EM Basic Lit Review for Medical Students/Residents Compiled

This is a compiled resource for medical students of 52 practice changing, high yield articles within Emergency Medicine. The articles were compiled by the website Academic Life in Emergency Medicine (aliem.com) where they polled academic attendings to compile a list of some of the most important articles to read during intern year. Here, we provide summaries of each article along with important take home points at the end. Our hope is that reading these blurbs will help to distill the take home point of each article into an easy to digest format while also facilitating learners on how to approach reading articles effectively and efficiently.

List of Articles reviewed:

1. Andersen HR, Nielsen TT, Rasmussen K, Thuesen L, et al; DANAMI-2 Investigators. A comparison of coronary angioplasty with fibrinolytic therapy in acute myocardial infarction. N Engl J Med. 2003 Aug 21;349(8):733-42. PMID: 12930925
2. Backus BE, Six AJ, Kelder JC, Bosschaert MA, et al. A prospective validation of the HEART score for chest pain patients at the emergency department. Int J Cardiol. 2013 Oct 3;168(3):2153-8. PMID: 23465250
3. McCullough PA, Nowak RM, McCord J, Hollander JE, et al. B-type natriuretic peptide and clinical judgment in emergency diagnosis of heart failure: analysis from Breathing Not Properly (BNP) Multinational Study. Circulation. 2002 Jul 23;106(4):416-22. PMID: 12135939
4. Nichol G, Leroux B, Wang H, Callaway CW, et al; ROC Investigators. Trial of Continuous or Interrupted Chest Compressions during CPR. N Engl J Med. 2015 Dec 3;373(23):2203-14. PMID: 26550795
5. Quinn J, McDermott D, Stiell I, Kohn M, Wells G. Prospective validation of the San Francisco Syncope Rule to predict patients with serious outcomes. Ann Emerg Med. 2006;47(5):448-54. PMID: 16631985
6. Sgarbossa EB, Pinski SL, Barbagelata A, Underwood DA, et al; GUSTO-1 (Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries) Investigators. Electrocardiographic diagnosis of evolving acute myocardial infarction in the presence of left bundle-branch block. N Engl J Med. 1996 Feb 22;334(8):481-7. PMID: 8559200
7. Wyse DG, Waldo AL, DiMarco JP, Domanski MJ, et al; Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) Investigators. A comparison of rate control and rhythm control in patients with atrial fibrillation. N Engl J Med. 2002 Dec 5;347(23):1825-33. PMID: 12466506

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10. de Gans J, van de Beek D; European Dexamethasone in Adulthood Bacterial Meningitis Study Investigators. Dexamethasone in adults with bacterial meningitis. N Engl J Med. 2002 Nov 14;347(20):1549-56. PMID: 12432041
11. Marik PE, Flemmer M, Harrison W. The risk of catheter-related bloodstream infection with femoral venous catheters as compared to subclavian and internal jugular venous catheters: a systematic review of the literature and meta-analysis. Crit Care Med. 2012 Aug;40(8):2479-85. PMID: 22809915
12. Weiss EA, Oldham G, Lin M, Foster T, Quinn JV. Water is a safe and effective alternative to sterile normal saline for wound irrigation prior to suturing: a prospective, double-blind, randomised, controlled clinical trial. BMJ Open. 2013 Jan 16;3(1). PMID: 23325896
13. Wong CH, Khin LW, Heng KS, Tan KC, Low CO. The LRINEC (Laboratory Risk Indicator for Necrotizing Fasciitis) score: a tool for distinguishing necrotizing fasciitis from other soft tissue infections. Crit Care Med. 2004 Jul;32(7):1535-41. PMID: 15241098

Musculoskeletal: page 18

14. Stiell IG, Greenberg GH, McKnight RD, Nair RC, et al. Decision rules for the use of radiography in acute ankle injuries. Refinement and prospective validation. JAMA. 1993 Mar 3;269(9):1127-32. PMID: 8433468

Neurosciences: pages 18-27

15. Hacke W, Kaste M, Bluhmki E, Brozman M, et al; ECASS Investigators. Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke. N Engl J Med. 2008 Sep 25;359(13):1317-29. PMID: 18815396
16. Hasbun R, Abrahams J, Jekel J, Quagliarello VJ. Computed tomography of the head before lumbar puncture in adults with suspected meningitis. N Engl J Med. 2001 Dec 13;345(24):1727-33. PMID: 11742046
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18. Johnston SC, Rothwell PM, Nguyen-Huynh MN, Giles MF, et al. Validation and refinement of scores to predict very early stroke risk after transient ischaemic attack. Lancet. 2007;369(9558):283-92. PMID: 17258668
19. Kattah JC, Talkad AV, Wang DZ, Hsieh YH, Newman-Toker DE. HINTS to diagnose stroke in the acute vestibular syndrome: three-step bedside oculomotor examination more sensitive than early MRI diffusion-weighted imaging. Stroke. 2009 Nov;40(11):3504-10. PMID: 19762709
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21. Nielsen N, Wetterslev J, Cronberg T, Erlinge D, et al; TTM Trial Investigators. Targeted temperature management at 33°C versus 36°C after cardiac arrest. N Engl J Med. 2013 Dec 5;369(23):2197-206. PMID: 24237006
22. Perry JJ, Stiell IG, Sivilotti ML, Bullard MJ, et al. High risk clinical characteristics for subarachnoid haemorrhage in patients with acute headache: prospective cohort study. BMJ. 2010 Oct 28;341:c5204. PMID: 21030443

