males (D'Angelo LJ, Mohla C, Sneed J et al. *J Adolesc Health Care* 1987; 4:344-348).

Pregnancy: The elimination of pregnant patients within this study makes it difficult to apply these results to the general population. The current standard of treatment with ceftriaxone is pregnancy category B, as is azithromycin. However, gemifloxacin and gentamicin are pregnancy category C and D, respectively, although these categories will be removed by the FDA in the future and replaced with alternative labeling, and it will be interesting to see the implications of these labeling changes with respect to recommended regimens in the management of all disease, including gonorrhea.

Diagnostic Testing: Results from gram stain and culture may be limited and inadequate for detecting infection in specimens obtained from the endocervical canal, urethra, or urine. Nucleic acid amplification tests (NAATs) obtained from these specimens may be necessary for detection of gonococcal infection (*MMWR Recomm Rep*. 2014; 63(RR-02):1-19).

Synergy: As per the CDC guidelines, azithromycin 2 g orally as a single dose can be offered as an alternative in those patients with a documented cephalosporin allergy.

This study incorporated the use of this treatment option along with either gentamicin IM or gemifloxacin PO. Future studies with these regimens may entail the evaluation to determine if efficacy and safety were associated with synergy between the combination of azithromycin with either agent or due to one drug alone.

RCT 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 groups to which they were randomized	☑
The study patients were recruited consecutively (i.e. 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	☑

Commentary

Patient History: The management of STIs is heavily dependent on patient history in addition to clinical signs and symptoms. In this study, pharyngeal and rectal specimens were only obtained if patients reported exposure, which may lead to an underestimation of the actual number of patients infected in these areas. The types of questions asked by clinicians of patients related to sexual history were not described. This may also be problematic since a period of 10 to 17 days elapsed before a follow up visit was conducted, which may have allowed for possibility for additional sexual activity and/or re-exposure.

Tolerability: The incidence of gastrointestinal adverse events across both treatment arms in this study was not insignificant, but did occur less frequently in those patients who received gentamicin in combination with azithromycin compared to those who received gemifloxacin in combination with azithromycin. Is it warranted and/or practical to provide suspected infected patients with a prophylactic antiemetic and/or small snack in the ED prior to treatment with either combination of agents?

Susceptibility Patterns: The authors do note that interpretation of the number of isolates demonstrating an elevated MIC breakpoint with gemifloxacin is not well defined. While this may require further analysis for determination of clinical relevance in in relation to treatment for gonococcal infection, interpretation of these values may not reasonably occur within the ED setting.

Implications with antimicrobial stewardship for STIs in the emergency department: Although antimicrobial stewardship is becoming a common practice for culture follow up in patients who are discharged from the emergency department, more often than not, these patients are often empirically treated prior to being discharged following the collection of gram-stains and/or Nucleic Acid Amplification Tests. For most EDs, nearly all culture results for gonorrhea and other STIs will return negative or positive with no further results provided related to antimicrobial susceptibility. Since resistance is becoming a growing issue related to this condition, additional mechanisms may need to be in place to allow for reported susceptibility patterns, which may lead to additional resources and costs associated with treatment.

CONCLUSION VS COMMENTARY

COMPARISON

Overall, this was a well-intentioned study aimed to evaluate the efficacy and safety of viable alternative treatment options in the era of increased resistance in gonococcal infection.

Although the authors did demonstrate similar rates of microbiological cure with combination treatment regimens consisting of gentamicin and azithromycin as well as gemifloxacin and azithromycin, due to better tolerability and superior antimicrobial susceptibility patterns, it may be reasonable to prefer the combination treatment regimen of azithromycin with gentamicin versus azithromycin with gemifloxacin.

However, it may be reasonable to conduct future studies evaluating the feasibility of these treatment regimens within the ED setting, since many practical factors associated with this study as pointed out above may need to be further delineated to determine overall applicability of the findings of this study to our patient population

Case Resolution

You offer your 28-year-old patient empiric treatment for his gonococcal infection, and highlight that two antimicrobial regimens may be used as a potential cure for his infection: two oral agents as a single dose or one parenteral and one oral agent as one-time doses.

You discuss with him that although the combination of these agents have not had widespread utilization for the treatment of this condition, they have been shown in small populations to be associated with cure of his infection, which may be especially helpful in his case given his previous history of infection as well as his allergy to cephalosporins, the standard treatment of this condition.

You counsel him related to the potential for adverse effects, mainly gastrointestinal in nature, and he decides to choose the combination of parenteral gentamicin and oral azithromycin for empiric therapy. He receives treatment with no adverse effects noted, and prior to discharge, you advise him related to safe sexual practices.

You also inform him that it is essential that he notify his sexual partner regarding the need for evaluation and treatment for the same infection.

Clinical Application

This study provides us with potential alternative options that may be used for the management of suspected uncomplicated gonococcal infection in patients who may be at increased risk for resistance or in those patients who have a cephalosporin allergy.

References

Kirkcaldy et al. The Efficacy and Safety of Gentamicin Plus Azithromycin and Gemifloxacin Plus Azithromycin as Treatment of Uncomplicated Gonorrhea. Clinical Infectious Diseases 2014

WHAT DO I TELL MY PATIENT?

The combination of azithromycin with either gentamicin or gemifloxacin administered as one-time doses will likely cure your suspected gonococcal infection, as the combination of agents has been found to be safe and effective in otherwise healthy patients.

Guest Skeptic: Dr. Nadia Awad
Nadia is an assistant professor of emergency medicine at the Ernest Mario School of Pharmacy at Rutgers University, and the emergency medicine pharmacist at Robert Wood Johnson University Hospital Somerset.

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Does this Woman Have An Ectopic Baby, Baby?

Case Scenario:

23-year-old woman presents to the emergency department with sudden onset of vaginal bleeding and lower abdominal pain. There has been no change in her bowel or bladder habits. She has a history of irregular periods, does not know when her last *"normal"* period was and has never been pregnant. She is sexual active and sometimes uses condoms.

Her vitals are blood pressure 110/70, heart rate 90, afebrile and oxygen saturation 99% on room air. Abdominal exam reveals a tender suprapubic area, volunteer guarding with positive bowel sounds. The pelvic exam is normal. Urine pregnancy test is positive. You are concerned about an ectopic pregnancy.

Q:

Does this woman have an ectopic pregnancy?

BOTTOM LINE

Transvaginal ultrasonography is an excellent test for diagnosing ectopic pregnancy.

Does this Woman Have an Ectopic Pregnancy? Crochet et al. JAMA 2013

P Medline and EMBASE for English articles from 1965-Dec 2012. Included 14 studies (n=12,101) of women with confirmed pregnancy, abdominal pain, vaginal bleeding or clinical suspicion of ectopic in early gestation.

I Physical exam findings, lab tests (bHCG) and transvaginal sonogram

C None

O Diagnosis of ectopic pregnancy, confirmed by surgical visualization and/or clinical follow-up

Authors' Conclusion:

"Symptoms of abdominal pain and vaginal bleeding in early pregnancy warrant an trans-vaginal ultrasound in order to rule out ectopic pregnancy. This is the single best diagnostic modality in making the diagnosis." (Crochet et al., 2013)

Background

- Ectopic pregnancies represent approximately 2-3% of all pregnancies
- Leading cause of 1st trimester maternal death
- Higher incidence in in vitro fertilization population
- Less than half of emergency department patients present with the classic abdominal pain and vaginal bleeding
- 50% of patients with ectopic pregnancies have no identifiable risk factor

Ectopic pregnancies represent a significant medical-legal risk. The Canadian Medical Protection Association (CMPA) reviewed all the ectopic cases from 2003 to 2007. They found 23 total open and closed cases. Of the 17 closed cases, delayed diagnosis was the number one reason for the medical/legal problem. There were 10 tubal ruptures and no maternal deaths in this series.

Table 1: Risk factors for ectopic pregnancy[9,17,18]

Factor	OR (and 95% CI)		
	Ankum et al[17]	Mol et al[18]	Dart et al[9]
Previous tubal surgery	21 (9.3–47)	–	–
Previous ectopic pregnancy	8.3 (6.0–11.5)	–	–
In utero DES exposure	5.6 (2.4–13)	–	–
History of PID	2.5 (2.1–3.0)	–	–
History of infertility	2.5–21*	–	5.0 (1.1–28)
History of chlamydial or gonococcal cervicitis	2.8–3.7*	–	–
Documented tubal abnormality	3.5–25*	–	–
Tubal ligation	–	9.3 (4.9–18)	18 (3.0–139)
Current IUD use	–	4.2–45*	5.0 (1.1–28)

Note: OR = odds ratio, CI = confidence interval, DES = diethylstilbestrol, PID = pelvic inflammatory disease, IUD = intrauterine device.
*Range; summary OR not calculated owing to significant heterogeneity between studies.

Experts thought the following factors contributed to the diagnostic delay:

- Delay in attending the patient
- Failure to perform a pelvic examination
- Failure to perform appropriate diagnostic investigations in women of reproductive age who presented with abdominal pain and vaginal bleeding
- Inadequate systems for the follow up of diagnostic investigations and/or patients

Results

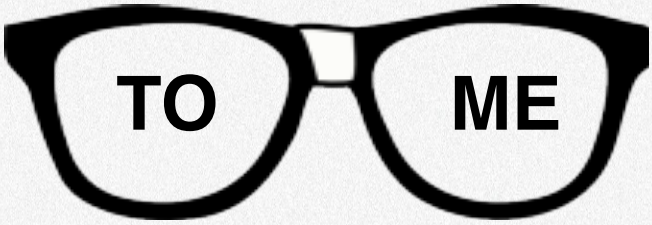
Among the 14 articles that were chosen to be included, the summary prevalence of ectopic pregnancy was 15% (IC 10-22%, I=96%). The positive likelihood ratios (+LR) for history and symptoms were less than 1.5, indicating limited clinical value.

A discriminatory zone for beta HCG levels is still not determined, and a single level cannot rule out ectopic pregnancy. Transvaginal ultrasonography was the best diagnostic modality with a +LR of 111 when there was an adnexal mass or no intrauterine pregnancy. The –LR was also very good at 0.12 but with wide confidence intervals (0.03-0.55).

Table 2. Summary Measures for Findings of Ectopic Pregnancy[a]

Finding	No. of Patients	Sensitivity	Specificity	LR+ (95% CI), I^2	LR− (95% CI), I^2
Physical examination					
Cervical motion tenderness[b]	1435[20,22,51]	0.45 (0.33-0.57)	0.91 (0.80-0.96)	4.9 (1.7-14), I^2 = 93%	0.62 (0.47-0.83), I^2 = 82%
Peritoneal findings[c]	868[41,51]	0.23-0.27	0.94-0.95	4.2-4.5	0.78-0.81
Adnexal mass[b]	1378[22,41,51]	0.09 (0.02-0.27)	0.96 (0.92-0.98)	2.4 (1.6-3.7), I^2 = 0	0.94 (0.87-1.0), I^2 = 79%
Adnexal tenderness[b]	1435[20,22,51]	0.61 (0.52-0.69)	0.65 (0.42-0.83)	1.9 (1.0-3.5), I^2 = 95%	0.57 (0.48-0.67) I^2 = 11%
Imaging					
Transvaginal sonography[d]	6885[50,54,59]	0.88 (0.52-0.98)	0.99 (0.96-1.0)	111 (12-1028), I^2 = 88%	0.12 (0.03-0.55), I^2 = 95%

TALK NERDY TO ME



Commentary

As a systematic review, this study was well conducted with a good array of studies and minimal biases present. The clinically relevant outcomes of maternal and fetal mortality make the diagnosis of ectopic pregnancy an important issue.

The robust positive likelihood ratio for transvaginal ultrasonography makes this diagnostic modality excellent for diagnosing ectopic pregnancy, if and when it is available. The common clinical conundrum comes from differentiating between ectopic pregnancy and miscarriage, for which this study provides useful exam and diagnostic tools.

Out of 10,890 abstracts that were initially reviewed, 14 articles were chosen for analysis based on the inclusion and exclusion criteria. The studies were found using only MEDLINE and EMBASE, therefore a selection bias would be present, as all non-published studies or negative studies would not be included.

Also, all non-English trials would also be excluded; however, ectopic pregnancy is a universal concern. The search strategy "previously published in The Rational Clinical Examination series" is not easily accessible.

In the studies that were included, some were based on "clinical impression" based on symptoms, however, the symptoms were not specifically stated. This could underestimate the effect of the specific symptoms, thereby leading the readers to rely more heavily on diagnostic modality and forgoing important clinical examination techniques.

The review is aimed at emergency medicine and primary care physicians; however, clinical setting was not identified in the studies chosen. As most early pregnancies would generally present to the ED or clinic setting, this can be assumed, however, deviation from this would affect the generalizability of the study. Their length of follow up was also uncertain.

There is heterogeneity amongst who is performing the ultrasound. Furthermore, the study aimed to look at ultrasounds performed by the *"bedside clinician"*, as noted by the authors could account for the large heterogeneity (I2=88%) with the test results. The operator variables were also not explored here; therefore we are unable to say how this translates to bedside ultrasonography in the ED.

Systematic Review Quality Checklist

The clinical problem is well defined	☑
The study population represents the target population that would normally be tested for the condition included	☑
The study population included or focused on those in the emergency department	
The study patients were recruited consecutively	
The diagnostic evaluation was sufficiently comprehensive and applied equally to all patients	☑
The reference standard was appropriate	☑
All undiagnosed patients underwent sufficiently long and comprehensive follow up	
The likelihood ratios of the tests in question are presented or can be calculated from the information above	☑
The precision of the measure of diagnostic performance is satisfactory	☑

Case Resolution

You perform a bedside transvaginal ultrasound and identify an ectopic pregnancy.

You page the gynecology team who comes and takes over her care. Then it's off to an ultrasound on a man suspected of renal colic before someone orders another CT.

CONCLUSION VS COMMENTARY

COMPARISON

Would be wary with who is performing and interpreting the ultrasound, but the strength of the +LR (111) makes this an excellent diagnostic modality for ectopic pregnancy regardless.

Clinical Application

In women with early pregnancy who present with abdominal pain and vaginal bleeding, physical examination findings of cervical motion tenderness, peritoneal findings, adnexal mass and adnexal tenderness are not useful enough to rule in or rule out the diagnosis of ectopic pregnancy.

However, transvaginal ultrasonography is the single best test for diagnosis. Clinical disposition and follow up can then be determined based on the stability of the patient and the findings on exam.

WHAT DO I TELL MY PATIENT?

I am concerned that you are having a pregnancy outside the uterus. This is called an ectopic pregnancy. These pregnancies are often in the tube and are called tubal pregnancies. It is a very serious condition and can even be deadly. We have a test called an ultrasound, which is very good at finding out if you have an ectopic/tubal pregnancy.

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Guest Skeptics:
Dr. Matt Dawson
Director of Point of Care Ultrasound at the University of Kentucky. Co-creator of Ultrasound Podcast.

Dr. Mike Mallin
Director of Emergency Ultrasound and the Emergency Ultrasound Fellowship at the University of Utah.

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O Canada:
Canadian CT Head Rule for Patients with Minor Head Injury

Case Scenario:

62-year-old woman who has an unwitnessed fall while walking on ice and hits her head. There was a possible brief loss of consciousness..
Her daughter brought her to the emergency department right away. The patient complains of a headache, but has not vomited and denies other complaints. The daughter feels her mother is acting appropriately. On your evaluation, the patient has a posterior scalp contusion, but no palpable step-off, and otherwise has Glasgow Coma Scale 15 and a non-focal neurological examination.

Q:

Does this patient need a head CT to rule out a clinically significant brain injury?

BOTTOM LINE

The Canadian CT Head Rule is a simple clinical decision tool with 100% sensitivity to identify patients with head injuries in need for neurological intervention. Being a Level 4 derivation study it will need to be validated in large prospective studies with impact analysis demonstrating change in clinician behavior with benefit and ready for prime time.

The Canadian CT Head Rule for Patients with Minor Head Injury

Stiell et al. Lancet 2001

P Adult patients presenting to the ED at 10 large Canadian hospitals with GCS 13 or greater within 24h after blunt head trauma resulting in witnessed LOC, amnesia or disorientation.

I Standardized clinical assessments were performed on all consecutive eligible patients before performing a CT scan at the discretion of the attending physician

C All the pre-CT variable were compared with the CT and outcomes at 14 days looking for associations. Overall, 44 variables were assessed.

O Need for neurological intervention, defined as need for neurologic intervention as death within 7 days due to the head injury or need with 7 days for craniotomy, elevation of skull fracture, increased ICP monitoring or intubation for head injury.

Excluded Patients:

- *<16 years of age*
- *Minimal head injury with no LOC, amnesia or disorientation*
- *Unclear history of trauma as primary event*
- *Obvious penetrating skull injury*
- *Acute focal neurological deficit*
- *Unstable vital signs*
- *Seizure prior to ED assessment*
- *Anticoagulation or bleeding disorder*
- *Pregnancy*

Authors' Conclusion:

We have developed the Canadian CT Head Rule, a highly sensitive decision rule for use of CT. This rule has the potential to significantly standardise and improve the emergency management of patients with minor head injury." (Stiell et al., 2001)

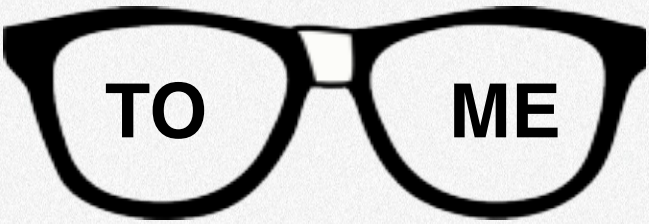
Background

CT scans are frequently done after head injury to evaluate for intracranial hemorrhage, which can be costly and causes radiation-exposure. Much of the time, these are negative, or find injuries for which no intervention is ever done and do not clinically affect the patient. CT Head decision rules help clinicians decide when to order a CT.

Results

- 3121 patients were enrolled and they were able to assess their primary outcome measure, need for neurological intervention, in 100% of patients.
- Mean age of the population was 39 with two-thirds being male
- The most common mechanisms were fall, MVC, assault and head hit by object, sports-injuries, and pedestrian versus vehicle.
- Initial GCS was 15 in 80% of patients.
- 2078 were scanned (67%) meaning 1043 were not scanned (33%)
- A tool (rule) was created including 7 variables formed through logistic regression followed by recursive partitioning.
- 5 high-risk variables (need for neurosurgical intervention)
- 2 medium-risk variables (for brain injury on CT)
- The 5 high-risk criteria had 100% sensitivity and 68.7% specificity to identify need for neurological intervention
- There were 44 patients (1%) who needed neurosurgical intervention and all were picked up with the tool.
- The sensitivity and specificity of the overall rule (all 7 variables) were 98.4% and 49.6%.
- There were 254 patients (8%) were judged to have a clinically important brain injury. The tool identified 250 of the 254 cases. The four patients not identified with the tool were small contusions. None required neurosurgical treatment and none had neurological sequelae.

TALK NERDY TO ME



Commentary

Ian Stiell and his team published another classic paper. They seemed to have worked their way up the body starting with the Ottawa Ankle Rules, moving to the Ottawa Knee Rules, the Canadian C-Spine Rules and finally the Canadian CT Head Rules.

This group from Ottawa was ahead of the curve on this topic. They started this project in the 1990's when people were only beginning to talk about increased utilization of CT (cost) and the risk of radiation. Ian and his team were looking for ways to help EM docs choose wisely a decade before the choosing wisely campaign was initiated.

Their methods were outstanding, as you would expect from a group that has been putting out such classic papers. There was no selection bias, the population represented a broad spectrum of patients, it was a multi-site study, results were robust for sensitivity and the primary outcome was patient oriented. In addition, the tool they derived was simple with only 5 high-risk need for neurosurgical intervention items.

What about all the patients who did not have a CT scan? They represented 33% of the population. More than 1,000 patients in total did not get a CT.

All patients, CT or not, were assessed for the primary outcome of need for neurosurgical intervention. The five-high risk variables did not miss any of the 44 patients who had this primary outcome.

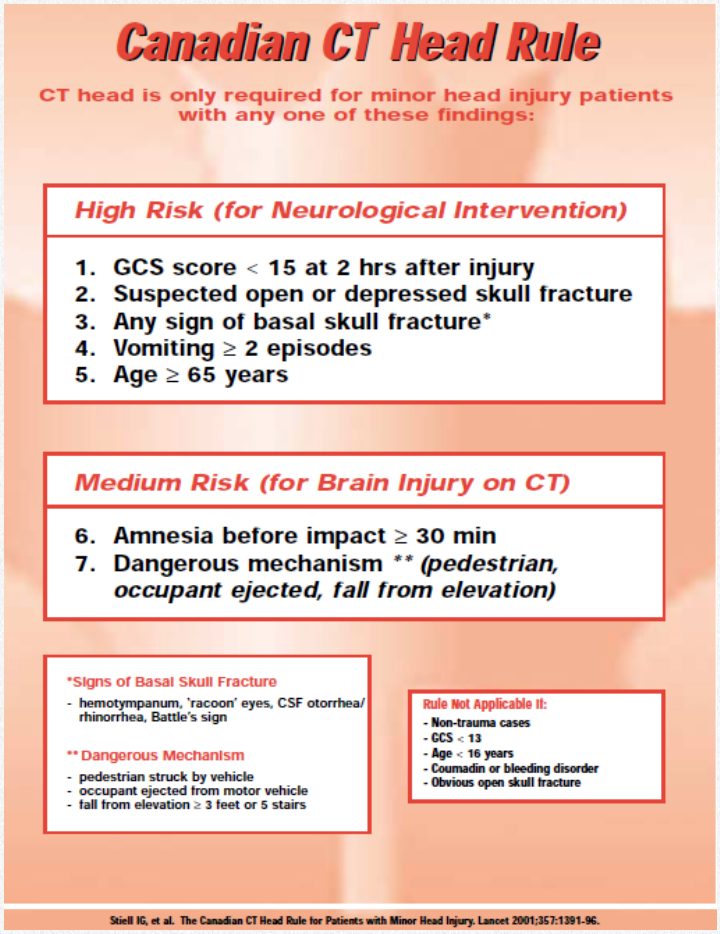
All patients who did not have CT underwent telephone assessment at 14-days post-injury, which classified patients as having no clinically important brain injury if had no or only mild headache, no memory or concentration problems, no seizure or focal motor problems, good performance on the Katzman Short Orientation-Memory-Concentration Test, and they had return to normal daily activities.

Telephone criteria had 100% sensitivity for identifying patients requiring neurological intervention and 87% sensitive for patients requiring clinically important brain injury.

The validity of these criteria was confirmed by applying these to a random sample of 172 study patients who had undergone CT.

What about the issue of intoxication either from drugs or alcohol? These were not part of the clinical decision tool.

Their data showed that examination of patients suspected of intoxication was not reliable or discriminating. In addition, blood alcohol level was not associated with important brain injuries. That is why they did not automatically scan patients with CGS of 13 or 14 but waited 2hrs to see if GSC increased to 15.
Not including alcohol as an indication for head CT is in contrast to the New Orleans' Rule that we will discuss shortly.



Clinical Decision Tools Quality Checklist

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

Case Resolution

Using the Canadian CT Head Tool, given the patient does not have any of the 5 high-risk criteria; you decide not to do a CT scan of their head. However, if you used the New Orleans Rule, she would have warranted herself a CT scan given her age was over 60 and she complained of a headache. You discuss it with the patient and her daughter, and opted not to do a CT scan.

Clinical Application

A main issue with New Orleans is that the specificity is so low that what we see is increased testing when you use this rule. The Canadian CT rule has a considerably higher specificity and you only miss CT findings that don't need neurosurgical intervention. These findings don't really matter . . . except, possibly to a plaintiff's lawyer.

The bottom line is that I think both rules can be used to help you establish your clinical reasoning early in training but I don't know that either performs better than a seasoned clinicians evaluation and assessment.

CONCLUSION VS COMMENTARY

COMPARISON

We agree that the tool has good sensitivity, both with and without the medium-risk variables, and it is meant to rule in patients with concerning head injuries, rather than rule out those that don't.

Overall, we feel it was a good quality study with a decent sample size. Their power calculation was to get 2,500 patients for a precision of 100% sensitivity for clinically important brain injury. The sensitivity of the high-risk criteria was 100%, which is good enough for me.

This rule was developed to insure that all injuries needing neurosurgical intervention were identified. This is a good, important, patient centered outcome. However, while the injury may not need neurosurgery, it may be important to know about other injuries as far as patient expectations for recovery. Also, in a different medico-legal environment, missing significant, albeit non-neurosurgical lesions, may be important.

WHAT DO I TELL MY PATIENT?

We have done a good job of checking out your head injury. The good news is you do not need a CT scan of your head. There is a special tool called the Canadian CT Head Rule. It has been shown not to miss any patients with a head injury requiring neurosurgery that should have a CT scan.
The bad news is I think you have a concussion and you may experience a range of symptoms due to this injury. Here is some information on concussion and what to watch for in the next few days. If you are getting worse, have any of these new symptoms listed or are concerned please come back to the emergency department to be re-assessed.

DARE To Compare

Two Validation Studies Comparing Canadian CT Head Rules to the New Orleans Criteria:

Papa et al (2012) compared both rules in patients with GCS 15 at a single U.S. Level 1 trauma center for outcomes of "any traumatic intracranial injury," clinically important brain injury, and need for neurosurgical intervention.

431 patients were enrolled; 7% had traumatic injury on CT, 3.5% had clinically important brain injury, and 1% required neurosurgical intervention.

Both the New Orleans and the Canadian rules had 100% sensitivity, but the Canadian Rule had a higher specificity for all three outcome measures (36.3 versus 10.2 to identify traumatic intracranial lesions on CT, 35 versus 9.9 for clinically important brain injuries, and 80.7 versus 9.6 to identify need for neurosurgical intervention).

Smits et al (2005) compared both rules in Dutch patients with GCS 13-15 for the same 3 outcome measures.

3181 patients were enrolled; positive CT findings were present in 9.8% of patients and 0.5% required neurosurgical intervention.

Both rules had 100% sensitivity to identify need for neurosurgical intervention. The New Orleans Rule had a higher sensitivity for identifying positive CT scan findings and clinically important injuries (97.7-99.4% versus 83.4-87.2% in the Canadian study).

The Canadian Rule had higher specificities for all three outcome measures (37.2-39.7% versus 3.0-5.6% in the New Orleans study).

They concluded the estimated potential reduction in CT scan ordering was 3.0% for their adapted New Orleans Rule versus 37.3% for their adapted Canadian Rule.

A recent smaller study by Kavalci et al was just published last year with 175 patients from a tertiary care center in Turkey. The CCHR had higher specificity, Positive Predictive Value and Negative Predictive Value for important clinical outcomes than does the NOC. (Free access open article)

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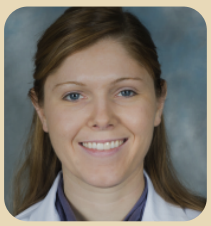

Guest Skeptics:

Dr. Anand Swaminathan

Anandi is an Assistant Program Director at NYU/Bellevue Hospital in the department of EM

Dr. Emily Junck

She is a third year Emergency Medicine resident physician at University of Washington.

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Can't Touch This: Hands on Defibrillation

Case Scenario:

A 55-year-old male goes into cardiac arrest minutes after arriving in the ED. He 's rushed into the shock room and CPR is started. Chest compressions are ongoing and as soon as the monitor pads are attached, you notice the patient to be in ventricular fibrillation. A resident next to you says that he has read that the patient can be shocked without stopping chest compressions. Everyone in the room immediately turns their eyes on you to make the call and the intern doing CPR asks if it's really safe to do so.

Q:

Is it safe to shock a patient during ongoing chest compressions (so-called hands-on defibrillation)?

BOTTOM LINE

Performing hands on defibrillation poses a risk and it's a practice that should NOT be performed

Electrical Exposure Risk Associated with Hands-on Defibrillation

Lemkin et al. Resuscitation 2014

P Eight cadavers, neither frozen nor embalmed, with BMI between 12-29

I Resistance measurements taken from eight cadavers and two investigators using a calibrated multi-meter connected to monitoring electrodes placed 40cm apart on the chest. The anterior and posterior defibrillation pads were attached to a defibrillator and 360J biphasic discharges were given, with the subsequent voltages measured.

C There was no control group

O With the variables measured (resistance and voltage), they estimated the rescuer-received dose to estimate energy received during the defibrillation

Authors' Conclusion:

"Hands-on defibrillation using currently available personal protective equipment and resuscitative procedures poses a risk to rescuers. The process should be considered potentially dangerous until equipment and techniques that will protect rescuers are developed." (Lemkin et al., 2014)

Background

Defibrillation is the treatment of choice for rhythm disturbances like ventricular fibrillation and ventricular tachycardia without a pulse. Rapid and early defibrillation has been shown to increase survival after cardiac arrest.

There was some suggestion that a short period of CPR should be done prior to defibrillation in out of hospital cardiac arrest. However, a systematic review by Simpson et al in Resuscitation 2010 on this topic demonstrated no superiority of delayed vs. immediate shocking.

High quality chest compressions have also been shown to improve outcomes in cardiac arrest, to the extent that delays in starting them and even brief interruptions are associated with worse survival rates.

Having this in mind, the use of hands-on defibrillation to reduce interruption of chest compressions after cardiac arrest has been suggested as a means of improving resuscitation outcomes.

Lloyd et al 2008 looking at the electrical current flow through the rescuers who had their hands on patients being defibrillated.

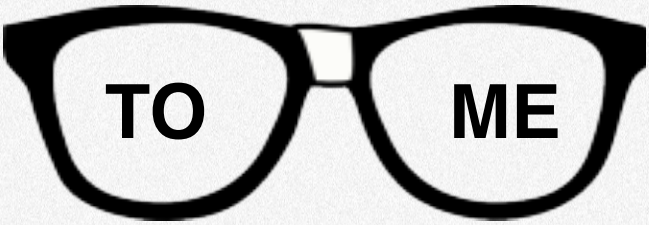
- 43 hands-on shocks with most at 200j but a few at 360j
- None of the rescuers felt the shocks who wore polyethylene gloves
- About 10% of the shocks were above the allowable 0.5mA
- The authors concluded shocking while doing CPR was feasible

The potential dangers of this strategy in regard to exposing rescuers to electrical energy are still being debated. There is a study on how much protection different glove types might provide. Sullivan and Chapman in 2012 study called Will medical examination gloves protect rescuers from defibrillation voltages during hands-on defibrillation?

Results

Defibrillation resulted in rescuer exposure voltages ranging from 827V to ~200V, depending on cadaver and anatomic location. The rescuer received dose under the test scenarios ranged from 1 to 8 J, which is in excess of accepted energy exposure levels.

TALK NERDY TO ME



Commentary

This study adds to the literature on the topic of hands on defibrillation. However, it is not patient oriented or provider oriented literature. The key message is to perform high quality chest compression and defibrillate early.

Case Resolution

You quickly state to the team that a recent study in resuscitation demonstrates that hands-on defibrillation is potentially dangerous and should not be done. You keep the compressions going while you charge the defibrillator to avoid longer pauses but do stop compressions for the electrical discharge and immediately resume CPR.

Clinical Application

Although you can find many case reports of people doing hands on defibrillation, this study shows that there's a risk involved and that this practice should be avoided. Instead, you can charge the defibrillator during the compressions and just stop for a brief period to give the discharge and resume compressions immediately.

Critical Appraisal for Study

Was this study based on a random or pseudo-random sample?	
Were the criteria for inclusion in the sample clearly defined?	☑
Were confounding factors identified and strategies to deal with them stated?	
Were outcomes assessed using objective criteria?	☑
If comparisons are being made, was there sufficient descriptions of the groups?	N/A
Was follow up carried out over a sufficient time period?	N/A
Were the outcomes of people who withdrew described and included in the analyses?	N/A
Were outcomes measured in a reliable way	☑
Was appropriate statistical analysis used?	☑

CONCLUSION VS COMMENTARY

COMPARISON

We agree with the authors conclusion in that even thought the amount of energy transferred during hands-on defibrillation might not be that much, it's sufficient to post a threat to the medical personnel and therefore it shouldn't be done for now.

WHAT DO I TELL MY PATIENT?

The evidence available to this day shows that hands-on defibrillation is potentially dangerous and should not be done.

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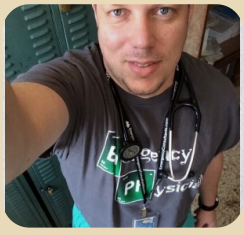

Guest Skeptic: Dr. Manrique Umana

He is s an Emergency Physician from San Jose, Costa Rica and the Residency Program Director. He is the co-author of a Spanish-based blog called www.ViaMedEM.com and an active person in #FOAMed world.

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You Spin Me Right Round Baby: Like Benign Paroxysmal Positional Vertigo

Case Scenario:

58-year-old woman with diabetes and hypertension presents with two days of feeling "*dizzy*". Her symptoms worsen when she turns her head. She has also noticed that is much worse when bending over and looking up while turning her head. She has extreme nausea and has had several episodes of vomiting. She has had some improvement in her symptoms with lying flat and closing her eyes. She is worried about something serious and asks what can be done to help with her symptoms.

Q:

Is the Epley Manoeuvre effective in the treatment of posterior canal BPPV?

BOTTOM LINE

The Epley Manoeuvre is a safe and effective procedure that can reduce/alleviate the symptoms of BPPV in ED patients.

The Epley (canalith repositioning) Manoeuvre for Benign Paroxysmal Positional Vertigo

Hilton et al. Cochrane Database Syst Rev. 2014

P 745 patients (11 RCTs) ranging from 18 to 90 years old presenting to either primary care settings or tertiary care with complaints of dizziness, ultimately diagnosed BPPV by a positive Dix-Hallpike and classical features with nystagmus

I The use of the Epley Manoeuvre in treatment of posterior canal BPPV and a subsequent conversion of a positive Dix-Hallpike test to a negative test

C RCTs evaluated looked at Epley maneuver verses placebo (sham maneuver), Epley versus control or Epley vs. other active treatment

O Primary outcome: Complete resolution of vertigo symptoms. Secondary outcomes: conversion of positive Dix-Hallpike to negative; adverse side effects of treatment.

Authors' Conclusion:

"There is evidence that the Epley manoeuvre is a safe, effective treatment for posterior canal BPPV, based on the results of 11, mostly small, randomised controlled trials with relatively short follow-up. There is a high recurrence rate of BPPV after treatment (36%). Outcomes for Epley manoeuvre treatment are comparable to treatment with Semont and Gans manoeuvres, but superior to Brandt- Daroff exercises." (Hilton et al., 2014)

Background

Benign Paroxysmal Positional Vertigo (BPPV) is a short-lived condition characterized by the sensation of rotation or instability most often exaggerated by rapid movements of the head.

The etiology is believed to be from excessive movement of fluid (endolymph) and debris within one of the three semi-circular canals of the vestibular system of the inner ear. The debris causes the fluid to continue moving after head motion has stopped giving the sensation of continued motion causing the symptoms associated with vertigo. This mechanism is called canalithiasis.

Peak incidence is between 50-70 years and affects between 11 and 67 per 100,000 each year. Symptoms often resolve spontaneously after a period of weeks but symptoms can be severe causing many to seek medical attention.

Symptoms can be provoked with the Dix-Hallpike maneuver which elicits symptoms and nystagmus. The nystagmus is torsional (superior pole of the eye directed towards the lower most ear) and up beating. There can be a latency period of up to 45 seconds with duration of less than 1 minute. Repeated positioning causes fatigue of this finding.

Once the diagnosis of BPPV is made on history and physical examination a canalith repositioning maneuver can be attempted.

It was Epley who described one of the technique used to relocate and redistribute the debris within the posterior semi-circular canal thereby eliminating symptoms. The Epley Maneuver as it is commonly called is a sequence of four head positions that use gravity to treat the BPPV or canalithiasis.

Results

Those treated with the Epley manoeuvre in pooled analysis showed a resolution of symptoms with OR of 4.42 (95% CI: 2.62 to 7.44), favouring treatment with the manoeuvre. There was also a high conversion to a negative Dix-Hallpike test in the treatment group with OR 9.62 (95% CI: 6.0 to 15.2).

Analysis 1.1. Comparison 1 Epley versus control or placebo manoeuvre, Outcome 1 Complete resolution of vertigo symptoms (subjective report).

Review: The Epley (canalith repositioning) manoeuvre for benign paroxysmal positional vertigo

Comparison: 1 Epley versus control or placebo manoeuvre

Outcome: 1 Complete resolution of vertigo symptoms (subjective report)

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Froehling 2000	12/24	5/26		17.5 %	4.20 [1.19, 14.83]
Lynn 1995	11/18	3/15		9.3 %	6.29 [1.29, 30.54]
Munoz 2007	12/38	10/41		48.1 %	1.43 [0.53, 3.84]
von Brevern 2006	28/35	3/31		4.6 %	37.33 [8.75, 159.22]
Yimtae 2003	16/25	7/20		20.5 %	3.30 [0.97, 11.29]
Total (95% CI)	**140**	**133**		**100.0 %**	**4.42 [2.62, 7.44]**

Total events: 79 (Treatment), 28 (Control)

Heterogeneity: Chi^2 = 13.73, df = 4 (P = 0.01); I^2 =71%

Test for overall effect: Z = 5.58 (P < 0.00001)

Test for subgroup differences: Not applicable

Analysis 1.2. Comparison 1 Epley versus control or placebo manoeuvre, Outcome 2 Conversion of a positive to a negative Dix-Hallpike test.

Review: The Epley (canalith repositioning) manoeuvre for benign paroxysmal positional vertigo

Comparison: 1 Epley versus control or placebo manoeuvre

Outcome: 2 Conversion of a positive to a negative Dix-Hallpike test

Study or subgroup	Treatment n/N	Control n/N	Odds Ratio M-H,Fixed,95% CI	Weight	Odds Ratio M-H,Fixed,95% CI
Lynn 1995	16/18	4/15		3.9 %	22.00 [3.41, 141.73]
Froehling 2000	16/24	10/26		25.8 %	3.20 [1.00, 10.20]
Yimtae 2003	22/25	13/20		14.0 %	3.95 [0.87, 17.99]
Munoz 2007	13/38	6/41		30.6 %	3.03 [1.01, 9.07]
von Brevern 2006	28/35	3/31		5.1 %	37.33 [8.75, 159.22]
Bruintjes 2014	20/22	10/22		7.3 %	12.00 [2.24, 64.28]
Liang 2010	42/43	34/44		6.3 %	12.35 [1.51, 101.36]
Xie 2012	54/58	11/45		6.9 %	41.73 [12.29, 141.65]
Total (95% CI)	**263**	**244**		**100.0 %**	**9.62 [6.00, 15.42]**

Total events: 211 (Treatment), 91 (Control)

Heterogeneity: Chi^2 = 18.83, df = 7 (P = 0.01); I^2 =63%

Test for overall effect: Z = 9.40 (P < 0.00001)

Test for subgroup differences: Not applicable

0.005 0.1 1 10 200

No treatment Epley manoeuvre

TALK NERDY TO ME

Commentary

The overall quality of the study is good and conforms to the standards and methods employed by other Cochrane reviews. This study is an update of previous reviews that had similar findings adding 6 new trials. A majority of the studies included had good methods for randomization and allocation but some had problems with blinding and adequate, meaningful follow up.

Seupaul talks nerdy about heterogeneity. This is a rough guide to interpret heterogeneity:

- 0% to 40%: might not be important
- 30% to 60%: may represent moderate heterogeneity
- 50% to 90%: may represent substantial heterogeneity
- 75% to 100%: considerable heterogeneity

It appears that the Epley Manoeuvre does have good success in resolving symptoms and should be used more often in ED settings to treat BPPV. One of the biggest drawbacks to the use of the Epley Manoeuvre is the time that it takes and the level of comfort that the practitioner has with the procedure. The Epley maneuver was found to be equal to or modestly superior to other repositioning manoeuvre.

Case Resolution

The patient was treated with the Epley Manoeuvre and had near complete resolution of her symptoms and was discharged home with positional restrictions and ENT follow-up as needed.

Clinical Application

Treatment with the Epley Manoeuvre is an effective method of treatment for cases of BPPV.

References

Hilton MP, Pinder DK. The Epley (canalith repositioning) manoeuvre for benign paroxysmal positional vertigo. Cochrane Database Syst Rev. 2014

Quality Checklist for Therapeutic Systematic Review

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 and precise enough to be clinically significant	☑

CONCLUSION VS COMMENTARY

COMPARISON

We feel the author's conclusions are appropriate and consistent with those of the SGEM.

WHAT DO I TELL MY PATIENT?

I know you are feeling terrible. The good news is there is a safe and effective treatment for your vertigo. It is called the Epley Manoeuvre. We can do it right here in the emergency department. All it takes is you lying down on the stretcher. I move your head gently through a series of positions. This resets the problem in your inner ear and people are often 100% cured.

Guest Skeptics:

Dr. Tony Seupaul
Tony is the Chair of the Department Emergency Medicine, University of Arkansas.

Dr. Chris Fowler
Chris is a second year EM resident in Arkansas.

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One Platelet, One Plasma, One RBC: PROPPR Trial

Case Scenario:

28-year-old male is involved in an altercation and shot multiple times in the chest and presents to the ED. His vital signs include a BP 72/46, HR 140, RR 30, O2 sat 89% on NRB and a temp of 98.7F. You intubate the patient successfully, begin IV fluids, and place bilateral chest tubes with significant blood return from the right chest tube. Due to the patients blood loss you initiate damage control resuscitation including: permissive hypotension, source control of bleeding, and a massive transfusion protocol.

Q:

What is the effectiveness and safety of transfusing adult patients with severe trauma and major bleeding using plasma, platelets, and red blood cells in a 1:1:1 ratio vs. with a 1:1:2 ratio?

BOTTOM LINE

A 1:1:1 transfusion strategy is a reasonable approach to adult patients who require a massive transfusion and seems to achieve more hemostasis and less death from exsanguination at 24 hours without increased complications.

Transfusion of Plasma, Platelets and Red Blood Cells in a 1:1:1 vs. a 1:1:2 Ratio and Mortality in Patients with Severe Trauma. The PROPPR Randomized Clinical Trial. Acute Migraine: A Systematic Review.

Holcomb et al. JAMA 2015

P 680 patients age 15 years of age and older and/or 50kg or greater meeting highest level of trauma activation. Patient must require at least 1 U of any blood component within the first hour of arrival or during pre-hospital transport.

I Platelet, plasma and red blood cell transfusion in a 1:1:1 ratio

C Platelet, plasma and red blood cell transfusion in a 1:1:2 ratio

O All cause mortality at 24 hour and 30 days. Ancillary outcomes were time to hemostasis, blood product volumes transfused, and complications.

Authors' Conclusion:

"Among patients with severe trauma and major bleeding, early administration of plasma, platelets and red blood cells in a 1:1:1 ratio compared with a 1:1:2 ratio did not result in significant differences in mortality at 24 hours or at 30 days. However more patients in the 1:1:1 group achieved hemostasis and fewer experienced death due to exsanguination by 24 hours. Even though there was an increased use of plasma and platelets transfused in the 1:1:1 group, no other safety differences were identified between the 2 groups." (Holcomb et al. 2015)

Background In the United States, trauma is the leading cause of death among patients between the ages of 1 and 44 years of age and the third leading cause of death overall. Approximately 20 to 40% of trauma deaths occur after hospital admission and are a result of massive hemorrhage.

There have been no large, multi-center, randomized clinical trials with survival as a primary end point that support optimal trauma resuscitation practices with approved blood products and therefore there are many conflicting recommendations.

The Prospective Observational Multicenter Major Trauma Transfusion (PROMMT) Trial demonstrated that many clinicians were transfusing patients with blood products in a ratio of 1:1:1 or 1:1:2 (plasma, platelets, RBC) and that early transfusion of plasma and platelets was associated with improved 6-hour survival after admission.

Results

Primary Outcome Mortality:

24 hours: 12.7% in 1:1:1 group vs. 17.0% in 1:1:2 group (CI -9.6% – 1.1%) [p=0.12]

30 days: 22.4% in 1:1:1 group vs. 26.1% in the 1:1:2 group (CI -10.2% – 2.7%) [p=0.26]

Secondary Outcomes:

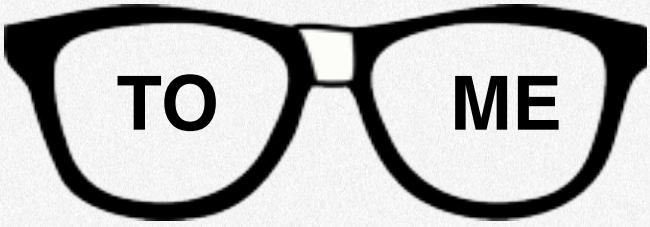
Exsanguination in first 24 hours significantly decreased in the 1:1:1 group (9.2%) vs. the 1:1:2 group (14.6%) [p=0.03]

More patients achieved hemostasis in the 1:1:1 group vs. 1:1:2 group (86% vs. 78%) [p=0.006]

More plasma (median 7 U vs. 5 U) and platelets (median 12 U vs. 6 U) were used in the 1:1:1 ratio vs. 1:1:2 ratio respectively

No difference in complications between the two transfusion strategies

TALK NERDY TO ME



Commentary

It is great to have a large randomized control trial looking at such an important topic. These studies take a tremendous effort to coordinate and do well. Congratulations to Dr. Holcomb and his team at University of Texas.

This trial was designed to test if a 1:1:1 protocol was superior to a 1:1:2 protocol and safety. They powered the study at about 600 patients to detect a 10% difference. Their primary outcome of all cause mortality at 24hr and 30days was not statistically significant.

This does not mean there is no difference between the two protocols. The only conclusion that can be made is there was not a >10% difference.

This is an important concept of trial design and evidence based medicine. A 10% mortality difference would be huge. They demonstrated only a difference of about 4% at 24hrs and 30days favouring 1:1:1. They would have needed a much larger trial (n=3,000) to confirm this 4% difference that would give an NNT of 25.

There was a problem of un-blinding of the trial once the transfusion protocol was started. This had the potential for interfering with the treatment of the patients once they were assigned to each of the protocols.

Another concern about PROPPR is why compare 1:1:1 to 1:1:2? The hypothesis was generated from the PROMMTT study but this was a prospective observational trial showing an associated benefit of earlier and higher ratios of plasma and platelets. There could have been confounding factors responsible for this observed mortality benefit.

Others may argue that they should have compared 1:1:1 to a goal direct approach or *"usual care"* to find out if this protocol was superior. They addressed this briefly in their discussion. This trial cannot speak to usual care or a goal directed approach.

We have seen sepsis care over the last decade go through a transition. It started with usual care not being that great. Dr. River's paper demonstrated a protocol with a bundle of steps could be significantly better in treating septic patients. However, last year major trials like ProCESS and ARISE showed two things. Usual septic care is now much better and that all parts of the bundle are not necessary.

A similar story could emerge as more information becomes available on what is the best approach to patients requiring massive transfusions.

Another issue is the two different transfusion protocols can be deceiving if not read in detail. They say they study compares a 1:1:1 protocol to a 1:1:2 protocol. However, there were some important differences not just in the ratios but in the order patients received blood products.

Initial containers were as follows:

- 1:1:1 got PLATELETS first (6 units) followed by alternating RBC and plasma.
- 1:1:2 got 2 units of RBC first and 1 unit of plasma. Platelets were not transfused until after 9 units of other blood products

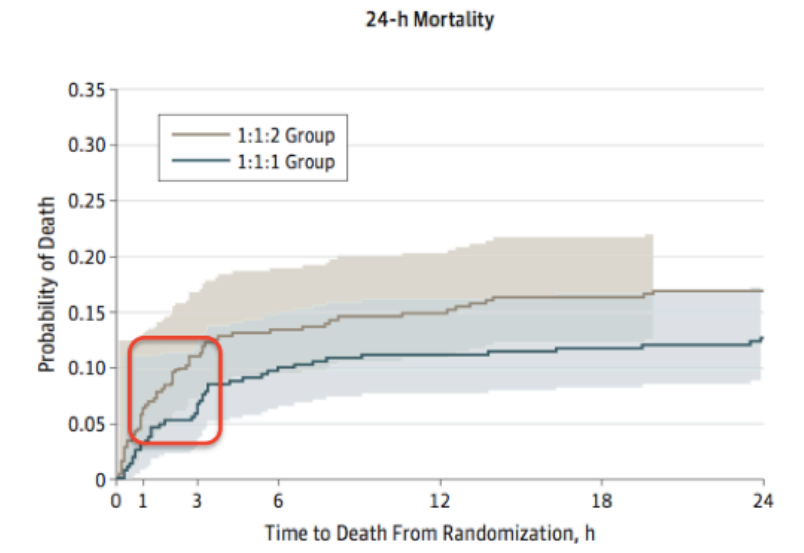
Subsequent Containers:

- Even number – 3 units plasma, 1 dose (6 units) platelets and 6U RBC with platelets given first then alternating 2 units RBC and 1 unit plasma
- Odd Numbers – 2 units of RBC and 1 unit plasma

I think this is a key piece of information and could explain why the 1:1:1 achieved homeostasis and fewer exsanguinations. It is possible the platelets given first in the 1:1:1 treatment group was responsible for the earlier hemostasis and fewer deaths due to exsanguination by 24 hours.

Looking at the Kaplan-Meier Curves the lines deviated between one and three hours but otherwise remained parallel. Could it have been the earlier transfusion of platelets in the 1:1:1 protocol that explains this anomaly in the results?

Figure 2. Kaplan-Meier Failure Curves for Mortality at 24 Hours and 30 Days



A minor point is they used the definition of *"massive transfusion"* as those patients requiring ≥10U RBC in the first 24hrs. The median transfusions of RBCs in the study were only 9 units. There are other definitions for massive transfusions but at least half their patients in their study did not reach the definition they decided to use.

Another comment about this study is that it was a *"pragmatic"* trial. This has both strengths and weaknesses. After the randomization process they left the treatment decisions up to the attending physician. This would be more "real" world practice but makes it more difficult to interpret the results. A more rigorous but less pragmatic approach would have been to treat both groups equally except for the intervention.

Their study objective was to compare the effectiveness of a 1:1:1 transfusion ratio of plasma, platelets and RBCS to a 1:1:2 ratio. They did appear to achieve these ratios with plasma to RBC. However, the median ratios of platelets to RBCs were 1.5 for the 1:1:1 group and 0.4 for the 1:1:2 group. So patients received more platelets than they were supposed to in the 1:1:1 group and less platelets than they were supposed to in the 1:1:2 group.

An online supplemental eTable 2 showed total blood products up to 24hrs after admission. The 1:1:1 group got a mean of 7 units plasma, 12 units platelets and 9 units RBC. In comparison the 1:1:2 group received a mean of 5 units plasma, 6 units platelets and 9 units RBC.

eTable 2. Resuscitation Products by Treatment Group up to 24 hours after Admission

Resuscitation up to 24 hours after Admission[1]		Group 1:1:1 (N = 338)	Group 1:1:2 (N = 342)	p-value[2]
Plasma (units)	Median	7 (3,13)	5 (2,10)	<.001
	>0, n (%)	325 (96.2)	320 (93.6)	
Platelets (units)[3]	Median	12 (6,18)	6 (0,12)	<.001
	>0, n (%)	333 (98.5)	205 (59.9)	
RBC (units)	Median	9 (5,15)	9 (6,16)	0.30
	>0, n (%)	338 (100)	341 (99.7)	
Cryoprecipitate (units)	Median	0 (0,0)	0 (0,9)	0.01
	>0, n (%)	73 (21.6)	100 (29.2)	
Crystalloids (liters)	Median	6.3 (3.8,9.5)	6.6 (3.5,10.5)	0.58
	>0, n (%)	333 (98.5)	338 (98.8)	
Colloids (liters)	Median	0 (0,0.3)	0 (0,0.3)	0.70
	>0, n (%)	90 (26.6)	88 (25.7)	
Tranexamic Acid (TXA)	>0, n (%)	64 (18.9)	68 (19.9)	
Other Procoagulants	>0, n (%)	19 (5.6)	15 (4.4)	

They explain this in the discussion suggesting that after the intervention stage of the study there was a catching up of products based on laboratory-directed care. This resulted in the 1:1:2 group receiving more plasma and platelets products and a final ratio approaching 1:1:1.

The other objective of the PROPPR study was to determine the safety of the transfusion strategies. It is important to note that they found no differences in the 23 pre specified complications.

Case Resolution

Unfortunately our patient did not survive. He was started on a massive transfusion protocol of 1:1:1 and had an emergency department thoracotomy performed, but ultimately all the bleeding could not be stopped and the patient coded.

Clinical Application

For adult patients who require massive transfusions a 1:1:1 is not superior to a 1:1:2 strategy. The PROPPR data suggests giving platelets earlier and in higher ratios. Local protocols will need to be developed using available resources and expertise to guide care of these critically ill patients.

RCT 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 groups to which they were randomized	☑
The study patients were recruited consecutively (i.e. 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 a plasma:platelet:red blood cell massive transfusion protocol in a 1:1:1 vs. 1:1:2 does not result in a greater than 10% difference in mortality at 24 hours or at 30 days, but smaller differences in mortality may be possible.

WHAT DO I TELL MY PATIENT?

Your family member has been shot. They are critically injured. There is a lot of bleeding and they require a massive transfusion. The US Department of Defense has come up with a treatment called damage control resuscitation. It involves early transfusion of different types of blood products (platelet cells that help stop bleeding, red blood cells that carry oxygen to the body and plasma that fills up their tank). We are going to use this balanced approach to try and save their life.

References

Holcomb JB et al. Transfusion of Plasma, Platelets, and Red Blood Cells in a 1:1:1 vs. a 1:1:2 Ratio and Mortality in Patients with Severe Trauma: The PROPPR Randomized Clinical Trial. JAMA February 2015

Holcomb JB, del Junco DJ, Fox EE, Wade CE, Cohen MJ, Schreiber MA, et al. The prospective, observational, multicenter, major trauma transfusion (PROMMTT) study: comparative effectiveness of a time-varying treatment with competing risks. JAMA Surg. 2013 Feb;148(2):127-36.

Guest Skeptic: Dr. Salim Rezaie
Salim is a faculty member at University of Texas Health Science Center at San Antonia, Texas. He is currently the creator/founder of REBEL EM blog and REBEL Cast

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I Saw the Signs of Angioedema

Case Scenario:

65-year-old African American male presents to the ED complaining of swelling of the tongue/lips. It started when he woke at 08:30. He went to Urgent Care and was treated with intramuscular steroids, benadryl and epinephrine. The swelling did not get any better. The patient was referred to emergency department. Swelling started >4 hours ago when you see him. He states no change in the swelling. On examination is vital signs are normal, no stridor, no respiratory distress, no hypoxia but he does have a swollen tongue and slightly slurred speech. He has a history of hypertension and the only medication he takes is Lisinopril

Q:

Is icatibant of any benefit in ACE-I associated angioedema?

BOTTOM LINE

Icatibant is an expensive drug that appears to work well for the off-label use of ACE-I induced angioedema but should be reserved for those rare cases of impending airway compromise.

A Randomized Trial of Icatibant in ACE-inhbitor-Induced Angioedema

Baset al. NEJM 2015

P Emergency department patients (n=27) between the ages of 18 and 95 who were on ACE-I and exhibited angioedema affecting the upper aerodigestive tract after excluding those with other causes of angioedema

I 30mg Icatibant subcutaneously

C Intravenous prednisone 500mg and clematastine 2 mg

O Medium time to complete resolution of edema as evaluated by investigator-assessed and patient –assessed symptom score. Secondary outcomes: Proportion of patients who did not have response to treatment, proportion of patients with complete resolution of edema at 4 hours, time to onset of symptom relief

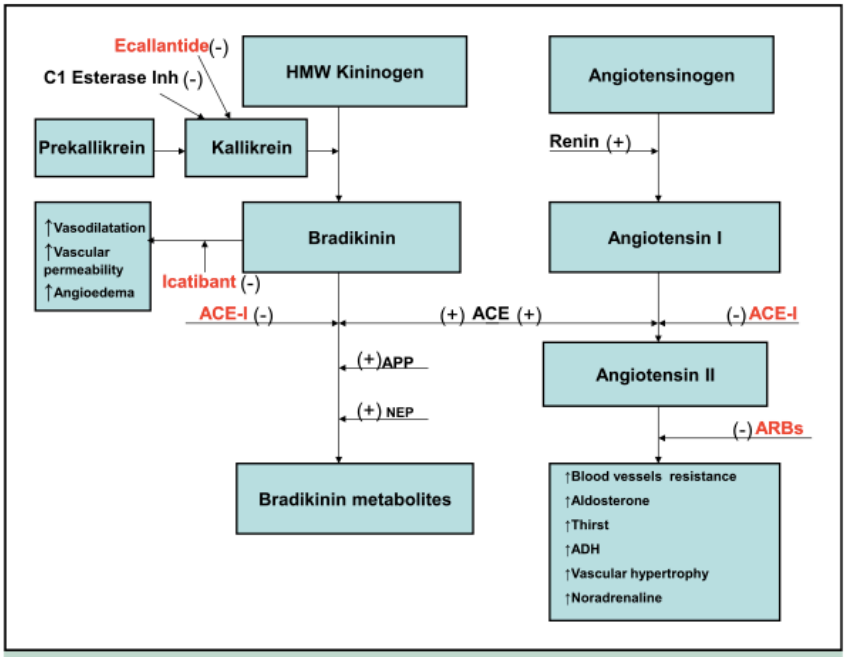
Authors' Conclusion:

"Among patients with ACE-inhibitor–induced angioedema, the time to complete resolution of edema was significantly shorter with icatibant than with combination therapy with a glucocorticoid and an antihistamine." (Baset et al., 2015)

Background

Angiotensin-Converting Enzyme Inhibitors (ACE-Inhibitors), such as Lisinopril, were approved by the FDA in the 1980's. ACE-I are common medications used for hypertension, congestive heart failure, post myocardial infarction, chronic kidney disease and diabetic nephropathy.

They inhibit the renin-angiotensin-aldosterone system. Angiotensinogen is converted to Angiotensin I by renin. Angiotensin I is then converted to Angiotensin II by angiotensin converting enzyme (ACE) that is mainly produced in the lung.



Angiotensin II has many biological effects including:

- increased blood vessel resistance
- increased aldosterone
- increased thirst
- increased antidiuretic hormone (ADH)
- increased vascular hypertrophy
- increased noradrenaline

Angiotensin converting enzyme also breaks down bradikinin. So if you block ACE with an ACE-I you can get a build up of bradikinin. ACE-I have side effects like all biologic agents. Because it causes lower blood pressure patients can get hypotension causing people to be weak/dizzy and even cause syncope.

Hyperkalemia is another well-recognized side effect of ACE-I. Urinary potassium excretion is stimulated by aldosterone and ACE-I decrease aldosterone. The estimated incidence of hyperkalemia secondary to ACE-I use is approximately 3%.

Then there is the classic ACE-I cough. This is thought to happen from in 5-35% of patients. This chronic dry could can start after the first dose but interestingly can not show up for weeks, months or even years.

No one knows the exact mechanism by which ACE-I cause cough but it is though to be due to the increased concentration of bradykinin, substance P, prostaglandins and thromboxane. Stopping the ACE-I is the treatment but the cough can persist for months in some patients.

The build up of bradykinin is also though to be the mechanism behind angioedema. The incidence of angioedema is seen in up to 0.7 % of users. It is usually self-limiting and has a very low fatality rate. The angioedema occurs in the mucosal tissue of the tongue, lips, eyelids, GI tract or genitalia that all have rich capillary blood supply.

An interesting fact is that angioedema is up to five times more common in those of African descent.

Angioedema can be divided up into two main types:

Allergic-histamine-mediated Angioedema:

Insect bites (bees), foods (peanuts/shellfish), drugs (many)
Fast onset, pruritus, rash and potential systemic effects
Responds to anaphylaxis therapy (antihistamines/steroids/epinephrine)

Non-allergic Angioedema:

Hereditary angioedema (HAE) and ACE-I angioedema
Gradual onset, non-pruritic, without rash and effects face, GI tract, genitals
Responds poorly to anaphylaxis therapy (antihistamines/steroids/epinephrine)

Again, most patients with ACE-I induced angioedema will have mild swelling, no airway obstruction and will resolve within several hours after stopping the drug.

Antihistamines and steroids are often given for the more serious cases of ACE-I angioedema but probably do not have much impact if any because the problem is bradykinin-mediated.

A new drug called icatibant is a bradykinin type 2 receptor antagonist labeled for use with hereditary angioedema. It blocks bradykinin receptors resulting in a rapid reduction of the edema and can prevent the need for intubating patients with significant airway involvement.

Results

Primary Outcome: Median time to complete resolution was 8hrs (3-16 range) icatibant vs. 27.1 (20.3-48) for standard care

Secondary Outcomes:

Complete resolution of edema at 4hr after treatment was 5/13 (38%) for icatibant vs. 0/14 (0%) standard care
Median time to onset of symptom relief (according to a composite investigator-assessed symptom score) was 2hr (1-8.1) for icatibant vs. 11.7 (8-18) for usual care

Table 2. Clinical Outcomes.*

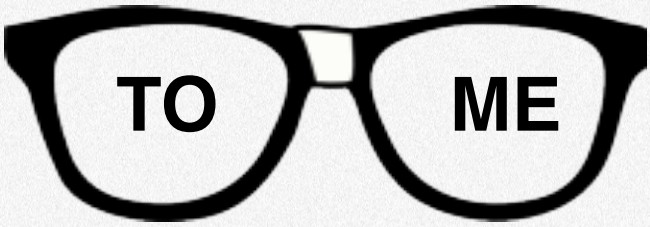
Outcome	Icatibant (N=13)	Standard Therapy (N=14)	P Value
Median (IQR) time to complete resolution of edema: primary end point — hr	8.0 (3.0–16.0)	27.1 (20.3–48.0)	0.002†
Patients with complete resolution of edema at 4 hr after treatment — no. (%)	5 (38)	0	0.02‡
Median (95% CI) time to onset of symptom relief — hr§			
According to composite investigator-assessed symptom score	2.0 (1.0–8.1)	11.7 (8.0–18.0)	0.03¶
According to composite patient-assessed VAS score	2.0 (2.0–6.3)	7.9 (1.2–11.8)	0.36¶
According to composite investigator-assessed angioedema score	2.0 (2.0–12.0)	12.0 (11.3–NE)	0.003¶

Table 3. Adverse Events and Injection-Site Reactions.*

Outcome	Icatibant (N=15)	Standard Therapy (N=15)
	no. of patients (%)	
Any adverse event	1 (7)†	4 (27)
Drug-related adverse event	1 (7)	1 (7)
Serious adverse event	0	1 (7)
Injection-site reaction‡		
Redness	12 (80)	4 (27)
Swelling	8 (53)	3 (20)
Pain	7 (47)	2 (13)
Itching	4 (27)	1 (7)
Sensation of warmth	4 (27)	0

- Three patients in standard-therapy group required rescue therapy (icatibant and prednisolone)
- One of these patients needed a tracheotomy
- There were some minor injection site reactions of redness, swelling, pain and itching (see table)

TALK NERDY TO ME



Commentary

This was a very small study of only 27 patients using icatibant for the off-label use of ACE-I angioedema. Here are five things to consider when evaluating this study:

1) Consecutive Enrolment: We were not sure whether there was consecutive enrolment in this study. This is important to minimize selection bias.

They report three patients had treatment initiated before randomization. Were there other patients that were either too sick or not sick enough who were excluded? They did remove these patients from the efficacy data set and did a per-protocol analysis.

Another point to make about enrolment was all of the patients were Caucasian. ACE-I angioedema is five times more common in patients of African descent. Will they respond differently to icatibant?

2) Blinding: The study was partially un-blinded. Specifically the study drug administrators and the assessors of injection site reactions knew which group patients were assigned. Why were they not blinded? This could introduce some bias when determining whether the active drug or saline subcutaneous injection cause a local reaction. However, the patients and the investigators who assess efficacy outcomes were blinded to treatment groups.

3) Patient Oriented Outcomes: The time to complete resolution 8hrs vs. 27hrs (19hr difference). Median time to onset of symptom relief was 2hr vs. 12hrs.

What about intubation or death? This was a much too small study, which they acknowledge, to assess these rare but very important patient oriented safety outcomes.

How about the need for admission? This might be a very patient oriented outcome. What about cost? These drugs cost $5,000-$10,000. Talk about a very expensive drug to use when most cases are mild, self-limiting, resolve in hours and rarely result in airway compromise.

There is a very big risk of indication creep and that everyone with some facial swelling will be treated with this drug rather than those rare patients heading towards airway obstruction.

4) Usual Care: The standard care was IV steroid (prednisolone) and antihistamine (clementine). I wish they had included epinephrine. This is because if someone is crashing or I'm not sure if it is ACE-I vs. anaphylaxis I would give epinephrine a try. I might also consider fresh frozen plasma.

5) Funded by Shire: Shire did not have a role in the study design. However, Shire did review and provide comments on the manuscript before submission for publication. However, just because a study is pharma funded does not mean the results are wrong but it raises my skeptical radar.

RCT 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 groups to which they were randomized	
The study patients were recruited consecutively (i.e. 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

Icatibant had significantly shorter time to symptom improvement and resolution of edema. What I don't know is if this therapy will prevent intubation or surgical airways. I can't generalize to a population of African Descent, who is disproportionately affected. And I can't necessarily generalize to standard care that may include epinephrine or fresh frozen plasma.

Case Resolution

This gentleman's swelling had not gone down over a course of a few hours with Epinephrine, Steroids and Antihistamines. He had no respiratory distress. He was not intubated as he had been stable over hours, but given severity of tongue swelling, he was admitted for observation with a trach kit at bedside, with ENT and Anesthesiology aware of him. He had no deterioration, did not require intubation, and went home the following day, knowing not to take any more ACE-inhibitors.

Clinical Application

I am not able to use this clinically because it is not available in places I work.

WHAT DO I TELL MY PATIENT?

You have swelling of your tongue, which is likely caused by your medication, Lisinopril. This can occur any time after starting the medicine. There is a medication that may decrease the swelling of your tongue, but I don't know if it will improve your breathing such that you won't need your airway protected. Harms of the medicine may include pain, swelling, itching and redness at the injection site. One dose of this medicine costs thousands of dollars.

References

Bas et al. A randomized trial of Icatibant in ACE-Inhibitor-Induced Angioedema. NEJM January 2015

Guest Skeptic: Dr. Eric Schneider
Eric is a Community Emergency Medicine Physician in Kansas City, Missouri, who has a drive to bring the most pragmatic, evidence-based and cost-effective care to his patients at an inner city trauma hospital. He's a father of three, married to a Pathologist, and an avid musician,

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Comfortably Numb:
Lose Dose Ketamine as Adjunct for ED Pain Control

Case Scenario:
27-year-old woman presents to the emergency department again with severe back pain radiating to her legs. She has tried analgesics, anti-inflammatories, narcotics and even trigger point injections. You have been reading more and more papers suggesting a sub dissociative-dose of ketamine (SDDK) could work.

Q:
Is the administration of subdissociative dose ketamine for acute pain control safe and effective compared with placebo?

BOTTOM LINE

High-quality published evidence to support the use of subdissociative-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.

The Use of Subdissociative-dose Ketamine for Acute Pain in the Emergency Department. Sin et al. Acad Emerg 2015

P English-language randomized controlled trials assessing adult or paediatric emergency department patients with acute pain (fracture, dislocation, abscess, burns).

I Ketamine 0.20-0.30 mg/kg IV over 3-10 minutes versus placebo. One trial used morphine (0.1 mg/kg) with the ketamine

C One trial used morphine (0.1 mg/kg IV + 0.1 mg/kg every 4 hours), one used morphine + placebo, one used midazolam (0.1 mg/kg IV) + fentanyl (0.5 microgram/kg), and one used fentanyl 1.5 microgram/kg

O Primary Outcome: Difference in pain scores. Secondary Outcome: Incidence of adverse events and reduction in adjuvant opioids

Authors' Conclusion:

"The data failed to provide convincing evidence to either support or refute the use of subdissociative-dose ketamine for management of acute pain in the ED. The decision to initiate subdissociative-dose ketamine should be based on assessments of potential risks and benefits of therapy on a case-by-case basis".

Background

Ketamine was developed more than 50 years ago and been used mainly as an anesthetic agent. It has a number of other medical uses including procedural sedation in the ED as well as chronic pain syndromes like neuropathic pain or cancer pain.

Ketamine is a N-Methyl-D-aspartate (NMDA) receptor antagonist that exerts sedative, amnestic, and analgesic effects as a dissociative anesthetic.

Ketamine also has some other non-medical uses. It is used as a street drug and goes by some other names such as Special K and cat valium. If recreational users take too much they referred to it as heading down the K-hole.

Ketamine historically had a bad reputation of raising intracranial pressure. EM Pharmacist, Meghan Groth debunked that myth on SGEM#93.

The bottom Line from that episode was: *"Ketamine seems to be a reasonable alternative induction agent for undifferentiated patients requiring RSI in the ED. Evidence to show that ketamine has negative effects on neurologic outcomes is weak and has been largely extrapolated from non-ED patients. This systematic review found no compelling evidence that ketamine worsens ICP, CPP, or neurologic outcomes as measured."*

There are a group of doctors out there who like to combine ketamine with propofol into Ketofol. We have a podcast coming up on that topic with Steve Carroll from EM Basic.

Results

Four randomized controlled trials totaling 428 patients were identified and met inclusion criteria.

Using the GRADE Criteria, the authors noted that the overall quality of evidence was low to moderate with potential biases including small sample sizes, lack of (or compromised) blinding, and lack of randomization.

In addition, the various trials used various doses of ketamine and comparator opioid analgesics, as well as different pain scales.

For the primary outcome, two studies (Messenger 2008 and Galinski 2007) demonstrated no detectable differences in pain scores.

One study (Gurnani 2007) reported, *"significantly lower pain scores"* but systematic review authors do not provide absolute values or number needed to treat estimates.

The only paediatric paper (Kennedy 1998) reported reduction in Observational Scale of Behavioral Distress (OSBD) scale scores in ketamine compared to fentanyl.

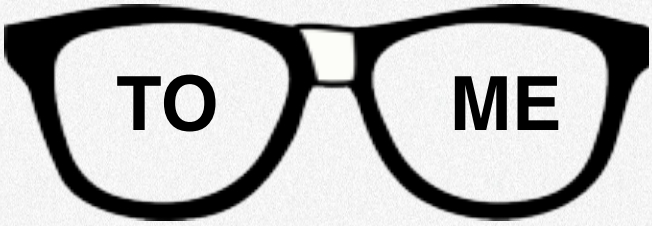
For the secondary outcome of adverse effects, Kennedy et al. reported higher incidence of post-treatment pediatric vomiting in ketamine vs. midazolam (NNT 17, 95% CI 10 to infinity), but Gurnani reported no vomiting in adults.

Gurnani reported significantly increased use of rescue therapy (which is undefined in the systematic review) with morphine (18/20) compared with ketamine (0/20), equating to a NNT approaching 1.

Across all 4 studies only one case of emergency phenomenon was reported and all reported adverse events were transient without requiring prolonged evaluation or hospitalization.

For the secondary outcome assessing the amount of adjuvant opioids consumed, both Galinski and Gurnani reported a significant reduction in the amount of morphine consumed or requested.

TALK NERDY TO ME



Commentary

1. Only searched two electronic databases (MEDLINE and EMBASE).
2. No search of the grey literature (research abstracts and experts in the field).
3. Did not explicitly follow the PRISMA Guidelines (Preferred Reporting Items for Systematic Reviews and Meta-Analyses).
4. Used the GRADE instrument to assess quality as opposed to the Cochrane instrument designed for systematic reviews of randomized controlled trials.
5. Did not include observational studies and conduct pre-planned sub-study analyses of randomized control trials and observational trials to broaden readers' understanding of the published literature on this topic.
6. We would have like to have seen more specific recommendations for future investigators in this field.
7. One of the studies included was by Dr. Bo Kennedy who noted that the dose of ketamine used for sub-dissociative purposes is still uncertain. Dr. Sri Chinta has an in-press manuscript at *Annals EM* that finally tests the appropriate paediatric ketamine dose (answer ED_{50} = 0.5-0.7 mg/kg and ED_{95} = 0.7 mg/kg).
8. Dr. Kennedy also raised the concern that none of the studies controlled how fast the ketamine was given (pushed or titrated to effect).
9. Dr. Kennedy also hypothesized that ketamine's effectiveness might depend on the type of pain based being studied.
10. Dr. Bill Dribben researches NMDA receptors. He believes that low dose ketamine such as that used in subdissociative doses, can produce schizophrenia-like symptoms in some patients.

Quality Checklist for Therapeutic Systematic Review

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 and precise enough to be clinically significant	

CONCLUSION VS COMMENTARY

COMPARISON

Agree that published randomized control trial data neither supports or refutes the emergency department effectiveness or safety of subdissociative-dose ketamine to manage acute pain in children or adults.

Case Resolution

You discuss the issue of subdissociateve-dose ketamine with the patient. She agrees to give it a try to see if it will help her back pain.

Clinical Application

The current published evidence should neither encourage nor dissuade use of subdissociative-dose ketamine as an adjunct to acute pain control in emergency department patients, but keep in mind that the absence of evidence is not evidence of absence.

WHAT DO I TELL MY PATIENT?

Many options exist to alleviate your pain in the emergency department today. One choice is intravenous ketamine, which several small and potentially flawed studies indicate may quickly reduce your pain, while reducing the amount of other pain medications that you require today. In children, 1 in 17 may vomit as a result of ketamine who otherwise would not have vomited, but few other significant side effects have been reported.

References

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2.Messenger DW, Murray HE, Dungey PE, van Vlymen J, Sivilotti ML. Subdissociative-dose ketamine versus fentanyl for analgesia during propofol procedural sedation: a randomized clinical trial. Acad Emerg Med. 2008 Oct;15(10):877-86.

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5.Kennedy RM, Porter FL, Miller JP, Jaffe DM. Comparison of fentanyl/midazolam with ketamine/midazolam for pediatric orthopedic emergencies. Pediatrics. 1998 Oct;102(4 Pt 1):956-63.

Guest Skeptic: Dr. Billy Sin

Billy is an Assistant Professor of Pharmacy Practice Arnold & Marie Schwartz College of Pharmacy and Health Sciences, Long Island University, Clinical Pharmacy Educator Emergency Medicine, The Brooklyn Hospital Center

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Bang your Head:
Paediatric Concussions

Case Scenario:
11-year-old snowboarder fails to land epic jump. She was wearing helmet. There was a brief loss of consciousness and she is amnestic to the event. The only complaint is a mild headache. Her examination is normal and a shared decision is made to observe her rather than getting a CT scan. She is ultimately diagnosed with a concussion. When leaving the department she wants to know when can she go back shreddin' the gnar?

Q:

Is there benefit to recommending strict rest after a child has a concussion?

BOTTOM LINE

In children with concussion, two days of rest followed by a gradual return to activity is preferred over five days of rest followed by a gradual return to activity. The longer strict rest period appears to cause more post-concussive symptoms.

Benefits of Strict Rest After a Child has a Concussion: A Randomized Controlled Trial

Thomas et al. Pediatrics 2014

P Patients aged 11-22 years old presenting to the emergency department with acute (<24 hours) diagnosis of concussion.

I Strict rest at home for five days (no school, work or activity) followed by stepwise return to activity

C Rest for 1-2 days (at the discretion of the treating physician) followed by a return to school and stepwise return to activity.

O Compliance with physical and mental activity recommendations, symptoms, neurocognitive performance (ImPACT) and balance.

Excluded Patients:

- Could not speak English
- Couldn't consent
- Had pre-existing intellectual disability or mental health issue, had a previously diagnosed intracranial injury, were being admitted.
- Patients were also excluded if they lived >1 hour from the investigation center or at the discretion of the recruiting physician.

Authors' Conclusion:

"Recommending strict rest for adolescents immediately after concussion offered no added benefit over the usual care." (Thomas et al. 2014)

Background

Pediatric traumatic brain injury (TBI) is a leading cause of death and disability. The Center for Disease Control (CDC) has called it a national health problem. TBIs are responsible for close to 500,000 ED visits, over 35,000 hospitalizations and more than 7,000 deaths/yr in the USA. TBI is considered mild 75% of the time. Most patients with TBI are discharged from the ED with active concussive symptoms.

TBI represents a challenging situation to emergency physicians. We do not want to miss a significant intracranial lesion while at the same time want to avoid ionizing radiation.

So how do you decide when to get neuroimaging? The best clinical decision instrument and the one we use at McMaster Children's Hospital is PECARN (Pediatric Care Applied Research Network). It has been externally validated and found to be better than the CHALICE Tool and the CATCH Tool (Easter et al Annals Emergency Medicine).

PECARN has been collecting data on patients with head trauma since 2004. It is a federally funded multi-institutional network for research in pediatric emergency medicine.

They successfully enrolled 34,000 patients for the derivation of two clinical decision rules (one for children < 2 years and one for children > 2 years), and an additional 9,000 patients to validate the decision rules. This was published by Kuppermann N et al in the Lancet 2009.

Assuming no patients with significant intracranial injury were missed with their follow-up mechanism, the rule had the following to predict the lack of ciTBI:

- 97% sensitivity and 59% specificity for older children
- 99% sensitivity and 54% specificity for age <2yrs old

The overall prevalence of ciTBI was 0.9% (less than 1/100). Patients requiring neurosurgery was 0.14% (1/700). No patients died out of 34,000.

Results

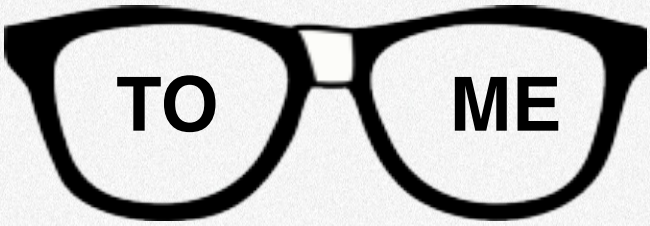
Both groups reported a ~20% decrease in physical activity and energy expenditure for the 5 days post-injury. There was more reported high and moderate mental activity in the usual care group on days 2-5 (8.33 vs. 4.86 hours, P = 0.03).

With regards to efficacy, 67% of patients in the usual care group experienced symptom resolution during follow-up compared to 63% in the strict group (P = 0.82) so no difference.

It took 3 days longer for 50% of patients in the strict group to report symptom resolution. The strict group had more post-concussive symptoms compared to the usual care group over the 10 day follow-up period (70 vs. 50, P <0.03) and had greater post-concussive symptom scale (PCSS) scores (188 vs. 132, P < 0.03).

There were no significant differences noted in computer-based neurocognitive tests and balance scores noted and no significant differences in neuropsychological assessments except for the Symbol Digit Modalities Test for which the usual group performed worse at day three and better at day ten.

TALK NERDY TO ME



Commentary

This is a novel, single-center study examining a topic that we often struggle with in the emergency department, specifically, how long to keep someone resting post-concussion.

There are some minor limitations of this study: The patients were aged 11-22 years. It is questionable whether this study can be generalized to younger pediatric patients;

The two groups did differ significantly in terms of age with the strict rest group being older. The impact of this difference is unknown;

Outcome measures such as re-presentation to emergency department and proportion of patients with symptoms beyond 10 days were not described. In addition, 11% of patients were lost to follow-up.

This study has opened the door to a very interesting line of inquiry, and further research will be very useful.

RCT 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 groups to which they were randomized	☑
The study patients were recruited consecutively (i.e. 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	☑

For the time being, however, there is evidence to support a two-day rest period following a concussion with a gradual return to activity. Keeping a child at strict rest for five days post-concussion appears to offer no benefit, and there is evidence of harm from this strategy.

Case Resolution

You send the shredder home with your hospital's standard concussion information.

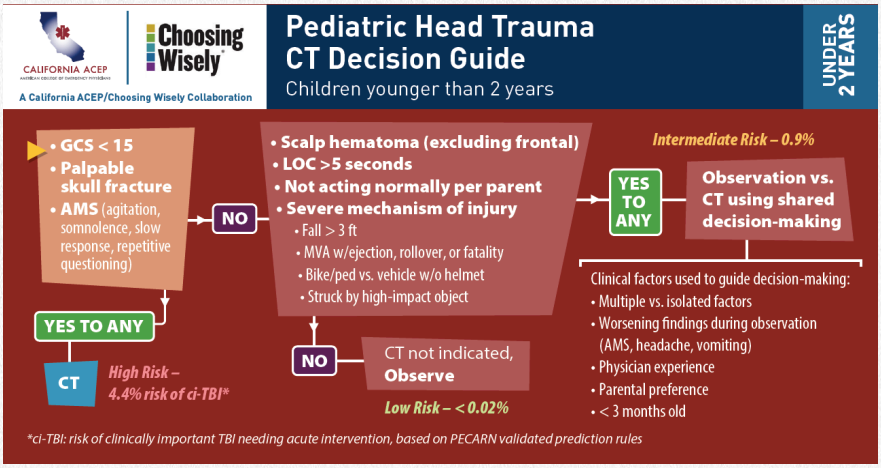
Clinical Application

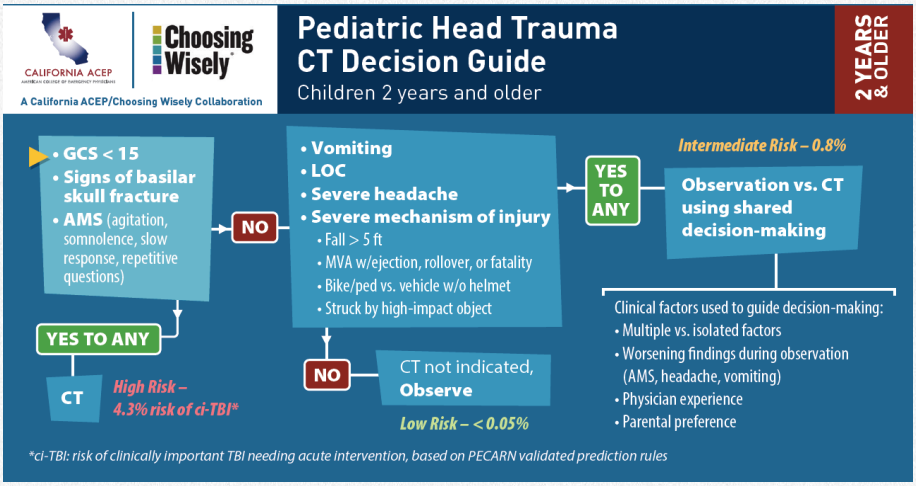
In children presenting with concussion we can limit the rest period, post-concussion, to two days followed by gradual return to activity.

CONCLUSION VS COMMENTARY

COMPARISON

We would agree with the authors that there is no added benefit to five days of strict rest over two days and we would add that the five-day strict strategy appears to cause more harm.





WHAT DO I TELL MY PATIENT?

Your child has a concussion and they need to take two days off school and sports. They can slowly return to activity after that period of time.

Two for the Price of One

Case Scenario:

Same 11-year-old snowboarder who has a mild headache after her concussion. The mother wants to know if there is anything else besides acetaminophen or ibuprofen to treat her daughter's headache?

Q:

What about using intravenous hypertonic saline as a therapy for paediatric concussive pain?

BOTTOM LINE

Although an interesting therapeutic modality to be further studied, IV hypertonic saline is not ready for routine use in children with moderate-severe concussions.

Hypertonic Saline as a Therapy for Pediatric Concussive Pain: A randomized controlled trial of symptom treatment in the emergency department

Lumba-Brown et al. Pediatric Emergency Care 2014

P Children 4-17 years old with acute closed head injury, GCS>13, moderate to severe concussive symptoms and had a CT scan prior to enrollment

I Standard care + 10cc/kg of 3% hypertonic saline (max 1L) over 1 hour

C Standard care + 10cc/kg of normal saline (max 1L) over 1 hour

O Change in self reported pain using Wong-Baker FACES Pain Rating Scale.

Excluded Patients:

- GCS<13
- CT bleed
- Seizure
- Chronic migraines
- EtOH
- Drugs
- Associated injuries
- Needing narcotics
- Trauma patients
- Intubated or pregnant

Authors' Conclusion:

Three percent HTS [hypertonic saline] is more effective than NS [normal saline] in acutely reducing concussion pain in children." (Lumba-Browen et al., 2014)

Background

Hypertonic saline as a therapy for increased intracranial pressure was first described almost 100 years ago by Weed and McKibben in the American Journal of Physiology symptoms.

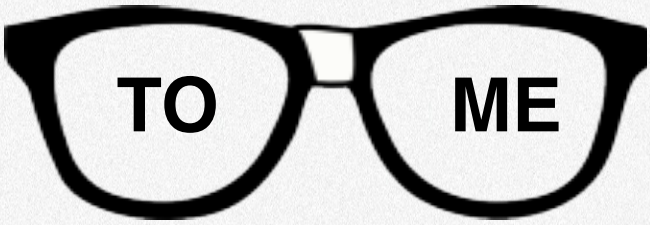
Results

The change in pain from pre-treatment to 1 hour post-treatment was significantly better at 3.52 for the HTS group than 1.14 for the NS group ($p<0.001$). In addition the change in pain at 2-3 days was significantly better in the HTS group (4.61) compared to the NS group (3) with a $p = 0.01$.

TABLE 2. Pain Scale Reports in HTS and NS Treatment Groups

	3% HTS Therapy (n = 23), mean (SD)	NS Therapy (n = 21), mean (SD)	Mann-Whitney *U* Test (*P*)	Independent *t* Test (95% CI)
Pretreatment pain (FPS1)	5.74 (2)	4.29 (1.1)	0.02	—
Pain within 1 h posttreatment (FPS2)	2.22 (1.6)	3.14 (2.2)	0.11	—
Change in pain; FPS2 − FPS1	3.52 (1.6)	1.14 (1.5)	>0.001	(−0.3. to −1.4)
Pain within 2–3 d after ED discharge; (FPS3)	1.13 (1.5)	1.29 (1.5)	0.73	—
Change in pain; FPS3 − FPS1	4.61 (2.3)	3 (1.7)	0.01	(−2.9 to −0.3)

TALK NERDY TO ME



Commentary

This study explores an interesting therapeutic possibility for children with moderate to severe concussions after an acute head injury. The authors' conclusions are over-ambitious and careful consideration of the paper's limitations needs to be addressed.

The sample size was too small. The original plan was to recruit a total of 104 patients for this trial. The authors failed to reach this number and only recruited a total of 44 patients.

Commentary

The low number of patients put the study at risk of significant differences between study groups, which we see. Specifically, in this study, the HTS group had higher initial pain scores which could made it easier to see an greater absolute change in pain scores over time.

Generalizability is an issue for these patients to our patients. This study only included patients who had a CT scan and therefore it is questionable whether these results can be applied to all patients presenting with concussive symptoms. Also, it would be unethical to perform an unnecessary CT scan just to ensure the utility of this therapy. The authors also had a number of exclusion criteria, including post-traumatic seizure and history of chronic migraines, which may preclude the generalizing of these results to the average ED patient.

Follow-up was not as planned. The initial plan was a 2-3 day follow-up. The average follow-up was 5 days with many patients being followed up at 7 days. This may have instilled recall-bias, undermining the results from the 2-3 day pain scales.

RCT 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 groups to which they were randomized	☑
The study patients were recruited consecutively (i.e. 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	?

Clinical Application

None at this time.

CONCLUSION VS COMMENTARY

COMPARISON

We disagree with the authors. Based on significant limitations of this study, hypertonic saline is not ready for prime-time use in patients with moderate-severe concussion.

References

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Guest Skeptic: Dr. Anthony Crocco

Associate Professor, McMaster University, Medical Hospital Emergency Department. Director and Division Head McMaster Children's

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EGDT:
ProMISe(s) ProMISe(S)

Case Scenario:

You see a 62-year-old man sent from a nursing home with a three day history of a productive cough, intermittent fevers and today is a bit confused. The transfer notes include a history of congestive heart failure, chronic obstructive pulmonary disease, gout, hypertension, type 2 diabetes, and mild dementia. His emergency department vitals are as follows: Temperature 39.1C, heart rate 103, blood pressure 115/100, respiratory rate 26, oxygen saturation is 92% on room air, and capillary blood sugar is normal.

Q:

Does an emergency department patient with septic shock need aggressive EGDT or is *"usual"* resuscitation just as good?

BOTTOM LINE

There is no need to provide invasive expensive EGDT in the emergency department for septic shock patients

Trial of Early, Goal-Directed Resuscitation for Septic Shock, NEJM 2015

P Adult patients presenting to the emergency department with early septic shock (SIRS 2+ criteria with refractory sBP<90mmHg despite fluid resuscitation 1L within 6 0minutes, or hyperlactatemia >4mM). Patients recruited from 56 hospitals (approximately 25% of total hospitals) in England (29% teaching hospitals)

I Early goal-directed therapy (EGDT). Note – all patients received antibiotics before randomization

C *"Usual care"* including monitoring, investigations and treatment as determined by treating clinician(s)

O Primary: 90 day all-cause mortality.
Secondary: SOFA scores (6, 72hrs), organ support (cardiovascular, respiratory, renal) in critical care up to 28days, length of stay (emergency department, intensive care unit, hospital), all-cause mortality 28d/hospital /1year, survival duration, health-related quality of life (HRQOL, measured on EQ-5D-5L), resource usage, costs at 90d and one year.

Excluded Studies:

- Age<18yo
- Pregnant
- Primary acute diagnosis (stroke, acute coronary syndrome, congestive heart failure, status asthmaticus, arrhythmia, seizure, over-dose, burn/trauma)
- Unstable GIB
- Need immediate surgery
- History of AIDS
- Do not resuscitate/other advanced directives restricting resuscitation
- Contraindications to line placement/blood transfusions,
- Transfer from another in-hospital setting, not able to commence within 1hr emergency department arrival or complete 6hr protocol
- Physician discretionary exclusion.

Authors' Conclusion:

In patients with septic shock who were identified early and received intravenous antibiotics and adequate fluid resuscitation, hemodynamic management according to a strict EGDT protocol did not lead to an improvement in outcome."

Background

Sepsis can be defined as a "*clinical syndrome complicating severe infection characterized by inflammation remote from the site of infection. Dis-regulation of the inflammatory response can lead to multiple organ dysfunction.*"

Systemic Inflammatory Response Syndrome (SIRS) Criteria:

- A temperature over 38C or less than 36C
- A heart rate over 90 beats/min
- A respiratory rat e over 20 breaths/min or PCO2 less than 32mmHg
- A WBC count less than 4,000 or over 12,000 or greater 10% immature forms

Sepsis: At least two of the four SIRS + infection.
Severe Sepsis: Sepsis + hypotension and end organ failure
(Hypoxia, renal failure, hepatic failure, coagulopathy, hypotension, lactate greater than 2 mmol/l)
Septic Shock: Severe sepsis and hypotension refractory to fluid treatment or lactate greater than 4 mmol/l

Results

This was a parallel arm superiority trial, 1:1 randomization in permuted blocks of 4/6/8. 1260 patients needed for sample size, 1243 completed trial (>98% follow-up) for primary outcome of interest. Baseline characteristics well matched in both arms, including infection sources.

Only 1/3 patients screened were successfully recruited with poor recruitment on weekends and nights. Recruitment rate of eligible was similar to the two other trials (note: recruitment by day-of-week/time-of-day was not reported by the other two trials). Lower recruitment at weekends and nights indicates the challenges faced in conducting emergency and critical care research.

The economic evaluation was based on 2012 GB pound/US dollar values. Cost effectiveness determined on threshold willingness to pay for QALY gains as per NICE guidelines (GBP 20,000 / USD $28,430 per QALY).

Primary outcome from ProMISe Trial:

No statistically significant difference in 90d all cause mortality (EGDT 29.5% vs. Usual Care 29.2%)

ED Protocol Adherence (0-6 hrs)

	EGDT	Usual Care
SCVO2	87.3%	0.3%
Arterial line placement	74.2%	62.2%
Any central line	92.1%	50.9%
Median IV fluids	2000ml	1784ml
Colloids equal	31.6%	46.6%
Vasopressors	53.3%	46.6%
Dobutamine	18.1%	3.8%
RBC Transfusions	8.8%	3.8%
Platelet/FFP Transfusion	<2.5%	<2.5%
ICU admission	88.2%	74.6%
Invasive measures (CVP, MAP, sBP, Hgb)	Similar at 6hr	Similar at 6hr

Relative risk in the EGDT group, 1.01; 95% confidence interval [CI], 0.85 to 1.20; P=0.90 for an absolute risk reduction in the EGDT group of −0.3 percentage points (95% CI, −5.4 to 4.7)

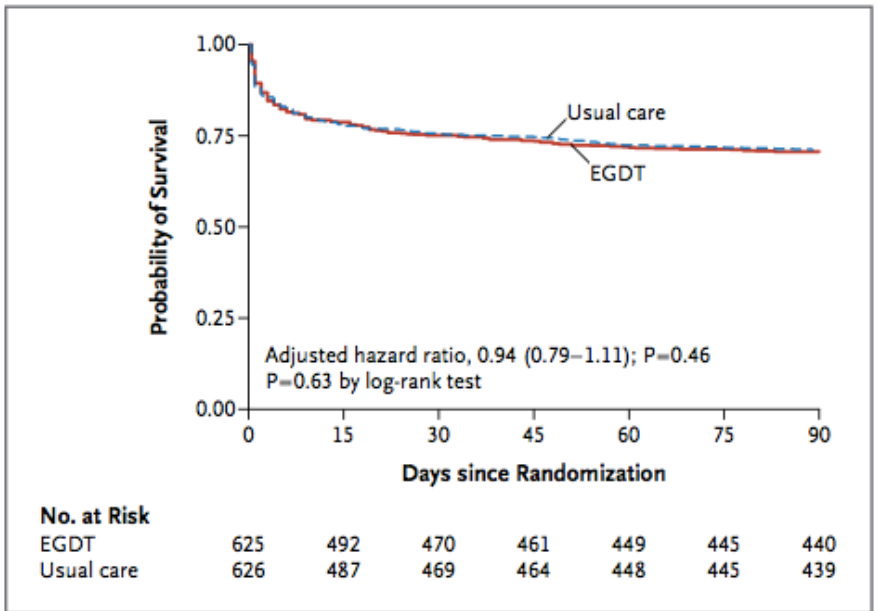


Figure 2. Kaplan–Meier Survival Estimates.
Shown is the probability of survival for patients with severe sepsis receiving early, goal-directed therapy (EGDT) and those receiving usual care at 90 days.

Secondary Outcomes:

Mortality:
No difference – 28 days: 24.8% vs. 24.5%
No difference – Hospital discharge: 25.6% vs. 24.6%

Median length of stays (LOS):
No difference – ED LOS: 1.5hrs vs. 1.3hrs
ICU LOS: 2.6 days vs. 2.2 days
No difference – Hospital LOS: 9d vs. 9d

Days free from life support:
No difference – Cardiovascular 37.0% vs. 30.9%, Respiratory 28.9% vs. 28.5%, Renal 14.2% vs. 13.2%

Quality of Life:
No difference – Health related quality of life
No difference – QALY up to 90d

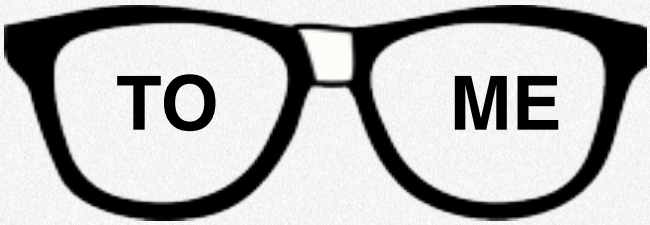
Expense/Cost of EGDT vs. *Usual Care?*
No difference – Average costs up to 90d: $17,647 EDGT vs. $16,239 UC
It was about £1,000 more to do EGDT – mostly associated with the ½ day increased LOS in the ICU

Harm:
No difference in serious adverse events: 4.8% vs. 4.2%

Table 3. (Continued.)

Outcome	EGDT (N=625)	Usual Care (N=626)	Incremental Effect (95% CI)	P Value
Cost-effectiveness				
Health-related quality of life on EQ-5D at 90 days††	0.609±0.319	0.613±0.312	−0.004 (−0.051 to 0.044)§	0.88
Quality-adjusted life-yr up to 90 days	0.054±0.048	0.054±0.048	−0.001 (−0.006 to 0.005)§	0.85
Costs up to 90 days				0.26
Pounds	12,414±14,970	11,424±15,727	989 (−726 to 2,705)§	
Dollars	17,647±21,280	16,239±22,356	1,406 (−1,032 to 3,845)§	
Incremental net benefit up to 90 days‡‡				0.25
Pounds	NA	NA	−1,000 (−2,720 to 720)§	
Dollars	NA	NA	−1,422 (−3,866 to 1,023)§	
Serious adverse events — no. (%)	30 (4.8)	26 (4.2)	1.16 (0.69 to 1.93)¶	0.58†

TALK NERDY TO ME



Commentary

The trifecta on EGDT for sepsis has been completed. This is the final nail in the coffin for EGDT for adult septic shock in the emergency department.

A nail with caveats. From a population standpoint, in institutions where usual care entails a system of consistent early identification (recognized with 1.5 hr, randomized in under 3 hours from presentation). Early IV fluids. Remember that about 2 liters prior to randomization. Early antibiotics (had to be started prior to randomization – median within 3 hours from presentation). Early lactate measurement. When this is your usual care, you can expect similar outcomes as ProMISe.

We still need to further explore usual care in our study. For example, what is unclear is if there are certain populations that may benefit from the other components of the protocol and this will be worked out in a combined analysis among the three trials.

These results mirror the earlier results of the ProCESS (US) and ARISE (Aus/NZ/Finland) trials comparing EGDT vs. *"usual care"* protocols, and showing no differences between any of the arms worldwide. Again, trial planners agreed to harmonize the endpoints of all 3 trials, so future metaanalyses should confirm these results using individual patient data.

The failure to reproduce the original 2001 Rivers/ early EGDT results in all 3 trials likely reflects the increased attention and aggressive treatments (albeit non-invasively) that most ED physicians now use worldwide in treating septic shock patients. It is now clear that an expensive and invasive care for these patients is not necessary.

Given the attention focused on sepsis, it seems highly unlikely that usual resuscitation has not improved in the 10-15 years since the study by Rivers and colleagues.

An important consideration, however, when interpreting the results from ProMISe (and those from the harmonised trilogy of trials including ProCESS and ARISE) is that the patients recruited to ProMISe were identified early and received a median of 2L of IV fluids and antimicrobial drugs prior to randomisation. Then, in this group of patients, subsequent, algorithm-driven EGDT (as defined by the six-hour resuscitation protocol from the study by Rivers and colleagues) including continuous central venous oxygenation monitoring did not lead to an improvement in outcomes and increased the costs of care.

Of note, this trial did calculate utility measures for HRQOL using a validated tool, and found that EGDT was more expensive than usual care (not significantly so), and the incremental net benefit of EGDT over usual care was negligible. It is rare to have simultaneous real-time economic evaluations done in large randomized control trials, so when they are done (and done properly as it was here), the results are even more informative.

RCT 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 groups to which they were randomized	☑
The study patients were recruited consecutively (i.e. 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	

Case Resolution

Having recognized the sepsis potential of this patient and confirming a high lactate, you initiate broad-spectrum antibiotics for what is most likely a clinical pneumonia. You give aggressive fluid resuscitation with IV normal saline or ringers lactate. Then call your consultant to arrange admission to the intensive care unit.

Clinical Application

If it is 02:00 and you are working in a single coverage emergency department you can start with IV fluids, antibiotics and lactate measurement. If you have volume refractory shock requiring vasopressors, then most guidelines support administering them through a central line. Given that about half of the usual care group received central lines within about 2 hours after being randomized indicates that emergency department providers are both decisive and capable when they feel central lines are needed.

References

1. Trial of Early, Goal-Directed Resuscitation for Septic Shock. NEJM March 2015.
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CONCLUSION VS COMMENTARY

COMPARISON

We agree with the ProMISe authors conclusions. However, as in previous trials, this is NOT a refutation of any protocolized care, but only EGDT in its original 2001 version (Rivers NEJM). Every study group and the Surviving Sepsis Campaign still recommend the use of sepsis protocols that emphasize: 1) Early recognition 2) Copious IV crystalloid resuscitation, 3) Lactate screening and 4)Targeted (or at least broad-spectrum) antibiotic

Guest Skeptics:

Dr. Suneel Upadhye (BEEM Group)
Suneel is an Associate Clinical Professor Emergency Medicine at McMaster University and Associate Member of Clinical Epidemiology and Biostatistics. He is also the Chair CAEP standards committee and a sepsis researcher.

Dr. Tiffany Osborn
Tiffany is the second author on the ProMISe Trial. She is an Associate Professor in the Department of Surgery and the Department of Emergency Medicine at Washington University, St. Louis.

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Ketofol: Does it Take Two to Make a Procedure Go Right?

Case Scenario:

A 40-year-old male comes to the Emergency Department with a dislocated shoulder while playing football. He's a weekend warrior and has never had any shoulder dislocations in the past. It took him about an hour to get the Emergency Department. After some pain control, you try the Cunningham and scapular manipulation to get the shoulder back in but they are not working. You decide that he needs procedural sedation. One of your residents asks you "I've heard about ketofol thing, can we try it in this patient?"

Q:

How does propofol compare to ketofol mixed at 1:1 ratio compared to ketofol mixed at 4:1 (propofol to ketamine) for adults requiring procedural sedation in the Emergency Department?

BOTTOM LINE

Ketofol in a 1:1 or 4:1 ratio does not appear to have a greater than 20% benefit (less adverse respiratory/airway events) compared to propofol alone

Randomized, Double-Blinded, Clinical Trial of Propofol, 1:1 Propofol/Ketamine, and 4:1 Propofol/Ketamine for Deep Procedural Sedation in the Emergency Department

Miner et al. Annals of Emerg Med 2014

P Adults 18 and over presenting to the ED requiring procedural sedation for a painful ED procedure

I Propofol/ketamine at a 1:1 ratio or 4:1 ratio

C Propofol alone

O Primary Outcome: Number and proportion of subjects experiencing airway or respiratory adverse events leading to an intervention

Authors' Conclusion:

"We found a similar frequency of airway and respiratory adverse events leading to intervention between propofol alone and either 1:1 or 4:1 ketofol". (Miner et al. 2014)

Background

Ketofol's use has been rising in popularity in the EM and pediatric EM community. Ketofol refers to a combination of ketamine (which we talked about using in a sub dissociative dose for pain control recently) and propofol. It is often mixed in the same syringe but people some choose to give it separately. The theory is that the two medications can make a procedure go right by canceling out the bad effects of the other.

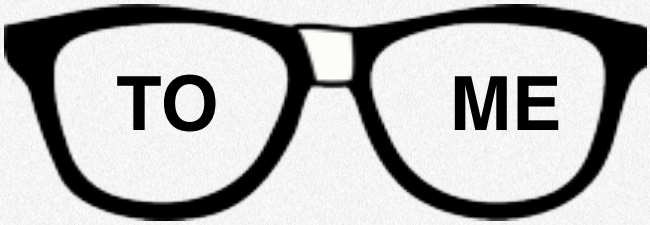
Propofol tends to cause hypotension and sometimes apnea whereas ketamine usually raises the blood pressure and doesn't affect the respiratory drive. On the flip side, ketamine tends to cause vomiting when emerging from its effects whereas propofol has some antiemetic properties.

Results

Primary Outcome:
There was no statistically significant difference in the primary composite outcome. Propofol 32% vs. 1:1 Ketofol 22% vs. 4:1 Ketofol 33%

Secondary Outcomes:
These were similar between the three groups. The only exception was that there was more recovery agitation in the ketofol 1:1 group and the ketofol 4:1 group compared to propofol alone. This is to be expected since ketamine is known to cause recovery agitation, however the clinical significance of this is uncertain. The authors didn't mention whether any patient had recovery agitation that was significant enough to require treatment or that the patient remembered after the procedure

TALK NERDY TO ME



Commentary

1. Composite Endpoint: While composite endpoints make the target bigger and easier to hit, each component may not be of equal importance to the patient. They had six components in their composite outcome: hypoxia, central apnea, subclinical respiratory depression, complete airway obstruction, laryngospasm and aspiration. There were zero events for half (three) of the components for any of the interventions. The most common adverse component was subclinical respiratory depression 51/271 (19%). How important is this event?

2. Surrogate Endpoints: They used definitions from previous studies. However, these do not represent patient oriented outcomes. The authors did recognize this as a limitation to their study.

3. Un-blinding: They did a good job in attempting to blind the physicians to the group allocation by having the syringes look identical. Despite the strategy physicians were able to guess group allocation more than chance. They guessed the 1:1 group 58% of the time. This could have un-blinded the study and introduced some bias. Bias being defined as moving the results away from the truth.

RCT 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 groups to which they were randomized	☑
The study patients were recruited consecutively (i.e. 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	☑

Power Calculation: The anticipated ~30% adverse composite outcome. When you look at their results they were pretty close with an observed range from a low of 19% in the 1:1 group to a high of 32% in the 4:1 group. However, they set their sample size on a 20% difference in their primary outcome. Why did they pick such a large number? There was a 10% difference between propofol vs. 1:1 ratio and 11% difference between the 1:1 ration vs. 4:1 ratio. If the sample size were larger would there be a regression to the mean or would this difference hold up. If the later, the NNT would be 10 favoring the 1:1 ratio.

Patient Oriented Outcomes: The composite adverse outcomes may not have been that important to the patients. Especially when the intervention to address the problems were; providing supplemental oxygen, bagging the patient, repositioning during the procedure and stimulating the patient to induce ventilation. No patient in any of the three groups needed an airway adjunct. An important patient oriented secondary was satisfaction with the procedure. More patients were satisfied with propofol alone (85%) compared to 1:1 ratio (71%). The study was not powered to make any conclusions on secondary outcomes but the results could generate a hypothesis for a future study.

Case Resolution

You and the resident both take a look at this article and decide to proceed with just propofol for the sedation since it will require less nursing time and less potential for medication errors in mixing as compared to propofol. As always, you do a good pre-procedure assessment of the airway as well as doing a good history and physical. You get all of your airway equipment to the bedside, check your equipment and size it appropriately. You also have the RSI kit at the bedside just in case. The patient receives the propofol and you successfully reduce the patient's shoulder on the first attempt without any respiratory issues.

CONCLUSION VS COMMENTARY

COMPARISON

The conclusion seemed a little misleading. A more accurate conclusion would be there was not a greater than 20% difference in composite outcome (respiratory and airway adverse events) between propofol alone vs. either 1:1 propofol/ketamine ratio or 4:1 ratio.

Clinical Application

I am generally going to use IV opioids for pain control followed by propofol for procedural sedations.

WHAT DO I TELL MY PATIENT?

We are going to use propofol to sedate you to help put your shoulder back in. Propofol is a very safe drug that we have a lot of experience using in our Emergency Department. Side effects are rare and may include having to breathe for you with a mask or put a tube down your throat but we will watch you closely and be prepared for any possible problem ahead of time.

References

Miner et al. Randomized, Double-Blinded, Clinical Trial of Propofol, 1:1 Propofol/Ketamine, and 4:1 Propofol/Ketamine for Deep Procedural Sedation in the Emergency Department. Annals of Emerg Med 2014

Guest Skeptic: Dr. Steve Carroll

Steve is an Emergency Medicine Physician and EM Core Faculty with the US Army at San Antonio Military Medical Center in San Antonio, Texas. He also does an awesome podcast called EM Basic that is your *"boot camp guide to emergency medicine"*. EM Basic reviews common EM topics at the level of a medical student or intern

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Complicated: Non-Operative Treatment of Appendicitis (NOTA)

Case Scenario:

A 35-year-old man presents to the emergency room with right lower quadrant pain for approximately 18 hours. You assess the patient and find that his Alvarado Score is 7. You then ask for an ultrasound, as his body mass index is in the normal range. The ultrasound shows that he has an enlarged appendix >6mm that is not compressible and there is no intraperitoneal fluid present. You make a presumptive diagnosis of uncomplicated acute appendicitis. You relay this finding to the patient and he turns to you and asks, *"Hey doc, I heard that you can treat appendicitis with antibiotics now. Is that true?"*

Q:

Are antibiotics in non-complicated acute appendicitis an effective and safe alternative to appendectomy?

BOTTOM LINE

Because of the diagnostic uncertainty of appendicitis, non-operative treatment of appendicitis (NOTA) will always be a very difficult thing to study. You will never know for sure in the antibiotics arm whether you were actually treating appendicitis. You will only know this in the surgical arm in which there is a pathology diagnosis. As a general practitioner with enhanced surgical skills, I would be concerned about treating suspected appendicitis with antibiotics because should it fail, this could lead to increased morbidity.

Safety and Efficacy of Antibiotics Compared with Appendectomy for Treatment of Uncomplicated Acute Appendicitis: Meta-Analysis of Randomised Controlled Trials BMJ 2012

P 4RCTs of adult patients (n=490)

I Antibiotics

C Appendectomy

O Complications (wound infection, perforated appendicitis, peritonitis)

Authors' Conclusion:

Antibiotics are both effective and safe as primary treatment for patients with uncomplicated acute appendicitis. Initial antibiotic treatment merits consideration as a primary treatment option for early uncomplicated appendicitis.

Background

Claudius Amyand did the first appendectomy in 1735. The standard treatment for acute appendicitis ever since Charles McBurney described it in 1889 has been appendectomy.

Omar et al (2008) showed just how safe laparoscopic appendectomies have become. They found in a study of over 230,000 UK patients under the age of 49 there were no deaths. Kluiber et al 1996) demonstrated the incidence of post-operative intra-abdominal wound infection to be about 2-5%.

Being that there are doctors out there without scalpels, and that diverticulitis has often been treated successfully with antibiotics (this also being an infection based on the same theory), some have put two and two together and postulated that perhaps acute appendicitis could be treated successfully with antibiotics.

Two meta-analyses have been done recently and interestingly enough; they looked at nearly the same studies on "uncomplicated" acute appendicitis and came up with two opposite conclusions. This is an example of why things in evidence-based medicine can be "complicated".

Results

Primary Outcome: Complications (wound infection, perforated appendicitis or peritonitis)
Relative Risk Reduction 0.69 (CI 0.54 to 0.89 P=0.004)-favouring antibiotics

Secondary Outcomes:
Length of Stay – No difference

Readmissions: 68/345 (20%) of patients treated with antibiotics were readmitted with recurrence of symptoms. If one were to include the studies with crossover (which I think should be considered failure) this number would be 158/438 (36%).

Efficacy: Antibiotics 274/470 (58%) and surgery 398/430 (93%). Failure as defined by normal pathology, which to me is a failure of diagnosis, not therapy.

Pain and temperature were not analyzed in a meta-analysis format

Quality Checklist for Therapeutic Systematic Review

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 and precise enough to be clinically significant	☑

Appendectomy for Suspected Uncomplicated Appendicitis is Associated with Fewer Complications than Conservative Antibiotic Management: A Meta-Analysis of Post-Intervention Complications. J of Infection 2015

P 3 RCTs of adult patients (n=531)

I Antibiotics

C Appendectomy

O Major complications (peritonitis or abscess formation after intervention). They excluded wound infection in this analysis.

Authors' Conclusion:

Suspected uncomplicated appendicitis has a lower rate of major post-intervention complications when managed with primary appendicectomy compared to antibiotic therapy."

Results

The primary outcome was major post-intervention clinical complications (peritonitis or abscess formation after intervention).

10.1% (27/268) with antibiotics vs. 0.8% (2/263) with appendectomy

You can alternatively report this as a Risk Ratio that was 7.71 (CI 2.3-25.5 p=0.0008) or a NNH =11. There was no statistical difference in perforated appendicitis in either group.

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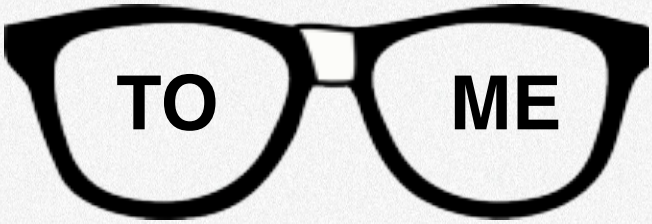

Commentary

Diagnosis of Acute Appendicitis:

In all studies this was different. There was no defined definition of the positive diagnosis of acute appendicitis. Some studies included certain lab tests (CRP etc.) others included +/- imaging that may have included CT or ultrasound or both. None of the studies used a defined scoring system for acute appendicitis (i.e. Alvarado Score).

We know that even in the best circumstances, the negative appendectomy rate still ranges from 6%-30%. Diagnostic certainty is still quoted between 70-97% depending on where you look. This is a huge range. And, if studies don't use rigorously defined diagnostic criteria for uncomplicated appendicitis with a known specificity, then we don't know how many patients in each study labeled as "acute appendicitis" actually have "acute appendicitis" or some other entity.

The only way to diagnosis appendicitis is on pathology. Thus, we will never truly know in any studies that randomize patients based on pre-pathology diagnosis whether we are treating a number of patients with *"acute appendicitis"* whom actually have another diagnosis. Thus, it will always be that the antibiotic arm will have an unknown in this regard as compared to the surgical arm that will always have a pathological confirmation of diagnosis.

Heterogeneity in Studies:
Populations were different and didn't include children, and didn't include women in one study.

Some studies used laparoscopic appendectomy, some used both, and others didn't define the type of surgery.

Each study used a different antibiotic regimen (though in the 2012 study, it showed that this didn't have an effect on efficacy).

Intention To Treat Analysis (ITT):

This means that patients were studied in the groups they were randomly allocated to even if they crossed over in the study.

A crossover from antibiotics to an appendectomy means a failure of antibiotic therapy, rather than other reasons patients would fall out of an ITT analysis. Neither of the metanalyses tried to do a per-protocol analysis (though they did exclude one study with significant crossover in the 2012 metanalysis). What it would look like if all the crossover patients were studied in the groups in which appendicitis was actually treated successfully?

Quality Checklist for Therapeutic Systematic Review

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 and precise enough to be clinically significant	☑

Treatment Difference:

The type of antibiotic used did not have an impact on the results for the patients assigned to the antibiotic group. However, only two of the four studies in the Varadhan review reported peri-operative antibiotics prophylaxis in the surgical group. If antibiotics were given the post-op wound infection rate was about 3%. In the patients' without documentation of antibiotics the infection rate was 12%.
It is now standard care to use antibiotics peri-operatively for appendectomies because it decreases infection rate from 15% to 5%. So if antibiotics were not used in the surgical cases it stacks the deck in favor of the non-operative group. This means their higher composite outcome of complications in the surgical group could have been driven by post-operative wound infections

Included Studies:

The systematic review by Kirby did not include the Hansson et al 2009 British Journal of Surgery study. This was an RCT of 369 patients with history, signs and laboratory tests suggestive of acute uncomplicated appendicitis. Not all the patients had imaging (CT and/or ultrasound) to confirm the diagnosis prior to randomization.

Kirby also excluded Hansson because they included patients irrespective of the risk of perforation. A perforated appendix is not an uncomplicated case of appendicitis anymore. Antibiotic treatment of a perforated appendicitis can delay the diagnosis of complicated appendicitis and result in increased morbidity.

Case Resolution

You look skeptically at the patient. Being a person who routinely does surgery for acute appendicitis, your pre-conceived bias takes over and you say that yes, there have been some studies recently that have shown promise in this regard, but there also have been studies that demonstrate potential harm. Therefore, you stick with what you feel comfortable with and offer the patient a laparoscopic appendectomy as it has the lowest complication rate in regard to surgical management of acute appendicitis. In addition, it also has been shown to significantly reduce the negative appendectomy rate.

Clinical Application

This represents a potential opportunity for shared decision making (SDM) between the patient and the surgeon. Barry and Edgman-Levitan NEJM 2012 describes SDM when the patient and the doctor collaborate on reaching a decision about a management strategy for a given clinical problem. For SDM to take place there must be more than one reasonable option. It also requires the physician give the patient the information they need to choose between competing acceptable strategies.

CONCLUSION VS COMMENTARY

COMPARISON

These two meta-analysis came to opposite conclusions. They did so by choosing different studies to include and the outcomes that they felt (subjective) were clinically relevant.

If you think wound infection isn't clinically relevant, then yes antibiotics increase risk of serious complications (abscess, peritonitis) compared to appendectomy. In contrast, if you think post-op wound infection is clinically relevant, then as a pooled outcome (wound infection, peritonitis and perforated appendicitis) overall it would look like antibiotics are safer in the treatment.

As long as you are not giving antibiotics prophylactically peri-operatively to prevent post-operative wound infections that is standard of care. And including studies that make no attempt to exclude patients with complicated appendicitis.

WHAT DO I TELL MY PATIENT?

here are some studies showing antibiotics can be effective in the treatment of acute un-complicated appendicitis. However, it's complicated, because there are other studies that show the opposite to be true. There are risks no matter what treatment you choose. I think the data still supports doing surgery right away but ultimately the decision is yours.

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Guest Skeptic: Dr. Bret Batchelor

Bret is a general practitioner with Enhanced Surgical Skills currently working in Vanderhoof, BC. He is the host of the newly created podcast that can be found on iTunes called Really Rural Surgery.

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Paramedics' Got a Squeeze Box

Remote Ischemic Conditioning

Case Scenario:

Your rural EMS unit is dispatched to a call for a 65-year-old man with chest pain. On scene a 12 lead ECG is acquired in six minutes, revealing ST elevation in V_3 through V6. The patient is given 324 mg of chewable aspirin, sublingual nitroglycerin which reduces his 9/10 chest pressure, oxygen by nasal cannula to maintain his SaO_2 above 94%. The EMS provider calls the hospital with a STEMI alert with a 30 minute ETA. You recall reading an article recently about remote ischemic conditioning, which is done by inflating a BP cuff on the patient's arm to 200 mmHg for 5 minutes, then release the pressure for 5 minutes, and repeat three more times. The article said this technique reduces myocardial damage from reperfusion injury after the PCI. It's not in your protocols so you call medical control to discuss it.

Q:

Does pre-hospital remote ischemic conditioning performed on STEMI patients decrease myocardial reperfusion injury and improve their long-term outcome?

BOTTOM LINE

The technique has promise as it is cheap and can be done by all levels of EMS provider. However, there needs to be a large multicentred trial using RIC showing improved patient oriented outcomes before this becomes a routine treatment in the pre-hospital setting for STEMI patients.

Improved Long-Term Clinical Outcomes in Patients with ST-elevation Myocardial Repurfusion Injury and Improve Their Long-Term Outcome

Sloth et al. European Heart Journal 2014

P Adults with symptoms <12hrs and STEMI on ECG

I Remote ischemic conditioning by inflating a blood pressure cuff on the patient's arm to 200 mmHg for 5 minutes, followed by release of pressure for 5 minutes. Performed a total of 4 times prior to PCI.

C Usual care

O Primary Outcome: MACCE (Major Adverse Cardiac and Cerebrovascular Events) that included a composite of all-cause mortality, myocardial infarction, readmission for heart failure and ischemic CVA/TIA.

Authors' Conclusion:

"Remote ischemic conditioning before primary percutaneous coronary intervention seemed to improve long-term clinical outcomes in patients with ST-elevation myocardial infarction". (Sloth et al., 2014)

Excluded Studies:

- Diagnosis not confirmed upon hospital arrival
- History of previous myocardial infarction, previous coronary artery bypass grafting (CABG), and chest pain > 12 hours prior to admission.
- Parent trial excluded LBBB,
- Fibrinolytic treatment in previous 30 days
- Left main stem stenosis, Severe heart failure needing mechanical ventilation, and intra-aortic balloon pump

Background

The phenomenon of ischemic preconditioning was reported almost 30 years ago in experiments done on dogs. These early studies looked at limiting infarct size. The technique involved a series of alternating periods of ischemia of a coronary artery with reperfusion sessions to render the myocardium more resistant to a subsequent ischemia event.

When a coronary vessel is occluded during an MI, myocardial cells distal to the occlusion suffer from ischemic injury. A reperfusion injury has been described once the flow has been restored via PCI that may increase the infarct size.

Unlike the dog experiments, the remote ischemic conditioning (RIC) involves placing a blood pressure cuff on an extremity. It typically is on the arm and inflated to 200 mmHg for 5 minutes, then released. This pattern is repeated three more times.

The exact mechanism behind remote ischemic conditioning (RIC) is not known. It is thought to be a neuroal and hurmoral interaction mediating the protective effect.
RIC has been investigated in a number of large cardiac surgery and PCI trials. These have reported benefit in improving cardiac markers and limiting infarct size.

Results

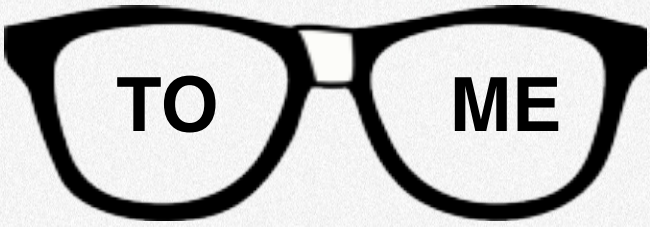
There were 333 patients with suspected STEMI randomized into the trial. Only 251 met trial criteria after randomization and these patients has a per protocol analysis performed. The 82 patients excluded were: Diagnosis of MI not confirmed (34), previous CABG (4), CP>12hrs (4) and previous MI (41).

Primary Outcome MACCE Per Protocol Analysis:

13.5% RIC vs. 25.6% control
HR 0.49 (0.27-0.89) p=0.018

Secondary Outcomes

All cause mortality HR 0.32 (0.12-0.88) p=0.027
Myocardial infarction HR 0.69 (0.28-1.71) p=0.423
Readmission HR 0.54 (0.16-1.85) p=0.327
CVA/TIA HR 0.72 (0.16-3.23) p=0.670

TALK NERDY  **TO ME**

Commentary

This study was a long-term follow up to a study by Botker et al published in the Lancet 2010. It looked at these same 251 patients who either received the RIC procedure or the control group, and looked at the short term outcome differences in post-PCI myocardial damage as measured by single photon emission CT.

They were pleased with their outcomes and went on to follow these patients through Danish nationwide medical registries up to five years after their MI, looking to see if there were any differences in Major Adverse Cardiac or Cerebrovascular Events (MACCE).

We identified five issues with the study:

Per-Protocol vs. Intention to Treat Analysis:
Both are tools to investigate the data and have strengths and weaknesses. Intentions to treat analysis tend to be a better method because it is not biased by non-compliant patients, dropouts and cross overs.Per-protocol analysis excludes patients who deviated from the protocol and only includes those who received the treatment. Doing a per-protocol analysis can introduce attrition bias. This is a form a bias in which those groups of patients being compared no longer have similar characteristics. It tends to be a lower form of evidence but better demonstrates the effects of a treatment when used in an optimal manner. These types of per protocol analyses can be helpful in interpreting non-inferiority trials.

They did both a per-protocol and intention to treat analysis but highlight only the per protocol results. This makes me skeptical of the results because if you look at the ITT for the primary composite outcome of MACCE the HR is not nearly as robust and barely meets statistical significance. HR 0.62 (0.39-0.99) p=0.45

The authors say they focused on the per protocol analysis because the parent trial showed benefit in myocardial salvage index per protocol. For more information on ITT vs. Per protocol check out this review by Dr.Gupta.

Where was the Benefit?

Their secondary outcomes were the components of the MACCE composite outcome. Only the all-cause mortality showed significant reduction in HR. Interestingly when they broke this down into subgroup analysis for cardiac mortality vs. non-cardiac mortality the benefit was seen in the later.

Cardiac mortality HR 0.39 (0.08-2.00) p=0.258

Non Cardiac Mortality HR 0.28 (0.08-1.03) p=0.056

The RIC intervention that was to decrease cardiac badness (death) did not seem to be superior to control. However, there were very few events in both groups that make the results difficult to interpret.

The ITT analysis on all cause mortality showed no statistical difference HR 0.51 (0.25-1.07) p=0.074

Not Blinded:

This was not a blinded trial for the providers or the participants. Only the outcome assessors were blinded to treatment group. This could have introduced bias into the experiment. The EMS personal may have treated the intervention group differently even if on a subtle level.

They could have attempted to blind the trial. An automatic BP cuff that automatically inflated to either 200mm Hg for temporary ischemia or a value significantly less. They could have even asked the paramedics and patients post intervention which "arm" of the trial they thought they were randomized. This would have confirmed the blinding was maintained.

Commentary

Time to Complete:

This has the potential to slow things down in the filed for a time dependent emergency. The protocol called for 5min of inflation followed by 5min deflation. This was done for four cycles taking 40 minutes in total.

Sixteen of the 251 (6%) could not complete the four cycles of inflation/deflation because the transportation time was insufficient. They continued the procedure in hospital while the patients were getting primary PCI.

So the question becomes can you apply these results to your practice environment. It may depend on how long your transportation times are and this could, if proven to be of benefit, may play a greater role in rural/remote areas with longer transport times.

External Validity:

This study was done in Denmark where the EMS system could be substantially different than in North America. In addition to the transport times what level of training do their EMS providers have compared to ours? What can be provided in the pre-hospital setting?

RCT 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 groups to which they were randomized	☑
The study patients were recruited consecutively (i.e. 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	?

Case Resolution

You discuss the recommendation with your EMS medical director via cell phone. You and the doctor decide not to perform the procedure, but agree to meet and review the literature to see if the procedure should be considered for inclusion in statewide protocols.

Clinical Application

None at this time.

CONCLUSION VS COMMENTARY

COMPARISON

The authors' conclusion that RIC *"seemed"* to show improvement in long-term clinical outcomes in patients with STEMI gives them some wiggle room. We would agree there *"seemed"* to be some benefit if you used the per protocol analysis but there did not *seemed* to be benefit if you used the ITT analysis, considered the lack of blinding and the other limitations mentioned.

WHAT DO I TELL MY PATIENT?

You are having a heart attack and we are taking you to the hospital as fast and safely as we can.

References

1. Sloth AD, Schmidt MR, Munk K, Kharbanda RK, Redington AN, Schmidt M, et al. Improved long-term clinical outcomes in patients with ST-elevation myocardial infarction undergoing remote ischaemic conditioning as an adjunct to primary percutaneous coronary intervention. Eur Heart J. 2014 Jan;35(3): 168-75.

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3. Gupta SK. Intention-to-treat concept: A review. Perspect Clin Res. 2011 Jul;2(3):109-12.

Guest Skeptic: Clay Odell

Clay is a paramedic and Executive Director of Upper Valley Ambulance, a regional EMS system covering nine communities in rural New Hampshire and Vermont. He's been involved in EMS for over 30 years in a variety of roles including urban paramedic, flight paramedic, an emergency nurse, and Chief of the State EMS Office in New Hampshire. Clay is very interested in EBM for EMS and says he's trying really hard to learn, but continues to procrastinate about actually taking a statistics course again.

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Diarrhea:
Hard to Spell, Easy to Smell and Easy to Cause with IV Antibiotics

Case Scenario:

A 58-year-old male presents to your ED complaining of a warm, painful, reddened area on his left thigh. His past medical history is only significant for generalized anxiety disorder and he has no known drug allergies. On exam, you find no evidence of an abscess, and you find his labs and vital signs are within normal limits. You confidently give him a diagnosis of uncomplicated cellulitis and need to determine an antibiotic regimen. You'd like to send him home with a five day course of cephalexin, but are thinking about giving him an intravenous (IV) dose of cefazolin before he leaves.

Q:

What is the risk of getting antibiotic associated diarrhea with an IV dose of antibiotics prior to discharging patients home with an oral course?

BOTTOM LINE

Administration of IV antibiotics in the emergency department is not without harms. In this small observational study, it looks like IV antibiotics are associated with an increased risk of AAD

Factors Influencing the Development of Antibiotic Associated Diarrhea in ED Patients Discharged Home: Risk of Administering IV Antibiotics

Haran et al. Am J Emerg Med 2014

P Adult patients from three emergency departments (2 large urban and 1 small community site).

I IV antibiotics as part of their emergency department and discharged home with a new prescription for antibiotics

C Patients who were not given IV antibiotics as part of their emergency department care and discharged home with a new prescription for antibiotics.

O Primary Outcome: Development of AAD, which the authors defined as three or more loose stools per day for at least two days

Authors' Conclusion:

"Intravenous antibiotic therapy administered to ED patients before discharge was associated with higher rates of AAD and with 2 cases of CDI. Care should be taken when deciding to use broad-spectrum IV antibiotics to treat ED patients before discharge home." (Haran et al., 2014)

Background

In certain infectious disease conditions, such as meningitis or septic shock, we know that rapid administration of antimicrobials in adequate doses is associated with improvement in patient outcomes.

Septic shock is a time dependent emergency. It has been demonstrated for every hour delay in providing antibiotics to patients with septic shock mortality increased by almost 8%. However, in patients who are well enough to be discharged home, this same relationship has not been demonstrated.

We all know that antibiotic associated diarrhea (AAD) is a common side effect of antibiotic therapy. The incidence in the literature has been reported to be between 5% and 39%. One of the most concerning types of AAD is Clostridium difficile (CDI). This has been on the increase.

There is such concern about C.diff that it has been one of the patient safety quality indicators in many organizations/jurisdictions.

There have been a number of factors that increase the risk of AAD/CDI including the type of antibiotic prescribed and the duration of use. While almost all antibiotics can cause AAD and CDI the cephalosporins, broad-spectrum penicillins and clindamycin are more often the cause. Patient factors are also thought to be involved: age greater than 65 years, co-morbidities and having a history of AAD.

Results

The authors of this study were able to complete analysis on 247 patients. Most of these patients were generally healthy with no significant past medical history.

The most common infection being treated with antibiotics was a skin/soft tissue infection. The patients who received IV or oral only antibiotics were similar at baseline with respect to emergency severity index, % tachycardia or febrile, and medical histories.

Primary Outcome of Antibiotic Associated Diarrhea:

45/247 (18%)

OR 2.73 (95% CI 1.38-5.43)

7% IV group vs. 12.3% Oral group

Absolute difference of 13.4%

NNH=7

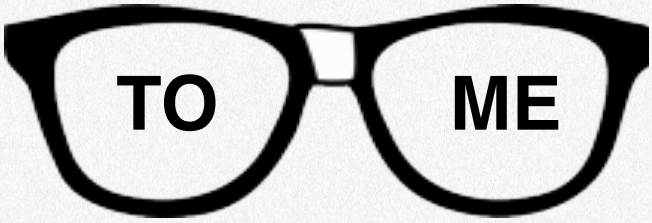
Secondary Outcome CDI:

2/247 (1%)

The rate of AAD tended to increase with the duration of antibiotic therapy. Clindamycin, vancomycin, cephalosporins, penicillins, and macrolides were associated with the highest rates of AAD; quinolones and doxycycline had the lowest rates.

Of patients who developed AAD, 27.9% stopped taking the antibiotic and 16.3% had a subsequent healthcare visit to address the diarrhea symptoms.

TALK NERDY TO ME



Commentary

In this small, observational trial the authors sought to determine risk factors for the development of AAD. The authors found that about 18% of patients in their analysis developed AAD, which fits into the range of 5-39% previously described in the literature.

The primary outcome was patient-oriented, but didn't necessarily take into account all potential confounders. It would have been nice to see a description of whether or not patients had any history of constipation, or were taking any medications that could have affected GI motility or the development of diarrhea/constipation (e.g. any sort of bowel regimen, iron supplements, opioids, naltrexone, metoclopramide, erythromycin, etc.).

Additionally, it's unclear if this primary outcome was accurately measured to minimize bias, because of how this data was collected. Patients were contacted in a follow up survey 4 weeks after finishing antibiotic therapy and asked about development of AAD. This is subject to not only recall bias, but may be different depending on the patient's perception of normal bowel movements.

Emergency Severity Index is endorsed by ACEP and the Emergency Nurses Association in the US, and used widely outside of the US as well. It has been shown to have an acceptable level of reliability, but may be subject to some variability in certain patient populations (e.g. pediatric patients) and a greater degree of variability observed in levels 3 through 5.

The tool has its limitations as it relates to describing the patients in this study, but represents the most feasible and widely recognized tool available for this population.

Despite its limitations, this study provides important information about potential risks of an intervention which has yet to demonstrate any benefit in this patient population (e.g. those well enough to go home with a course of oral antibiotics for their infection).

Additionally, if patients who receive IV antibiotics are more likely to develop AAD, and 28% of those patients stop taking the antibiotics early due the side effects, this could have implications not only for that patient but also the eventual development of antimicrobial resistance.

Observational Trials Checklist

Did the study address a clearly focused issue?	☑
Did the authors use an appropriate method to answer their question?	☑
Was the cohort recruited in an acceptable way?	☑
Was the exposure measured to minimize bias	?
Was the outcome accurately measured to minimize bias?	☑
Have the authors identified all important confounding factors?	
Was the follow up of subjects complete enough?	☑
How precise are the results/is the estimate of risk?	☑
Do you believe the results?	☑
Can the results be applied to the local population?	☑
Do the results of this study fit with other available evidence?	☑

If IV antibiotics don't result in a treatment benefit for these patients, are potentially harmful, and have greater cost implications, then why haven't we abandoned this practice?

What is needed is a double blinded, randomized, placebo controlled trial of patients being treated for infections in the ED and discharged home. The patients could receive IV antibiotics or saline and all be discharged home on a new oral antibiotic prescription. Then follow them for the primary outcome of AAD. Have secondary outcomes of CDI, discontinuation rate and clinical cure.

CONCLUSION VS COMMENTARY

COMPARISON

We agree that there was an association between IV antibiotics administration in the ED and increased rates of antibiotic associated diarrhea. Physicians should always think about the potential harm before providing any treatment.

Case Resolution

You decide to skip the IV dose of cefazolin and discharge your patient with a five day course of cephalexin for his cellulitis. You give the standard advice to return to the emergency department if they are getting worse (fever and/or increased redness/pain), not able to tolerate the oral antibiotic or are otherwise worried.

Clinical Application

For patients well enough to go home and a working gut an IV dose of antibiotics doesn't have any benefit over oral therapy, and may pose an increased risk of adverse effects.

WHAT DO I TELL MY PATIENT?

We are going to start you on antibiotics for your infection. Here is a prescription for some pills that are easily absorbed into your system and highly effective. One of the most common side effects of antibiotics is diarrhea. Giving you an intravenous dose of antibiotics before you leave could put you at a higher risk of developing diarrhea. Additionally, intravenous antibiotics for this type of infection do not result in a faster cure. Please take all your antibiotics as prescribed. This will ensure your best chance of being cured of this infection.

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Guest Skeptic: Meghan Groth
Meghan (@EMPharmGirl) is the emergency medicine pharmacy specialist at the University of Vermont Medical Center in Burlington, Vermont and an adjunct professor of pharmacy at the Albany College of Pharmacy and Health Sciences.

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I Hope You Had a Negative D-Dimer

ADJUST PE Study

Case Scenario:

An 84-year-old woman presents to the ED with vague symptoms of shortness of breath and mild chest discomfort for the last two days. She does not say "pain" but rather just an ache when taking a deep breath. Her past medical history includes hypertension, dyslipidemia, type-2 diabetes and osteoarthritis. Her vital signs are normal. She is Well's low but PERC positive due to her age. You do not want to order a D-dimer because of the high false positive rate but pulmonary embolism (PE) is on your differential.

Q:

Can an age-adjusted D-dimer threshold safely exclude PE in non-high risk ED patients with suspected PE?

BOTTOM LINE

Using an age-adjusted D-dimer cutoff in emergency department patients with suspected PE increases the diagnostic yield of D-dimer testing by 11.6%

Age-adjusted D-dimer Cutoff Levels to Rule Out Pulmonary Embolism: The ADJUST-PE Study

Righini et al. JAMA 2014

P Consecutive patients from 19 hospitals in 4 European countries with a clinical suspicion of PE. This was defined as acute onset or worsening shortness of breath or chest pain without another obvious etiology.

I Age adjusted D-dimer (age x 10)

C D-dimer as >500 µg/L

O Failure rate of each diagnostic strategy computed as number of adjudicated DVT + non-subsegmental PE divided by the number of patients with a negative D-dimer result that were left without any anticoagulant therapy.

Excluded Studies:

- Clinical suspicion for PE more than 24 hours after hospitalization.
- *Anticoagulated for another reason*
- *Creatinine clearance less than 30 mL/min*
- *Contrast dye allergy*
- *Life-expectancy less than 3 months*

Authors' Conclusion:

"Compared with a fixed D-dimer cutoff of 500 µg/L, the combination of pretest clinical probability assessment with age-adjusted D-dimer cutoff was associated with a larger number of patients in whom PE could be considered ruled out with a low likelihood of subsequent clinical venous thromboembolism." (Righini et al., 2014)

Background

A negative D-dimer has been shown to safely rule out pulmonary embolism in patients who are not high risk. It has a high sensitivity but low specificity. This means that there is a high false positive rate.

The false positive rate increases with age. This is because normal D-dimer levels increase with age. The result is older patients are subjected to more diagnostic image testing to rule-out PE.

There is a worldwide epidemic of over-testing with the downstream consequences of over-diagnosis and over-treatment. The problem of over-testing is complex. It stems from an imperfect mix of incomplete and flawed diagnostic evidence, constant malpractice threats (worse in some parts of the world than others), and clinicians struggling to balance clinical care (our day job) with maintaining awareness of the ever-evolving research landscape.

PE is a prime target to reduce over-testing and there have there have been a number of studies looking at age adjusting the D-dimer. The derivation study was done by Douma et al 2010. They suggested using a new cut off for patients over the age of 50 years of age.

The formula was patient's age x 10. So in our case it would be 84×10=840 µg/L

Conclusion: "*The age adjusted D-dimer cut-off point, combined with clinical probability, greatly increased the proportion of older patients in whom pulmonary embolism could be safely excluded.*"

The concept of age-adjusting the D-dimer to rule-out PE was validated in two trials (van Es et al 2011 and Penaloza et al 2012). Both of these studies demonstrated the clinical usefulness of this approach.

In 2013, Schouten et al in the BMJ published a systematic review and meta-analysis. It had over 12,000 patients and compared conventional D-dimer cut off of 500 µg/L vs. age-adjusted D-dimer.

Conclusion: "*The application of age adjusted cut-off values for D-dimer tests substantially increases specificity without modifying sensitivity, thereby improving the clinical utility of D-dimer testing in patients aged 50 or more with a non-high clinical probability.*"

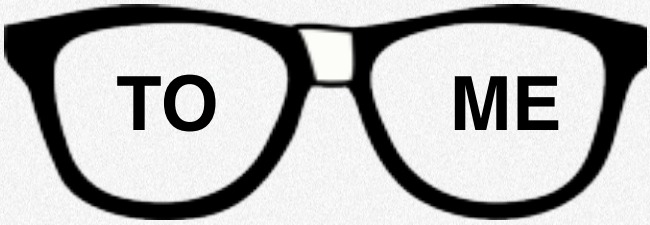
There were some concerns about this meta analysis expressed by some including Dr. Brent Thoma from Boring EM. His concerns seemed to focus on the heterogeneity of the studies and combining DVT studies with PE studies in the meta analysis.

Results

There were 3,346 patients with suspected PE included in the study of which 337 (10%) were over the age of 50 with a normal age-adjusted D-dimer and non-high clinical probability. The overall prevalence of PE was 19.0% (95% CI 17.7%-20.4%).

- 2898 patients were risk stratified as non-high risk or unlikely clinically to have a PE.
    - 1154/2898 (39.8%) had a negative D-dimer according to the age-adjusted cutoff
    - 817/2898 (28.2%) had a negative D-dimer using the <500 µg/L cutoff
    - This gives an absolute difference of 11.6%
- Three-month thromboembolic risk for patients <500 µg/L
    - 1/810 or 0.1% (95% CI 0%-0.7%)
- Three-month thromboembolic risk for patients with D-dimer >500 µg/L but < age-adjusted cutoff
    - 1/331 or 0.3% (95% CI 0.1%-1.7%)
- None of the elderly (age >75) with non-elevated age-adjusted D-dimer had confirmed VTE during follow-up
    - 0/195 or 0% (95% CI 0%-1.9%)

TALK NERDY TO ME



Commentary

Geriatric patients are assessed for possible PE worldwide every day. However, US and Canadian studies consistently report PE rates lower than European sites. Therefore, the European data likely represent spectrum bias skewed towards a "sicker" population relative to the U.S. that skews estimates of sensitivity upward, but does not affect specificity.

PE was a prime target in EM to quickly and safely reduce over-testing and this prospective, outcomes-based research provides strong evidence up which to do so for older adults. Their 3-month adjudicated outcomes provide compelling proof that age-adjusted D-dimers provide a rationale to use risk stratification plus appropriate D-dimer testing to safely reduce unnecessary ancillary PE testing – even in older adults.

They used the revised Genava score or the 2-level Well's score to risk stratified patients who they clinically suspected of having a PE. However, the authors do not explain who performed this risk stratification (research team vs. clinicians).

Based upon risk stratification, patients either proceeded to CTPA (high risk Wells or likely clinical probability Geneva), whereas non-high risk had D-dimer testing.

Neither the CTPA method or interpreting radiologist experience was detailed. Failure to report their CT instruments or radiologists' experience is technically a flaw (risk of bias) from a purist perspective. In addition, there were six different quantitative high sensitivity D-dimer assays used.

However, these *"flaws"* also increase the external validity and pragmatic applicability of this research since each of us is stuck with D-dimer assay used in our lab and radiologist that we have. Furthermore, their results did not seem to vary based on D-dimer assay.

Although only 1 of 7 deaths had autopsy to confirm whether PE caused death, the longitudinal 3-month follow-up using structured questionnaire provides strong patient-centric evidence of effectiveness. In addition, 3-month follow-up is standard in PE literature and at the outer range of timeframe within control of ED systems.

This was a management study and not a diagnostic study. Therefore, the authors did not report sensitivity, specificity, likelihood ratios, or interval likelihood ratios in their manuscript. Future diagnostic research should evaluate the sensitivity, specificity, likelihood ratios, and interval likelihood ratios for age-adjusted D-dimer, as well as implementation strategies to incorporate these new levels of abnormal into geriatric emergency care. This prospective, outcomes based research adds to an expanding volume of retrospective investigations indicating that age-adjusted D-dimer is ready for widespread use and ought to be incorporated into guidelines, textbooks, and routine bedside care.

The use of an age-adjusted D-dimer safely increases the proportion of non-high risk for PE patients from 28.2% (<500 µg/L) to 39.8% (age adjusted) with a non- elevated D-dimer and no further work-up required. This represents an 11.6% increase in D-dimer diagnostic efficiency.

CONCLUSION VS COMMENTARY

COMPARISON

The authors' conclusions seem very reasonable.

Clinical Application

This is ready for prime time. We should incorporate age-adjusted D-dimer into medical education, continuing medical education, electronic medical record protocols, and patient shared decision-making instruments.

Quality Checklist

The clinical problem is well defined	☑
The study population represents the target population	☑
The study population included or focused on those in the ED	☑
The study patients were recruited consecutively	☑
The diagnostic evaluation was sufficiently comprehensive and applied equally to all patients	
All diagnostic criteria were explicit, valid and reproducible	☑
The reference standard was appropriate	☑
All undiagnosed patients underwent sufficiently long and comprehensive follow-up	☑
The likelihood ratio(s) of the test(s) in question is 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?

Blood clots in the lung are called pulmonary embolisms. They can be hard to diagnose sometimes. We have a blood test for people like you who are not at high risk. We adjust the test based on your age. If the test is below your age-adjusted level you most likely do not have a blood clot in your lung and no further testing is needed. If the test is above your age-adjusted level we will need to do a CT scan to check for a blood clot.

References

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Guest Skeptic: Dr. Kerstin deWit

Kerstin did an Internal medicine and EM training in the UK. Since then she has worked in Thrombosis research and received a doctorate in the UK and a Masters in Epidemiology from the University of Ottawa. Kerstin currently works as a Thrombosis physician and Emergency Physician at McMaster University and member of Best Evidence in Emergency Medicine (BEEM).

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B-Lines: Diagnosing Acute Heart Failure with Ultrasound

Case Scenario:

78-year-old man with a history of diabetes, hypertension and coronary artery disease presents with a two day history of increasing shortness of breath. He does not have any chest pain or fever. You have been doing more and more with ultrasound and wonder whether you can make the diagnosis of acute pulmonary edema before getting the standard CXR, ECG and lab tests.

Q:

Can novice emergency medicine resident physician sonographers accurately identify B-lines in undifferentiated dyspnea patients to diagnose acute heart failure after a 30-minute training course?

BOTTOM LINE

Bedside ultrasound by inexperienced EM residents in a training program with an ultrasound fellowship to identify B-lines in non-critical ED patients with undifferentiated dyspnea is just as accurate as ultrasounds by experienced sonographers. Whether this applies to non-academic settings without ultrasound expertise is unknown. If the diagnostic accuracy is confirmed in less academic settings, future studies should assess more meaningful outcomes than diagnostic accuracy such as length of stay, admission rates, ancillary testing, and resolution of patient symptoms.

Comparison of Expert and Novice Sonographers' Performance in Focused Lung Ultrasonography in Dyspnea (FLUID) to Diagnose Patients with Acute Heart Failure Syndrome

Chiem et al. AEM 2015

P Sixty-six EM resident physicians from one inner-city ED with over 100,000 annual visits assessing patients >18 years old presenting with chief complaint of dyspnea.

I Bedside ultrasound by EM resident assessing for three or more B-lines using eight-zone thoracic ultrasound on thoracic exam preset and curvilenear transducer. All EM residents received 30-minute lecture on technique and recognition of sonographic B-lines by the ED director of ultrasonography.

C No comparison group

O Diagnostic accuracy (sensitivity, specificity, positive/negative likelihood ratio, positive/negative predictive value) of novice sonographers to identify B-lines by bedside ultrasound compared with an expert sonographer.

Excluded Studies:

- Included attending physician perspective that dyspnea due to cause other than CHF
- Incarcerated individuals
- Patients who were pregnant, on dialysis
- Patients on positive pressure ventilation, or receiving nebulizer treatment
- Patients too ill to provide written consent.
- Non-English speaking patients were also excluded

Authors' Conclusion:

"Inexperienced sonographers can identify sonographic B-lines with greater than 80% sensitivity and specificity as compared to an expert sonographer after a brief tutorial. Lung ultrasonography has fair predictive value for pulmonary edema from acute heart failure in the hands of both novice and expert sonographers." (Chiem et al., 2015)

Background

Acute heart failure is a condition where the heart cannot pump well enough to meet the demands of the body. It can be due to a number of different causes including: myocardial infarction, arrhythmias, valvular dysfunction, pneumonia, uncontrolled hypertension, anemia, hyperthyroidism and many other causes.

The diagnosis of heart failure before the 1990's was fairly grim with 60-70% of patients dying within five years of diagnosis.

Things have improved tremendously over the last couple of decades with respect to mortality but heart failure is still the most common re-admission diagnosis within one month for patients over 65 years of age. In the U.S. we spent roughly 25 billion every year on acute heart failure hospitalizations alone.

The diagnosis of acute heart failure can be challenging because the signs and symptoms are insensitive and/or non-specific.

Clinical gestalt alone is moderately specific, but not sensitive (LR+ 4.4, LR- 0.45). Chest x-rays have been used for years to diagnose heart failure, but is also imperfect. For example the presence of interstitial edema has LR+ 17.1 but LR- only 0.7. In addition, chest x-ray interpretation agreement between radiologist and emergency physician can be less than 50%.

This could result in many patients with acute heart failure being missed.

Serum markers of BNP and ProBNP sometimes help diagnose patients with acute dyspnea. A systematic review by Lam et al in Ann of Intern Med 2010 demonstrate ED testing may decrease hospital LOS by a day, and possibly reduce admission rates, but they did not really affect mortality rates

In 2012, BEEM and Dr. Peter Rosen published a review of 5 diagnostic RCTs that explored ED physician awareness of BNP or not (J Emerg Med). This study noted no consistent differences in any measurable outcome (diagnostic accuracy, ED length of stay, hospitalization rates, length of hospital admission, etc.)

POCUS is now part of the core curriculum for emergency medicine residents. Identifying B-Lines on thoracic ultrasound can be used to identify interstitial fluid.

Results

Although EM residents not mandated to participate, 92% did with range of 1 to 28 ultrasounds and median of 3 per sonographer.

Over 50% of 1200 dyspnea patients presenting between May 2009 and June 2010 were ineligible using the authors' criteria and 380 patients were included in the analysis (93% African American, mean age 55 years).

Acute heart failure syndrome was the cause of dyspnea in 35% of patients with a 92% agreement for CHF-as-cause between the two expert reviewers.

Primary Outcome: Diagnostic accuracy of novice sonographer to identify B-lines for each lung zone

Sensitivity 85% (95% CI 83%-88%) and Specificity 84% (95% CI 82%-85%)
LR+ 5.2 (95% CI 4.7-5.8) and LR- 0.2 (95% CI 0.1-0.2)

Secondary Outcome: Diagnostic accuracy of linking B-line identification to the correct diagnosis of CHF

Novice Sonographers:

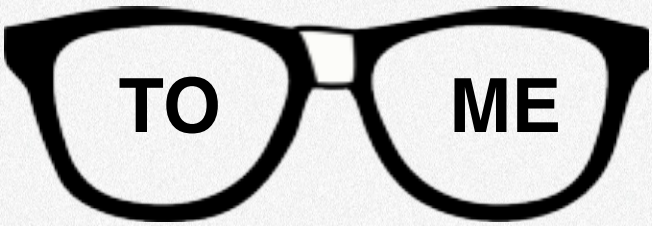
Sensitivity 87% (95% CI 81%-92%) and specificity 49% (95% CI 42%-55%)
LR+ 1.7 (95% CI 1.5-2.0) and LR- 0.3 (95% CI 0.2-0.4).

Expert Sonographers

Sensitivity 85% (95% CI 78%-90%) and specificity 58% (95% CI 52%-64%)
LR+ 2.1 (95% CI 1.7-2.4) and LR- 0.3 (95% CI 0.2-0.4)

The Receiver Operating Characteristic Area Under the Curve was 0.77 (95% CI 0.72-0.82) for novice sonographers and 0.76 (95% CI 0.71-0.82) for expert sonographer

TALK NERDY TO ME



Commentary

1) This was a fascinating Level II Diagnostic Accuracy study exploring the reproducibility of ideal setting bedside sonography (handful of experts) in the real-world of mostly inexperienced EM sonographers.

- *I would argue that we are not making the diagnosis of acute heart failure, especially as it relates to type and severity, in a timely manner. Acute heart failure syndrome, being a syndrome, can occur from several etiologies and there are guidelines as to how best to treat a specific phenotype.*
- *However, most clinicians assume that all patients with acute heart failure have the same hemodynamic issues and therefore manage them with nitrates and furosemide. This leads to complications such as hypotension and acute kidney injury, with associated increases in length of stay as well as mortality. This is one of the reasons that heart failure researchers are starting to look at ED-based enrollment, so that you can potentially identify acute heart failure type and severity, in order to tailor therapies and to potentially identify patients that improve dramatically in the ED for discharge.*
- *POCUS (especially focused echocardiography) can really help with this problem, because it looks as patients' hemodynamics in a way that no lab or imaging test can capture. I firmly believe that EP's can be trained to do an acute heart failure ultrasound protocol, and the UCLA Clinical Science Testing Institute has given me some funding to test this out.*

- *However, one of the key issues in POCUS is the balance between feasibility and accuracy. We want to be able to prove to clinicians that the amount of training involved in the ultrasound application is outweighed–and we hope by a large extent–the increase in clinical accuracy and efficiency. In using a large group of trainee physicians, this study is a good step in that direction, whereas the vast majority of studies use a small group of highly-trained clinician sonologists.*

Hierarch of Evidence for Diagnostic Studies

1. Technical Efficacy – can we obtain the measures for diagnosis
2. Diagnostic Accuracy Efficacy- sensitivity, specificity, likelihood ratios, predictive values and area under the curve
3. Diagnostic Thinking Efficacy – confidence in diagnosis
4. Therapeutic Efficacy – proportion of cases that further testing we avoided and changed management
5. Patient Outcome Efficacy – cost per unit of change in outcome variable, morbidity avoided by testing, mortality
6. Societal Benefit – cost effectiveness analysis from society perspective

2) The authors used appropriate chart review methods and adhered to the important elements of the Standards for Reporting of Diagnostic Accuracy (STARD) guidelines.

We attempted to follow the 25-point checklist, including reporting the number of patients excluded and exclusion reason, as well as blinding of ultrasound interpretation and ultimate primary diagnosis.

3) The reporting a kappa value rather than raw agreement in assessing the cause of dyspnea, as acute heart failure syndrome between two experts would have been more meaningful.

This was considered but was was not a primary outcome of interest. Rather, two expert reviewer diagnosis (which should take into account the clinical, laboratory, and imaging data presented) is the gold standard in acute heart failure studies.

4) We were uncertain whether expert chart reviewers were aware of the bedside ED ultrasound results when determining whether cause of dyspnea was congestive heart failure; if they were aware then incorporation bias would tend to increases estimates of sensitivity and specificity.

- *The expert reviewers were blinded to the ultrasound results. However, the study sonologists were not necessarily blinded to the clinical information at hand as they performed and interpreted the ultrasounds. However, the expert sonologist who reviewed the ultrasounds and made his own interpretation was blinded to all data. It is interesting to see the differences in false positive and negative rates among the two groups.*

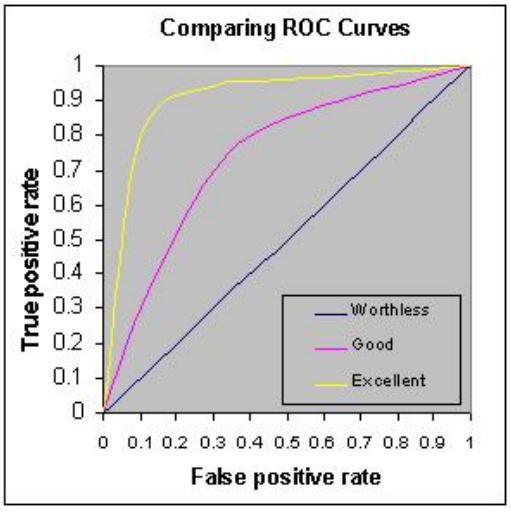
5) If ED clinicians used findings of B-lines to determine subsequent congestive heart failure (or other diagnostic) testing, partial verification bias increases estimates of sensitivity and decreases estimates of specificity.

- *This was largely avoided this issue because the ultrasound results were not available to the expert reviewers. We don't think it influenced diagnosis since the expert reviews are based on primarily laboratory and imaging data, as well as discharge summaries. In fact, most internists and cardiologists have no idea what a B-line is when you ask them. They assume that you are talking about Kerley B-lines on chest radiographs.*

6) You reported Receiver Operating Characteristics as Area Under the Curve (AUC). The AUC helps us estimate how good a test is at discriminating between disease and non-disease. To construct a ROC graph, we plot these pairs of values on the graph with the 1-specificity on the x-axis and sensitivity on the y-axis. The result can be between -1 and +1 with a perfect test having a value of 1. Your results were in the *"good"* range with both resident and attending having a value of 0.77 and 0.76 respectively.

ROC Curves

An ROC curve looks at the signal to noise ratio of a test, by graphing the true positive rate (or sensitivity) to the false positive rate (or 1-specificity) of various points of the test, in order to arrive at an optimal cut-off. However, you can look at the area under the curve and use it to see in general how accurate the test is.



CONCLUSION VS COMMENTARY

COMPARISON

We agree that inexperienced sonographers in a setting with ongoing ultrasound curricula and mentoring expertise can quickly acquire the skill to accurately identify B-lines by bedside ultrasound.

However, we are uncertain if this would be the same in settings without ultrasound experts to teach knobology, probe position, enhancing image quality, and facilitate balance between ED workflow and implementation of a new ultrasound skill.

Bedside ultrasound has two distinct skill requirements: (1) image acquisition and (2) image interpretation. Other imaging modalities (x-ray, CT, or MRI) do not require the ED provider to acquire the images.

That is true. It places imaging into the hands of clinicians and allows for expedited diagnosis in optimal circumstances. Both subsets need to be introduced relatively early in training, because we know that after training, it becomes more difficult to learn such a potentially powerful but difficult way to practice. That's why most of us ultrasound gurus are also busy introducing ultrasound to medical students in anatomy and physical diagnosis courses, as well as teaching our emergency medicine trainees and colleagues.

Part of *"knowledge translation"* in bedside ultrasound is learning how to efficiently obtain images without disrupting busy ED workflow. Doing so for congestive heart failure, where a reasonably accurate and readily available test (chest x-ray) already exists, requires research in non-academic, non-ultrasound training EDs.

Additionally, the clinical impact of bedside ultrasound was not assessed in this study. Using the most accurate measures of bedside US for B-lines (LR+ 2.1, LR- 0.3 for expert sonographer), the 35% pre-test probability for CHF would increase to 53% with a positive ultrasound and 14% with a negative ultrasound.

Is this post-test shift is CHF probability meaningful? What are the test- and treatment-thresholds upon which individual clinicians alter subsequent management decisions?

These questions will only be answered with a diagnostic randomized controlled trial where half the dyspnea patients ED provider point-of-care ultrasound, half do not. This diagnostic RCT should assess ED length of stay, admission rates, ancillary testing, and total costs, but also patient-centric outcomes like time to relief of symptoms

Case Resolution

You get out the ultrasound machine and find B-Lines suggestive of acute heart failure. These ultrasound findings are verified by your attending. While happy to have your skills confirmed you continue the work-up for the underlying cause of the patient's dyspnea.

Clinical Application

Bedside ultrasound in dyspnea patients by inexperienced EM residents to identify B-lines with minimal training is accurate relative to more experienced sonographers. However, using ultrasound B-lines to rule-in (LR+ 1.7) or rule-out (LR- 0.3) CHF is problematic and somewhat underwhelming.

WHAT DO I TELL MY PATIENT?

There are many potential causes for your shortness of breath. One possibility is heart failure and several tests will help to assess this possibility. One test that we can conduct right now is an ultrasound of your lungs. The results of this test may help me to more quickly determine the probability of acute heart failure while more definitive tests are pending.

References

1. Chiem AT, Chan CH, Ander DS, Kobylivker AN, Manson WC. Comparison of expert and novice sonographers' performance in focused lung ultrasonography in dyspnea (FLUID) to diagnose patients with acute heart failure syndrome. Acad Emerg Med. 2015 May;22(5):564-73.

2. Lam LL, Cameron PA, Schneider HG, Abramson MJ, Muller C, Krum H. Meta-analysis: effect of B-type natriuretic peptide testing on clinical outcomes in patients with acute dyspnea in the emergency setting. Ann Intern Med. 2010 Dec 7;153(11): 728-35.

3. Carpenter CR, Keim SM, Worster A, Rosen P, Beem. Brain natriuretic peptide in the evaluation of emergency department dyspnea: is there a role? J Emerg Med. 2012 Feb;42(2): 197-205.

Diagnostic Testing Quality Checklist

The clinical problem is well defined	☑
The study population represents the target population	☑
The study population included or focused on those in the ED	☑
The study patients were recruited consecutively	
The diagnostic evaluation was sufficiently comprehensive and applied equally to all patients	?
All diagnostic criteria were explicit, valid and reproducible	☑
The reference standard was appropriate	☑
All undiagnosed patients underwent sufficiently long and comprehensive follow-up	☑
The likelihood ratio(s) of the test(s) in question is presented or can be calculated from the information provided	☑
The precision of the measure of diagnostic performance is satisfactory	☑

Guest Skeptic: Dr. Alan Cheim

Alan is an assistant clinical professor and the director of ultrasound at UCLA Olive View.

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One Thing or Two?
For Community Acquired Pneumonia

Case Scenario:

62-year-old man presents to your ED with a four day history of increasing shortness of breath, purulent cough, fever, and generally feeling quite unwell. You measure her vitals, and he is mildly tachycardic and tachypneic, normotensive, O2 Sats are 96% on room air and his temperature is 38.2C.
A chest x-ray reveals a left lower lobe infiltrate in his lungs suggestive of pneumonia, and the decision is made to admit her to your general medicine floor You are about to start her on empiric antibiotics and wonder whether to use β-Lactam monotherapy or β-Lactam plus macrolide combination therapy

Q:

In adult patients admitted to hospital with moderately severe CAP, which is better at achieving clinical stability: β-Lactam monotherapy or β-Lactam plus macrolide combination therapy?

BOTTOM LINE

In patients presenting to the emergency department with community acquired pneumonia severe enough to warrant admission, we should continue to use β-Lactam + macrolide empiric therapy.

Beta-Lactam Monotherapy vs. Beta-Lactam-Macrolide Combination Treatment in Moderately Severe Community-Acquired Pneumonia: A Randomized Noninferiority Trial

Garin et al. JAMA Intern Med 2014

P Immunocompetent adults presenting to the ED with CAP and who were subsequently hospitalized

I Monotherapy (Cefuroxime 1.5g TID followed by cefuroxime 500mg PO OR Amoxicillin/Clavulanic acid 1.2g IV QID followed by amoxicillin clavulanic acid 625mg TID PO

C Combination Therapy (Monotherapy regimen PLUS clarithromycin 500 mg BID IV or PO)

O **Primary Outcome:** Percent of patients not reaching clinical stability at day-7 (All 5 vital signs reached and maintained for a minimum of 24 h: HR <100 bpm, SBP >90 mmHg, tympanic temperature <38.0 degrees C, RR <24 breaths/min, O2 sat by pulse oximetry >90% on room air)
Secondary Outcomes: Intensive care unit admission, complicated pleural effusion, length of stay, change in initial antibiotic treatment, in-hospital death, 30-day mortality, 90-day mortality, 30-day readmission, 90-day readmission, new pneumonia within 30 days

Authors' Conclusion:

"β-Lactam monotherapy was not found to be non-inferior to β-Lactam plus macrolide combination therapy in hospitalized adult patients with moderately severe CAP. However, "patients infected with atypical pathogens or with PSI category IV pneumonia had delayed clinical stability with monotherapy based on secondary outcome analyses" (Garin et al., 2014)

Background

Community-acquired pneumonia (CAP) is a common cause of emergency department visits and hospital admissions. Over the years, studies have looked at ways of scoring severity of illness to decide where a patient should be treated and how long a patient should receive antibiotics.

I remember starting out and having to calculate the FINE criteria to determine severity and whether or not to admit to hospital. Now we can just go to MD Calc and open up the PORT score or pneumonia severity index (PSI) App as a clinical decision tool to help us risk stratify patients for outpatient or in-patient management. This man scored 92 or moderate risk based on his age, sex, tachycardia and tachypnea.

There is still controversy surrounding what antibiotic(s) should be our empiric go-to. This has been increasingly difficult to pinpoint given the rise of antimicrobial resistance. In a 10-year span (1995 to 2005), Canada saw a dramatic rise in macrolide-resistant S. pneumoniae from 3.7% to 19.0%. Antimicrobial resistance is largely driven by overuse/misuse of antibiotics.

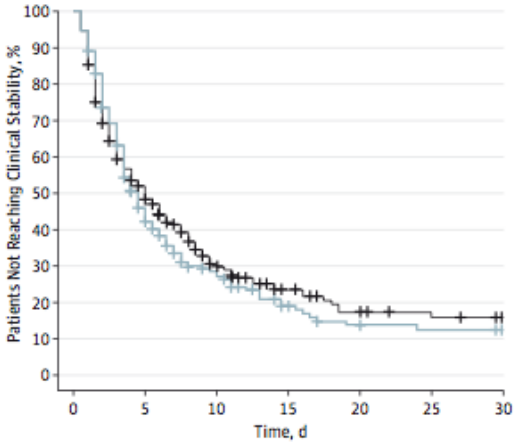
Results

A total of 580 patients were included in the analysis with 291 receiving monotherapy and 289 receiving combination treatment.

Primary Outcome
(Patients not reaching clinical stability at day 7):
41.2% in mono vs. 33.6% in combo (ARR= 7.6% NNT=14)

Subgroup Analysis: Combination better for atypical pathogens and pneumonia severity index category IV patients

Figure 2. Proportions of Patients Not Reaching Clinical Stability

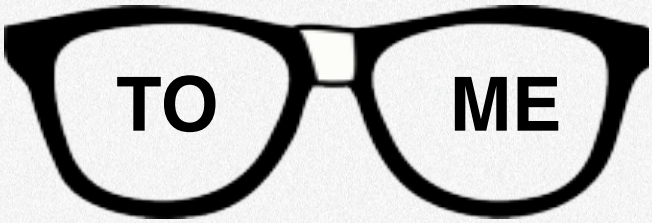


Black line indicates monotherapy arm; blue line, combination arm. *P* = .44 (log-rank test).

Monotherapy patients were more likely to be readmitted in 30 days

No difference in mortality, intensive care unit admission, complications, length of stay and recurrence of pneumonia within 90 days

TALK NERDY TO ME



Commentary

Study was designed well (good internal validity) with a reasonable primary outcome that was patient-oriented. The timing of patient follow-up makes sense, not many patients were lost to follow-up. In addition the data analysis was a true intention to treat analysis.

Even though the absolute difference was 7.6%, the upper limit of the 90% CI was 13%. Since this is above the a priori non-inferiority boundary of 8%, non-inferiority of monotherapy **was not** demonstrated.

There were some threats to validity. The study was supposed to target patients with moderately severe CAP, but actually accepted all CAP patients. This was evidenced by 10% PSI I, 50% II/III, and 40% IV; so the study artificially met its power because it accepted patients that were mild (I) as well as severe (IV).

It is important to note that there was more Legionella randomized to the monotherapy group. Legionella predisposes patients to being sicker. This imbalance at baseline could have contributed to the monotherapy being less effective.

A limitation of this study was the antibiotics used are not available in Canada (IV amoxiclav and IV cefuroxime). We also usually use azithromycin rather than clarithromycin as our macrolide in CAP. While the study was conducted across multiple sites, all were in Switzerland.

We need to consider the differences in antimicrobial resistance patterns compared to our own country. Ideally, we'd like to see a similar study done in Canada.

We contacted the authors and had them send us their antibiogram, which we compared to ours at own and surprisingly, the patterns was quite similar!

One final thing to comment upon was there were no safety differences between the two arms, which is reassuring for us.

RCT 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 groups to which they were randomized	☑
The study patients were recruited consecutively (i.e. 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	

Case Resolution

You decide to start the patient empirically on ceftriaxone IV + azithromycin PO. Two days later his blood cultures come back showing strep pneumo sensitive to cefuroxime.

At this point, he has improved clinically. You make the decision to write him a script for cefuroxime to complete his course of antibiotics, and discharge his home.

Clinical Application

According to the Ontario *"Anti-infective Guidelines for Community-acquired Infections"* – an evidence-based, peer-reviewed publication – community acquired pneumonia is divided into three categories: mild to moderate, severe requiring hospitalization and severe requiring intensive care unit.

Notice how none of these categories align 100% with the article's "moderately severe community acquired pneumonia". Recommended empiric therapies also differ. β-Lactam monotherapy is only recommended for mild to moderate community acquired pneumonia patients safely treated as out-patients.

Once admitted, the only monotherapy recommended is a fluoroquinolone. However, at our hospital, we are trying to decrease our fluoroquinolone use, as our antibiogram shows increasing resistance to it and also because it is associated with higher risk of C. difficile infection compared to other options.

For our community acquired pneumonia patients sick enough to be admitted, we empirically use β-Lactam + macrolide, which is supported by the results of this study.

CONCLUSION VS COMMENTARY

COMPARISON

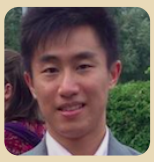
The author's conclusions are similar to our conclusion. The evidence shows β-Lactam monotherapy is not non-inferior to β-Lactam + macrolide combo therapy in admitted community acquired pneumonia patients. As such, this data re-affirms our current practice, which is to use β-Lactam + macrolide as empiric therapy in admitted community acquired pneumonia patients.

WHAT DO I TELL MY PATIENT?

You have community-acquired pneumonia and we need to admit you to hospital for treatment. You will be started on two different antibiotics to treat the infection (one oral and one intravenous). We will keep a close eye on you and hope to see some improvement in the next 24-48 hours. Some of the blood test we took may be able to tell us how to better treat your pneumonia but they will take a few days to get final results

References

Garin N, Genne D, Carballo S, Chuard C, Eich G, Hugli O, et al. beta-Lactam monotherapy vs beta-lactam-macrolide combination treatment in moderately severe community-acquired pneumonia: a randomized noninferiority trial. JAMA Intern Med. 2014 Dec;174(12):1894-901.



Guest Skeptics: Victor Tsang and Cassandra McEwan
Victor graduated from University of Waterloo School of Pharmacy and is currently doing a residency at London Health Sciences Centre in London, Ontario. Cassandra graduate of McGill University and University of Waterloo. She is also completing a residency program at London Health Sciences Centre.

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Internal or External Shoulder Immobilization (It Don't Matter to Me)

Case Scenario:

24 year-old man is goofing around on the Memorial Day long weekend at the beach. He falls and dislocates his shoulder for the first time. An examination shows it is an isolated injury and x-rays demonstrate an anterior dislocation of his shoulder without fracture. Procedural sedation is performed with no complications. Post procedure image shows a reduced shoulder joint. You are getting ready to immobilize him and wonder whether it would be best in external or internal rotation.

Q:

What is the best position to immobilize someone after a primary shoulder dislocation?

BOTTOM LINE

We do not know what is the best position for primary anterior shoulder dislocations to be immobilized.

Immobilization in External Rotation Combined with Abduction Reduces the Risk of Recurrence after Primary Anterior Shoulder Dislocation

Heidari et al. J Shoulder Elbow Surg 2014

P Patients age 15 to 55 years-old presenting with primary anterior dislocation of the shoulder

I External rotation (10^0) with ABduction (15^0) (AbER)

C Internal rotation with ADduction (AdIR)

O Recurrence rate of dislocation (humeral head completely or partially out of glenoid socket that reduced spontaneously or by manual maneuver)

Authors' Conclusion:

"Immobilization with the shoulder joint in abduction and external rotation is an effective method to reduce the risk of recurrence after primary anterior shoulder dislocations and should be preferred to the traditional method of immobilization in adduction and internal rotation in clinical practice."(Heidari et al. 2014)

Background

The shoulder joint has the widest range of motion of any joint in the human body. This makes it very useful and very susceptible to injury. These injuries include dislocation, fracture, rotator cuff tears and neurologic injuries.

The vast majority of shoulder dislocations are anterior. Young active men are at greatest risk for dislocating their shoulder.

Traditional treatment for primary anterior should dislocation has been to immobilize in a sling with the arm positioned in internal rotation and ADDuction. There is a high reoccurrence rate for instabilities especially in the young population.

"Immobilization with the arm in external rotation is effective in reducing the rate of recurrence after initial dislocation of the shoulder." (Itoi et al J Shoulder Elbow Surg 2003)

"Immobilization in external rotation after an initial shoulder dislocation reduces the risk of recurrence compared with that associated with the conventional method of immobilization in internal rotation. This treatment method appears to be particularly beneficial for patients who are thirty years of age or younger." (Itoi et al Joint Surg Am 2007)

Liavaag et al. found no reduction in the rate of recurrent instabilities for primary anterior shoulder dislocations, contradicting findings of Itoi et al.
"Immobilization in external rotation does not reduce the rate of recurrence for patients with first-time traumatic anterior shoulder dislocation." (Livaag et al J Bone and Joint Surg Am 2011)

In 2014 there were two studies looking at the issue of immobilization after primary should dislocation and came to different conclusions.

Results

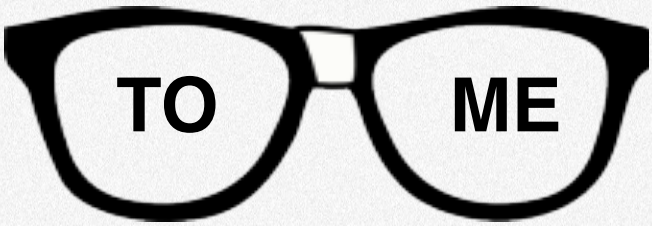
102 patients with a mean age of 36 years and 89% men (younger and mostly men, what a surprise)

Primary Outcome of Recurrence Rate by 24 Months:
3.9% in AbER vs. 33.3% in AdIR
Absolute Difference 29.4% or NNT=3

Secondary Outcome:

	External (AbER)	Internal (AdIR)
Apprehension Test	8%	18%
Discontinuation Rate	20%	6%
Return to Sport	84%	32%
WOSI Score	188	231

TALK NERDY TO ME



Commentary

This study was powered with the assumption of 30% recurrence rate for the AbER group and 60% in the AdIR group. It was not clear why these numbers were picked to select the sample size. Interestingly, their results demonstrated a much lower rate of recurrence than anticipated with only 4%in the AbER group and 33% in the AdIR group.

We also had some concerns with blinding. While the patient and clinicians were not blinded to the intervention, it was unclear whether the outcome assessors were aware of group allocation.

A lack of blinding may have impacted the primary and secondary outcomes. Patents had a telephone interview at 24 months and filled out a WOSI score at 33 months.

Recall bias could have been introduced and patients may have experience a placebo effect on the subjective WOSI assessment knowing they were in the intervention group.

The discontinuation or non-cooperation was higher in the AbER group (20%) vs. the AdIR group (6%).

This was thought to be due to the unpleasant effect on activities of daily living with an external immobilized upper limb. It made it difficult to sleep, walk through doorways and not hit people in a crowded environment.

However, the increased discontinuation rate in the AbER group would have favored the control by potentially increasing the reoccurrence rate for the AbER group.

Then there were no patients lost to follow up for their primary outcome at 24 months. This was different that Itoi 2007 who had 20% loss and Liavaag 2011 who had 2% lost to follow-up. While this could be true, 100% follow-up always make us a bit more skeptical.

They did have a few patients lost to follow up at their secondary outcome follow-up WOSI score at 33 months (3 from intervention and 2 from the control group).

RCT 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 groups to which they were randomized	☑
The study patients were recruited consecutively (i.e. 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

These results from a single centre seem too good to be true.

	N	AbER	AdIR	Lost to Follow-up
Itoi 2003	40	0%	30%	
Itoi 2007	198	26%	42%	20%
Livaag 2011	188	30%	24%	2%

External Rotation Immobilization for Primary Shoulder Dislocation: A Randomized Controlled Trial

Whelan et al. Clin Orthop Relat Res 2014

P Adults younger than 35 with primary anterior shoulder dislocation

I External rotation brace.

C Internal rotation sling.

O Recurrent instability defined by a documented episode of anterior shoulder dislocation with X-ray evidence requiring manipulative reduction in hospital or healthcare setting or multiple episodes of shoulder subluxation which was disabling enough to seek surgical stabilization. An Orthopaedic Surgeon was mandatory in the case of recurrent subluxations before categorized as having an adverse event

Authors' Conclusion:

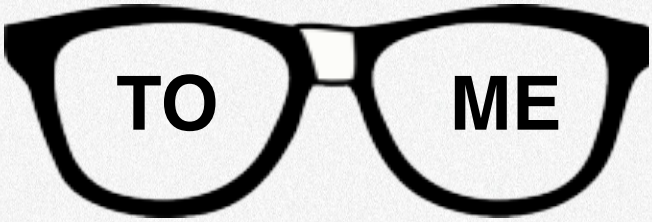
"Despite previous published findings, our results show immobilization in external rotation did not confer a significant benefit versus sling immobilization in the prevention of recurrent instability after primary anterior shoulder dislocation." (Whelan et al. 2014)

Results

There were a total of 60 patients randomized in this study with 31 in the external rotation and 29 in the internal rotation immobilization group.
Mean patient age was 23 years with 92% (55/60) men.

Primary Outcome Rate of Recurrent Instability
No Superiority with External Rotation
37% (10/27) ER vs. 40% (10/25) IR
No difference in WOSI between the two different immobilization strategies. There was a small statistical difference in ASES but we are not sure of the clinical significance.

TALK NERDY TO ME



Commentary

Recruitment/Blinding:

These were not consecutive patients but could that have introduced some selection bias?
You recruited not just ED patients but also Ortho clinic and primary care do you think that introduced referral bias?

Blinding (patients knew if their arm was sticking out but and you tried to hide this from physio. Do you think the study could have been unblinded to the treating clinician (physiotherapist) and would that impact the primary outcome of recurrence or secondary outcome of patient subjective scoring?

WOSI and WOSI vs. ASES:

WOSI was reported as a percent in your study but an absolute number in the Heidari study. How do we compare these two numbers?

Why do you think there was a difference between WOSI and ASES

Statistical Stuff:

You had less recurrence than expected a priori leaving you with an underpowered study.

Why did you decide to use means +/- standard deviation (SD) with p values rather than giving means with a 95% confidence interval (CI) and calculate a number needed to treat (NNT) to prevent one recurrence?

Why did you find no superiority to external rotation when Itoi and Heidari did find benefit?

Was it the age of patients (yours was younger)?
Do you think different populations/cultures (Japan/Iran) vs. Canadian/Norway played a role?
Itoi Included patients with fractures but your study specifically excluded fractures

How about the different external rotation immobilization devices/braces. They were not the same, could that have had an impact on the results?

Heidari had more abduction and more external rotation than your study. Would that explain the different findings between the two studies?

Large Randomized Control Trial or Systematic Review:

So there are conflicting results in the literature on what is the best position to immobilize a patient after a primary anterior shoulder dislocation. Do we just need a much bigger study or would a systematic review help sort this out?

RCT 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 groups to which they were randomized	☑
The study patients were recruited consecutively (i.e. 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	

Case Resolution

The patient is placed in a standard internal rotation immobilization sling. He is provided with specific instruction to wear the sling for 3-4 weeks and then return for re-assessment. He will then be started on a course of physiotherapy to restore range of motion, strength and function.

Clinical Application

This clinical situation makes an excellent opportunity for shared decision-making. This means collaborating with the patient about the two reasonable options. Provide information about the traditional internal rotation vs. the external rotation immobilization. Reassure the patient there is no right or wrong answer and what ever they decide will be fine.

CONCLUSION VS COMMENTARY

COMPARISON

We agree with the authors' conclusions that there is *"no benefit"* demonstrated with external rotation vs. internal rotation immobilization with the disclaimer that it was underpowered due to the lower than expected recurrence rate

WHAT DO I TELL MY PATIENT?

We have put your shoulder back in the joint. There is a high chance it can pop out again. You need to have it immobilized for the next month and then start physiotherapy. Traditionally we have put people in a sling. Some research suggests having your arm sticking out to the side could be better. Other researchers has said the opposite. The new way may turn out to be better but it is big device and can be awkward. What do you want to do?

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Guest Skeptic: Dagny Kane-Haas
Dagny is a physiotherapist who just completed her Masters degree in Clinical Science in Manipulative Therapy.

122. We Can Ondansetron if We Want To: But Should We?

Case Scenario:

Four year-old girl presents with diarrhea and three episodes of vomiting in the last 24 hours. The child has signs of mild dehydration. A diagnosis of gastroenteritis is made but you are concerned about ensuring the child takes enough fluids and wonder whether ondansetron is a good choice.

Q:

What has been the trend in ondansetron use in the last 10 years, and how has this related to intravenous rates and admission rates?

BOTTOM LINE

For the centers studied, the rates of ondansetron use increased from 0.1% to 42%. 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.

Impact of Increasing Odansetron Use on Clinical Outcomes in Children with Gastroenteritis

Freedman et al. JAMA Pediatr 2014

P Children <18 years old presenting to the emergency department with gastroenteritis

I Oral ondansetron use

C Time-trend retrospective analysis

O **Primary Outcome:** Rates of intravenous insertion.
Secondary Outcomes: Hospital admission rates, representation to the emergency department within three days, alternative diagnose within three days, cost analysis over time.

Authors' Conclusion:

Ondansetron use in children with AGE (acute gastroenteritis) has increased dramatically in pediatric centres during the past decade without a concomitant reduction in IV rehydration or hospitalizations." (Freedman et al., 2014)

Background

Dehydration in children is a common presentation to the emergency department. A main cause of dehydration in this age group is gastroenteritis that is characterized by acute onset diarrhea with or without nausea, vomiting, fever and abdominal pain.

The scope of the problem was quantified by Glass et al:
- 20-40 million episodes of diarrhea in children each year in the USA
- 2-4 million physician visits per year
- 10% of all hospital admissions of children < 5 yrs old

In the last few years there have been two systematic reviews on the use of ondansetron in children with vomiting from gastroenteritis.

The first was by DeCamp et al. in 2008 and the second was by Fedorowicz et al in 2011. We covered DeCamp in SGEM#12 that showed impressive results:

- NNT of 5 to stop vomiting
- NNT of 5 to prevent one IV insertion
- NNT of 14 to prevent one admission

Given the prevalence of gastroenteritis in the pediatric population, the concerns around preventing dehydration and the desire to avoid unnecessary invasive procedures or admissions, these results were very important.

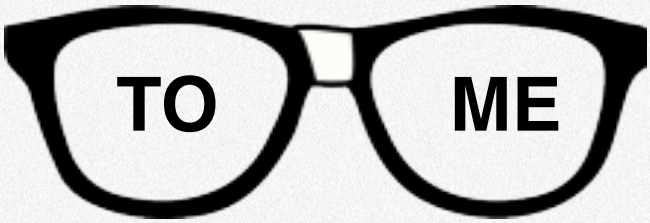
Results

During the timeframe of the study (2002-2011), there were 804,000 pediatric visits to the emergency department with gastroenteritis were included.

Ondansetron increased from 0.1% (2002) to 42% (2011)

The rates of intravenous use went from 18.7% in 2002 to 17.8% in 2011, a non-significant difference. In addition, the rates of admission to hospital did not change significantly during this time frame. There was however a significant drop in representation (bounce back) to the emergency department by 0.31% between 2002 and 2011. And finally, 13.5% of children who received an intravenous for rehydration had been given oral ondansetron.

TALK NERDY TO ME



Commentary

The remaining 18 institutions had ondansetron use that went from low to medium to high over the study time frame. This strategy compromises generalizability of the data to the average emergency department and may have had an unknown biasing effect on the data.

This is the first study of such design to examine this clinical question. As such it is hard to compare the authors' results.

Case Resolution

This girl was not given ondansetron, but rather was given oral rehydration (low and slow!) and was successfully able to tolerate this fluid. She was sent home with proper instructions on care and return to emergency department recommendations.

Clinical Application

In children with gastroenteritis, we need to save ondansetron for those patients who have failed oral rehydration.

CONCLUSION VS COMMENTARY

COMPARISON

We agree with the authors with the caveat that the results may not apply to centers that did not have an equivalent change in ondansetron use over that time frame. The results do highlight the concern that we as emergency department clinicians may be inappropriately using ondansetron in pediatric patients with gastroenteritis.

Oral rehydration fluids should be tried (low and slow) prior to ondansetron use. This strategy should be employed even in children with moderate dehydration. Only children who are severely dehydrated should receive an intravenous immediately.

Quality Checklist

Did the study address a clearly focused issue?	☑
Did the authors use an appropriate method to answer their question?	☑
Was the cohort recruited in an acceptable way?	☑
Was the exposure accurately measured to minimize bias?	☑
Was the outcome accurately measured to minimize bias?	☑
Have the authors identified all important confounding factors?	?
Was the follow up of subjects complete enough?	☑
How precise are the results?	☑
Can the results be applied to the local population?	?
Do the results of this study fit with other available evidence?	?

Your child has a viral infection and we need to make sure they can tolerate oral fluids. We want to avoid dehydration. We are going to start by giving your child oral rehydration fluid, small volumes slowly and frequently. If they vomit with this approach, we will try a medicine to stop the vomiting. If that fails, we will start an intravenous and give them fluid that way.

WHAT DO I TELL MY PATIENT?

References

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Guest Skeptic: Dr. Anthony Crocco
Anthony is the Medical Director & Division Head of Pediatric Emergency at McMaster's Children's Hospital. He is known on YouTube for his RANThonys and has recently developed a novel website to teach evidence based medicine called SketchyEBM.

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Intranasal Fentanyl
Oh What a Feeling

Case Scenario:

Thirteen year-old boy twists his leg at school. He presents to the emergency department with a laterally displaced patella. Prior to reduction of the dislocated patella, you wonder what you can give the child for pain management.

Q:

Can intranasal fentanyl be used in paediatric patients in pain to safely help control pain?

BOTTOM LINE

For children with acute moderate to severe pain, using intranasal fentanyl is a safe and effective way to manage the pain.

Intranasal Fentanyl for the Management of Acute Pain in Children

Murphy et al. Cochrane 2014

P Randomized control trials (RCTs) and quasi RCTs studying children in acute pain

I Intranasal fentanyl

C Any other pharmacological/non-pharmacological intervention

O Primary Outcome: Reduction in pain score.
Secondary Outcomes: Adverse events, tolerance, rescue analgesia use, satisfaction of parent/patient, cost, mortality

Authors' Conclusion:

"Intranasal fentanyl (INF) may be an effective analgesic for the treatment of patients with acute moderate to severe pain, and its administration appears to cause minimal distress to children."
(Murphy et al., 2014)

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).

Some groups of patients who are at great risk for oligoanalgesia (elderly, women, mentally ill, certain ethnic groups, and insurance status)

There are many options available to treat paediatric pain both pharmacologically (analgesics, NSAIDS, nerve blocks, sub-dissociative dose ketamine and opioids) and non-pharmacologically (distraction, sucrose, infant warmers and splinting).

Here are some references for more information on the topic of paediatric pain:

1. Cimpello LB et al. Practice patterns of pediatric versus general emergency physicians for pain management of fractures in pediatric patients. Pediatr Emerg Care 2004
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6. Gray L et al. Sucrose and warmth for analgesia in healthy newborns: an RCT. Pediatrics 2015
7. Hartling L et al. Music to reduce pain and distress in the pediatric emergency department: a randomized clinical trial. JAMA Pediatr 2013
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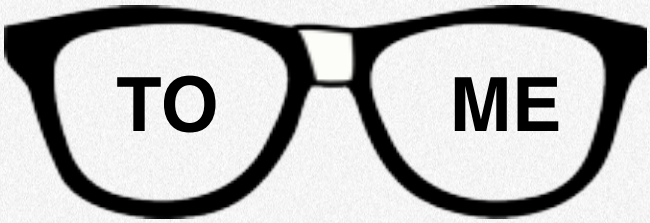
Results

Three studies were included in this systematic review. One study compared intranasal fentanyl to intramuscular morphine, another intranasal fentanyl to intravenous morphine and the last compared intranasal fentanyl given in two different concentrations. Given these methodological differences, combining data sets was not possible.

When intranasal fentanyl was compared to intramuscular morphine, intranasal fentanyl was found to have no significant difference in pain control, except at 10 minutes when intranasal fentanyl had a lower pain score ($p<0.014$). When intranasal fentanyl was compared to intravenous morphine, there were no significant differences noted in pain reduction between groups.

No adverse events or deaths were noted in any of the studies. There was one participant who experienced a bad taste and another who vomited from the intranasal fentanyl group. In comparison, one patient in the intravenous morphine group experienced flushing of the IV site.

TALK NERDY TO ME



Commentary

This is a really well performed systematic review. The search strategy was thorough and the included studies, albeit not many, were of good quality.

Sadly, all three studies were so different in their methodology, that their data could not be combined.

All three studies point towards intranasal fentanyl being an effective and safe method of managing moderate to severe paediatric pain.

Case Resolution

This child is administered intranasal fentanyl and shortly after a reduction of the child's dislocated patella.

Clinical Application

In children with acute moderate to severe pain, intranasal fentanyl can be used safely to manage their pain

CONCLUSION VS COMMENTARY

COMPARISON

Agree 100%

Quality Checklist for Therapeutic Systematic Review

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 and precise enough to be clinically significant	☑

WHAT DO I TELL MY PATIENT?

You have had serious trauma with significant bleeding. We are going to give you a drug that should help control the bleeding and improve your chances of survival.

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Guest Skeptics: Dr. Anthony Crocco
Anthony is the Medical Director & Division Head of Pediatric Emergency at McMaster's Children's Hospital. He is known on YouTube for his RANThonys and has recently developed a novel website to teach evidence based medicine called SketchyEBM.

124 Little Bones
Ultrasound for Skull Fractures

Case Scenario:

An 18-month-old male presents to your small ED having a witnessed fall off a couch and hit his head on a hardwood floor. He threw up once and cried immediately at the scene. There was no loss of consciousness.

The parents are concerned about a serious head injury, particularly with the large hematoma. He is alert with a Glasgow Coma Scale of 15 and has no neurological deficits. Remembering your PECARN pediatric CT decision rules you note that for children less than two years old a CT of the head is recommended if Glasgow Coma Scale<15, altered mental status, or palpable skull fracture.

This child looks great except for a large frontal hematoma and you want to be able to send him home but you know that the presence of a skull fracture increases the risk of an associated intracranial injury.

Q:

Is ultrasound in the emergency department useful to rule-in or rule-out skull fractures in children?

BOTTOM LINE

Ultrasound is a useful adjunct for detecting skull fractures and further risk stratifying minor head injuries when used along with a clinical decision rule like PECARN. However serious intracranial injuries can occur without fracture and the sensitivity of ultrasound for fracture is not yet sufficient to use it as the sole method for detecting injury and making discharge decisions.

Accuracy of Point-of-Care Ultrasound for Diagnosis of Skull Fractures in Children

Rabiner et al. Pediatrics 2013

P Patients 21 years old or younger presenting to the emergency department with suspected skull fracture undergoing CT scan

I Point of care ultrasound in the emergency department (60-minute training session to learn how to use ultrasound to evaluate the skull for fracture and a 30-minute hands-on practical session

C CT scan

O Test characteristics (Sensitivity, specificity, PPV, NPV, +LR and -LR)

Excluded:

- Patients presenting with completed radiologic studies
- A confirmed skull fracture
- An open fracture
- If urgent intervention was required

Authors' Conclusion:

"Clinicians with focused ultrasound training were able to diagnose skull fractures in children with high specificity" (Rabiner et al., 2013)

Background

Point of care ultrasound (POCUS) is becoming a popular method for detecting various types of fractures. It is fast, can be done on less stable patients you don't want leaving the department, can be directed to the area of injury, and can be repeated, particularly when fracture reduction is required.

Ultrasound has been found to have good accuracy when performed by clinicians for various fractures (Weinberg et al Injury 2010) POCUS has been found to be equal or superior to plain films and even bone scans involving fractures of some flat bones like the sternum (Jin et al J Ultrasound Med 2006 and You et al J Clin Ultrasound)

Head injuries are a common presentation in children and the push to reduce exposure to ionizing radiation in young brains is greater than ever. Decision rules like the PECARN CT Head rules help reduce the number of CT scans done on minor head injury patients but the presence of skull fractures is known to increase the risk of an intracranial injury by over four times.

Close observation or CT is going to be a consideration in these fracture patients. Finding fractures with skull X-rays is a problem as they are difficult to interpret and still miss a number of fractures.

The clinical exam is not accurate either for skull fracture as this study demonstrates with 5% found in the very low pretest probability group and 33% found in the low to moderate group. Thus it makes sense to consider the use of ultrasound that has no ionizing radiation, is well tolerated in children, and is not technically challenging to perform.

There have been several other studies now looking at using ultrasound for pediatric skull fractures. Sensitivities range from 82% to 100% and specificity from 94-100% (Weinberg et al Injury 2010, Riera and Chen Paediatr Emerg Care 2012 and Parri et al J Emerg Med 2013).

Results

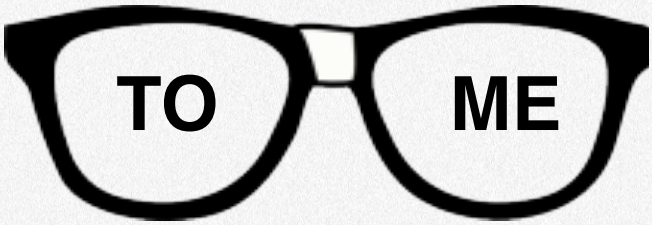
Point-of-care ultrasound was performed by 17 clinicians. There were 69 children under the age of 21years old with suspected skull fractures.

The patients' mean age was 6.4 years. The prevalence of fracture was 12% (8/69).

The test characteristics for detecting skull fractures were reported with 95% confidence intervals. More information on how to calculate these numbers can be found on MedCal.net.

Sensitivity 88% (53-98%) and Specificity 97% (89-99%)
PPV 0.78 (0.45- 0.94) and NPV 0.98 (0.91-1.0)
+LR 26.7 (6.7-106.9) and -LR 0.13 (0.02-0.81)

TALK NERDY TO ME



Commentary

Overall this is a well-performed study on an important topic. More and more we are trying to limit the radiation exposure in children with closed head injuries. Point-of-care ultrasound offers the availability of quick, radiation-free results.

The results of this study are somewhat limited by the small number of patients included, a limitation that is evident from the wide confidence intervals. Another limitation is the sample used was one of convenience and not consecutive.

However, this is the largest single study looking at this topic. They used clinicians with one-hour focused training in skull fracture scanning and a technique of only scanning over the hematoma region.

Their single false negative patient (missed fracture) had a fracture adjacent to the hematoma so using a better technique of scanning on and around a hematoma would have likely discovered this fracture. The authors describe the patient with the missed fracture or false negative as requiring observation only and no specific treatment.

The first false positive was performed by a novice but over-read as negative by the senior clinician suggesting that training may be important to accuracy. The second false positive was called as a positive by both physicians reading the scan and negative on CT.

However, with small, non-depressed fractures, CT is not 100% sensitive either as demonstrated in the studies of other fracture areas. Thus this patient may have had a true positive on ultrasound and false negative on CT.

Diagnostic Testing Quality Checklist

The clinical problem is well defined	☑
The study population represents the target population	☑
The study population included or focused on those in the ED	☑
The study patients were recruited consecutively	
The diagnostic evaluation was sufficiently comprehensive and applied equally to all patients	☑
All diagnostic criteria were explicit, valid and reproducible	☑
The reference standard was appropriate	☑
All undiagnosed patients underwent sufficiently long and comprehensive follow-up	☑
The likelihood ratio(s) of the test(s) in question is presented or can be calculated from the information provided	☑
The precision of the measure of diagnostic performance is satisfactory	☑

CONCLUSION VS COMMENTARY

COMPARISON

Agree with the authors' conclusions that emergency physicians with 60 minute ultrasound training were able to diagnose skull fractures in children with high specificity.

Case Resolution

You could order a skull Xray but you know they are hard to interpret, involve some radiation, will miss a significant number of fractures, and don't provide any information about intracranial injury. Instead you decide to use your department's portable ultrasound machine to look for a fracture and combine this with your clinical decision rules.

With Mom holding her son in her lap, you gently scan over and around the region of the frontal hematoma. There is no fracture visible so, along with PECARN rule support, you are happy to observe the child for a few hours in the ED and send him home with clear discharge instructions for the parents. They are reassured by your examination, seeing their son's intact skull on the ultrasound and are content to avoid doing a CT unless his clinical picture changes later.

Clinical Application

Point-of-care ultrasound, in the hands of competent physicians, appears to be a viable option to rule-in and rule- out skull fractures in children.

One concern, from a clinical standpoint, is that often children with enough findings to merit concern about a skull fracture, have enough clinical findings to warrant a CT scan to rule-out intra-cranial pathology. Also, the incidence of pathology below a skull fracture in children is high, so finding one on ultrasound may merit further investigation with CT scanning. Judicious use of radiation is encouraged, as there is evolving evidence of the long-term risks to mortality and development for children exposed to ionizing radiation.

WHAT DO I TELL MY PATIENT?

We can use an ultrasound device to check and see if your son has a skull fracture. This can help me decide if he is at risk of having a more serious injury and needs to get a CT scan.

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2. Weinberg ER, Tunik MG, Tsung JW. Accuracy of clinician-performed point-of-care ultrasound for the diagnosis of fractures in children and young adults. Injury. 2010 Aug;41(8):862-8.
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Guest Skeptic: Dr. Greg Hall
Greg is Director of EM Ultrasound at the Brantford General Hospital in Brantford Ontario and Assistant Clinical Professor at McMaster University. He is Vice President of the Canadian Emergency Ultrasound Society, co-author of Point-of-care Ultrasound for Emergency Physicians, co-creator of the EDE 2 Course: Advanced Emergency Department Echo, and director of the EDE 3 Course, a leading edge POCUS workshop.

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Special Edition

I'm So Excited

The goal of the Skeptics' Guide to Emergency Medicine (SGEM) is to shorten the knowledge translation window from over ten years down to less than one year. It accomplishes this by doing a critical appraisal of a recently published article using the Best Evidence in Emergency Medicine (BEEM) process. BEEM has the only validated audience rating tool in emergency medicine and to the best of my knowledge, the only known measure of clinical relevance.

The SGEM consists of a weekly podcast available for free on iTunes and a blog. It is also tied into a Facebook page, active Twitter feed and YouTube Chanel.
This is an SGEM Extra. This week I will not be doing a structured critical review; instead I will be discussing two very exciting things happening with the SGEM

Season 2 is now available for download as a PDF Book. SGEM Season 2 has all 42 episodes. Each chapter starts with a single page summarizing the episode. You get the case scenario, clinical question and the bottom line. Turn the page and you will find the PICO (population, intervention, control/comparison and outcome) and author's conclusions. This is followed by background information on the subject, key results and some *"talking nerdy"*.

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Take Me to the Rivaroxaban: Outpatient Treatment of VTE

Case Scenario:

A 55-year-old man presents with chest pain and shortness of breath. You risk stratify him to be non-high risk. His d-dimer comes back elevated at 720. A CT scan confirms a segmental pulmonary embolism.

Q:

Can low-risk emergency department patients with acute venous thromboembolsim be safely discharged home on rivaroxaban?

BOTTOM LINE

One observational study from two Indianapolis hospitals implies that rivaroxaban administered for variable durations of time for patients newly diagnosed with VTE in the emergency department is reasonably safe and effective. However, practice-change based on single non-randomized study is unjustified and multiple implementation barriers need to be evaluated and overcome prior to widespread application of this protocol.

Immediate Discharge and Home Treatment of Low Risk Venous Thromboembolism Diagnosed in Two U.S. Emergency Departments with Rivoraxaban: A One-Year Preplanned Analysis

Beam et al. Acad Emerg Med 2013

P Low-risk adult patients with newly diagnosed PE or DVT in academic emergency department

I Rivaroxaban 15 mg orally twice daily x 21 days then 20 mg daily for unspecified duration. Patients optionally got a first dose of enoxaparin 1mg/kg sub cutaneous

C None

O Recurrent venous thromboembolism (VTE) or hemorrhage. For bleeding they used the International Society of Thrombosis and Hemostasis definition of major or clinically relevant non major bleeding

Excluded:

- Systolic hypotension
- Contraindication to low-molecular-weight heparin or warfarin treatment Other medical condition requiring hospital treatment (sepsis, new or decompensated existing organ failure, intractable pain).
- Social condition requiring hospital treatment (homelessness with history of nonadherence to treatment, suspected neglect or abuse, untreated psychosis, severe alcohol or drug dependency).
- Coagulopathy, any INR > 1.7, or thrombocytopenia.
- Pregnancy.
- Incarceration.

Authors' Conclusion:

"Patients diagnosed with VTE and immediately discharged from the ED while treated with rivaroxaban had a low rate of VTE recurrence and bleeding." (Beam et al., 2013)

Background

Venous thromboembolism is a common diagnosis made in the emergency department. According to Rosen's textbook of Emergency Medicine, approximately 1 in every 500 to 1000 (0.1%-0.2%) emergency department patients have a pulmonary embolism (PE).

Per-patient inpatient admission costs for PE in the United States ranged from $25,000 to $44,000 between 1998 and 2006 with post-hospitalization warfarin and lab testing estimated at $2694.

Historically, these patients were all admitted to hospital for initial treatment (Simonneau). Washington University currently discharge ~1% of PE patients (and a few more DVT patients), but are asked to do so by admitting services in 21% of cases.

This situation is different in Canada. Papers starting coming out in the early 2000 demonstrating the safety of out-patient management of PEs (Kovacs). A pragmatic evaluation of the ambulatory management of PEs in Canada came out in 2010 (Kovacs). This showed 50% of patients being safely treated as out- patients.

Washington University in 2013 conducted a Knowledge Translation Journal Club on this topic with Hospitalists in an attempt to develop a mutually agreeable algorithm to those individuals appropriate for outpatient management. We developed an algorithm for outpatient management of low risk, non-pregnant, newly diagnosed PE patients that we still use today. One of our biggest uncertainties was if and how to manage these patients with newer anti-coagulants.

Results

A total of 106 patients discharged with venous thromboembolism (VTE) including 67% with DVT, 28% with PE and 5% with both DVT and PE. Of the total patients presenting with VTE they were able to discharge and treat as outpatients 27% of PE patients and 51% of DVT patients. Two patients died from causes unrelated to VTE or rivaroxaban therapy. There were three patients lost to follow-up and assumed to have a good outcome.

Primary Outcome

New VTE: None 0/106 (0%, 95% CI 0% to 3.4%).
Recurrent VTE: 3/106 (3%, 95% CI 0.6% to 8%) after discontinued therapy
Bleed: No patients had major bleeding events.

Commentary

We asked Dr. Kline a number of questions about the study. Listen to the SGEM Podcast to hear his answers.

A few things about the Anticoagulation Clinic:

You report two approaches that could be difficult to replicate. You did not use a one-size-fits all duration of rivaroxaban therapy. Instead, *"we used a combination of published criteria, evidence, clinician judgment, and shared-decision making to decide the duration of anticoagulation for each patient."* Would other healthcare settings without an emergency department-led anticoagulation clinic with access to the world's authority on VTE management be able to provide such individualized care?

You used an anticoagulation clinic staffed by the authors, to which most emergency physicians in other settings would not have access. In many urban settings, access to anticoagulation clinics can take months to schedule from the emergency department that serves as a significant barrier to discharge home for some patients.

Another point is you said: *"adoption (of the rivaroxaban protocol) by our ED faculty and housestaff was rapid and enthusiastic."* In other settings that lack an opinion leader with acknowledged expertise in the management of VTE, implementation processes and early adoption would likely be significantly more challenging.

Five Question about Bias in the Study:

You reported doing a chart review to identify VTE or bleeding events but report no chart review methods such as Gilbert and Lowenstein or Worster et al.

You used a modified Hestia criteria and the Prediction of Mortality from Pulmonary Embolism in Cancer (POMPE-C) criteria to identify *"low-risk"*, but they provide no evidence that the modified Hestia criteria predict VTE adverse outcomes or that the POMPE-C predict adverse outcomes in non-cancer patients.

You report no sensitivity analysis for the three patients who were completely lost to follow-up. Instead they assume that no adverse VTE events/outcomes occurred in these three patients. How about considering the worst case scenario and they all bled or died. How would that impact your data/conclusions?

You were able to provide rivaroxaban free of charge or at a deeply discounted rate for up to one year (www.jjpaf.org) for their largely indigent population. Whether manufacturers or state Medicaid programs would be willing/able to provide free or very cheap rivaroxaban on a much larger scale should the proposed protocol become standard of care everywhere is a key issue to widespread adoption of this protocol.

You did not compare this to "standard care" such as admitting these low risk patients to hospital and starting them on warfarin or rivaroxaban?

Quality Checklist

Did the study address a clearly focused issue?	☑
Did the authors use an appropriate method to answer their question?	
Was the cohort recruited in an acceptable way?	?
Was the exposure accurately measured to minimize bias?	☑
Was the outcome accurately measured to minimize bias?	☑
Have the authors identified all important confounding factors?	☑
Was the follow up of subjects complete enough?	☑
How precise are the results?	☑
Can the results be applied to the local population?	?
Do the results of this study fit with other available evidence?	☑

Case Resolution

The patient is presented with appropriate information. He is low risk, has a drug plan for rivaroxaban and can get follow-up in couple of weeks. You discuss the options including admission or out patient management. A shared decision is made for him to go home on rivaroxaban.

Clinical Application

It is certainly reasonable to discuss outpatient treatment with rivaroxaban (or warfarin) for appropriate low-risk emergency department patients with newly diagnosed VTE, but the discussion should include the degree of uncertainty associated with non-randomized, observational studies.

You have a blood clot in your lung. One early study suggests low-risk patients like you can be treated safely with a new pill that *"thins your blood"*. Sometimes early studies are later shown to be wrong by bigger and better studies. We should always be a little skeptical of small new studies. The usual treatment for blood clots is to admit you to the hospital. This is expensive and takes you away from home, family, and work for an extended period of time. You are a low-risk patient and have access to this new medication. You also can get seen in the special blood clot clinic in the next couple of weeks. Going home on the new pill or being checked into hospital are both reasonable options. What would you like to do?

CONCLUSION VS COMMENTARY

COMPARISON

We agree that this is a preliminary study demonstrating apparent efficacy and safety of rivaroxaban in urban, teaching emergency department settings for outpatient management of significant proportions of VTE patients. Additional studies from more heterogeneous emergency department settings and preferably from randomized controlled trials are needed before widespread application of this protocol is reasonable.

WHAT DO I TELL MY PATIENT?

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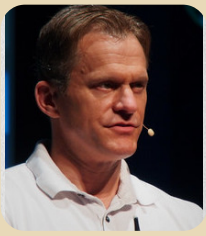


Guest Skeptic: Dr. Jeffrey Kline
Dr. Jeffrey Kline (@klinelab) is the Vice Chair of Research in Emergency Medicine and a professor of physiology, Indiana University School of Medicine.

Season#3: Theme Music

SGEMers know how important the theme music plays in the podcast. Marshall McLuhan was a well known Canadian Professor of Communication theory at the University of Toronto. One of his famous quotes was: *"Anyone who tries to make a distinction between education and entertainment doesn't know the first thing about either."*

I am often asked which comes first, the article or the theme music? Let me assure everyone that it is about the literature. After the paper has been selected I look to that rich era of music the 1980's. Only then do I try to find a song which fits the topic being discussed. While I try to get music from the 1980's there are a few times where a song from another era fits better.

Here is the list of the music used in Season #3 of the SGEM to help cut the knowledge translation window from over ten years to less than one year.

#	SGEM Title	Theme Song	Artist
85	Won't Get Fooled Again (tPA for CVA)	Won't Get Fooled Again	The Who
86	Achy Breaky Heart (Colchicine for Acute Pericarditis)	Achy Breaky Heart	Billy Ray Cyrus
87	Let Your Back Bone Slide (Paracetamol for Low-Back Pain)	Let Your Backbone Slide	Maestro Fresh Wes
88	Shock Through the Heart (Ottawa Aggressive Atrial Fibrillation Protocol)	You Give Love a Bad Name	Bon Jovi
89	Preventing Falling to Pieces	Breakeven (Falling to Pieces)	The Script
90	Hunting High and Low (Best MAP for Sepsis Patients)	Hunting High and Low	A-ha
91	French Version		
92	ARISE Up, ARISE Up (EGDT vs. Usual Care for Sepsis)	Rise Up	Parachute Club
93	Ketamine, A Bad Reputation?	Bad Reputation	Joan Jett
94	You Better Think Ultrasound for Acute Abdominal Aneurysm	Think	Aretha Franklin
95	Paediatric Fever	Fever	Peggy Lee
96	Machine Head – NIPPV for Out of Hospital Respiratory Distress	Machine Head	Bush
97	Hippy Hippy Shake – Ultrasound Vs. CT Scan for Diagnosing Renal Colic	Hippy Hippy Shakes	The Swinging Blue Jeans
98	Don't Stand So Close to Me (You have the flu)	Don't Stand So Close To Me	The Police
99	I Flip My Classroom Back and Forth	Whip My Hair	Willow Smith
100	Why Can' t This Be Love? Early Goal Directed Dating (EGDD)	Why Can't This Be Love?	Van Halen

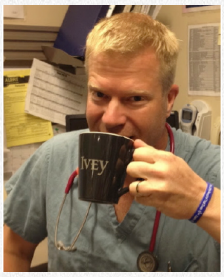
Season#3: Theme Music

#	SGEM Title	Theme Song	Artist
101	Puke – Antiemetics in Adult Emergency Department Patients	Puke	Eminem
102	Text Me for Emergency Department Follow-up	Call Me	Blondie
103	Just Breathe – Inhaled Corticosteroids for Asthma Exacerbations	Just Breathe	Pearl Jam
104	Let's Talk about Sex Baby, Let's Talk about STDs	Let's Talk About Sex	Salt-N-Pepa
105	Does this Woman Have an Ectopic Baby, Baby?	Baby, Baby	Justin Bieber
106	O Canada- Canadian CT Head Rule for Patients with Minor Head Injury	Canadian National Anthem	Adolphe-Basile Routhier
107	Can't Touch This – Hands on Defibrillation	Can't Touch This	MC Hammer
108	You Spin Me Right Round Baby Like Benign Paroxysmal Positional Vertigo	You Spin Me Round	Dead Or Alive
109	One Platelet, One Plasma and One RBC – PROPPR Trial	One Bourbon One Scotch One Beer	George Thorogood
110	I Saw the Signs of Angioedema	I Saw The Sign	Ace of Base
111	Comfortably Numb – Low dose Ketamine as Adjunct for ED Pain Control	Comfortably Numb	Pink Floyd
112	Bang Your Head – Paediatric Concussions	Bang Your Head	Quiet Riot
113	EGDT – ProMISe(s) ProMISe(s)	Promises Promises	Naked Eyes
114	Ketofol – Does It Take Two to Make a Procedure Go Right?	It Takes Two	DJ EZ Rock and Rob Base
115	Complicated – Non-Operative Treatment of Appendicitis (NOTA)	Complicated	Avril Lavigne
116	Paramedics' Got a Squeeze Box – Remote Ischemic Conditioning	Squeeze Box	The Who
117	Diarrhea – Hard to Spell, Easy to Smell and Easy to Cause with IV Antibiotics	Diarrhea: Hard to spell (easy to smell)	The Toilet Bowel Cleaners
118	I Hope you Had a Negative D-dimer (ADJUST PE Study)	Good Riddance (Time of Your Life)	Green Day
119	B-Lines (Diagnosing Acute Heart Failure with Ultrasound)	B line	Lamb

Season#3: Theme Music

#	SGEM Title	Theme Song	Artist
120	One Thing or Two for Community Acquired Pneumonia?	One Thing or Two	Bobby Bazini
121	Internal or External Shoulder Immobilization (It Don't Matter to Me)	It Don't Matter to Me	Phil Collins
122	We can Ondansetron if We Want To – But Should We?	Safety Dance	Men Without Hates
123	Intranasal Fentanyl – Oh What a Feeling	Oh What a Feeling	Crowbar
124	Ultrasound for Skull Fractures – Little Bones	Little Bones	Tragically Hip
125	I'm So Excited	I'm So Excited	The Pointer Sisters
126	Take me to the Rivaroxaban – Outpatient treatment of VTE	Take Me to the River	The Commitments

About the Authors



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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.

Christopher Carpenter, MD, MSc, FACEP, FAAEM, AGSF

Dr. Carpenter is the Director of EBM for the Division of EM Medicine at Washington University in St. Louis. He is the Chair of the SAEM EBM Interest Group and ACEP Geriatric Section. He is Associate Editor of Academic Emergency Medicine, as well as Associate Editor of Annals of Internal Medicine's ACP Journal Club. He co-authored the textbook "Evidence-Based Emergency Care: Diagnostic Testing and Clinical Decision Rules, 2nd Edition". Dr. Carpenter lives in St. Louis, Missouri with his wife, two children, and wonder-dog and is an avid St. Louis Cardinals fan.

David Kepecs, MSc

Mr. Kepecs is a fourth year medical student at the University of Toronto. He is extremely excited to be involved with the editing of SGEM: Season 3 because he has a strong belief in the enormous impact of FOAMed in the field of emergency medicine. He aspires to use future FOAMed projects to focus on health education projects for clinicians, students, and their communities. Outside of medicine, David enjoys golf, hiking and cheering on his last place fantasy football team.