Pediatrics: pages 27-33

23. Bjornson CL, Klassen TP, Williamson J, Brant R, et al; Pediatric Emergency Research Canada Network. A randomized trial of a single dose of oral dexamethasone for mild croup. N Engl J Med. 2004 Sep 23;351(13):1306-13. PMID: 15385657
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28. Spiro DM, Tay KY, Arnold DH, Dziura JD, et al. Wait-and-see prescription for the treatment of acute otitis media: a randomized controlled trial. JAMA. 2006 Sep 13;296(10):1235-41. PMID: 16968847

Pulmonary: pages 33-39

29. The Acute Respiratory Distress Syndrome Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. N Engl J Med. 2000 May 4;342(18):1301-8. PMID: 10793162
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Resuscitation: pages 39-42

36. De Backer D, Biston P, Devriendt J, Madl C, et al; SOAP II Investigators. Comparison of dopamine and norepinephrine in the treatment of shock. N Engl J Med. 2010 Mar 4;362(9):779-89. PMID: 2020038
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goals of early sepsis therapy: a randomized clinical trial. JAMA. 2010 Feb 24;303(8):739-46. PMID: 20179283.
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Toxicology: pages 42-43

40. Weaver LK, Hopkins RO, Chan KJ, Churchill S, et al. Hyperbaric oxygen for acute carbon monoxide poisoning. N Engl J Med. 2002 Oct 3;347(14):1057-67. PMID: 12362006

Trauma: pages 43-50

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Ultrasound: pages 50-52

49. Melniker LA, Leibner E, McKenney MG, Lopez P, Briggs WM, Mancuso CA. Randomized controlled clinical trial of point-of-care, limited ultrasonography for trauma in the emergency department: the first sonography outcomes assessment program trial. Ann Emerg Med. 2006 Sep;48(3):227-35. PMID: 16934640
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Urology: page 52

51. Smith-Bindman R, Aubin C, Bailitz J, Bengiamin RN, et al. Ultrasonography versus computed tomography for suspected nephrolithiasis. N Engl J Med. 2014 Sep 18;371(12):1100-10. PMID: 25229916

Vascular: page 53

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CARDIOLOGY

1. Andersen HR, Nielsen TT, Rasmussen K, Thuesen L, et al; DANAMI-2 Investigators. A comparison of coronary angioplasty with fibrinolytic therapy in acute myocardial infarction. N Engl J Med. 2003 Aug 21;349(8):733-42. PMID: 12930925

Study Question: Angioplasty has been shown to be superior to fibrinolytic therapy as a treatment option for acute myocardial infarction, but this paper wanted to investigate if angioplasty is also better when a patient needs to be transferred in order to get access to this intervention.

Demographics/Design: Multicenter, Danish study with 1,572 patients with AMI where the patients were randomized to either primary fibrinolysis with an accelerated tPA regimen or primary angioplasty. The study included patients presenting to one of 24 hospitals without angioplasty capability, or one of five hospitals with such capability. Transfer to an angioplasty center within three hours was necessary for patients to get randomized to angioplasty who presented to a center that did not offer it. This is a little complicated to follow, but basically patients could get randomized to angioplasty, or fibrinolysis no matter where they showed up as long as the transfer time from non-angioplasty capable facilities was fewer than 3 hours.

Inclusion criteria were age 18 or greater, the presence of symptoms for at least 30 minutes but less than 12 hours and cumulative ST segment elevation of at least 4 mm in two contiguous leads. **Exclusion** criteria included a contraindication to fibrinolysis, LBBB, acute MI and fibrionolytic treatment within the previous 30 days, pulseless femoral arteries, previous coronary bypass surgery, renal failure, diabetes treated with metformin, non-ischemic heart disease and non-cardiac disease associated with a life expectancy of less than 12 months. Also, patients who were judged to be at high risk during transportation due to cardiogenic shock (systolic BP< 65), persistent life threatening arrhythmia, or who needed mechanical ventilation were excluded.

Outcome: Primary composite endpoint of death, reinfarction, or disabling stroke within 30 days in those presenting to one of 24 hospitals without angioplasty, or one of five centers with angioplasty capabilities (transport time < 3 hours required for those presenting to one of the centers that could not do angioplasty).

- 14.2% bad outcomes for fibrinolysis vs 8.5% for angioplasty (p=.002) in patients presenting to a hospital without angioplasty capabilities but eventually transferred to such a center.
- 12.3% bad outcomes with fibrinolysis vs 6.7% with angioplasty among patients who presented to an angioplasty capable center (p=.05).
- Of note, transfer from a referral hospital to an invasive treatment center was accomplished within 2 hours in 96% of relevant cases.

Take home point: Get angioplasty over tPA for your MI even if you have to get transferred < 3 hours. Landmark study door to balloon time even with transfer.

2. A PROSPECTIVE VALIDATION OF THE HEART SCORE FOR CHEST PAIN PATIENTS AT THE EMERGENCY DEPARTMENT Backus, B.E., et al, Internat J Card 168(3):2153, October 2013

Study Question: To see if the HEART score could outperform available tools (TIMI, GRACE) as a predictor of bad outcomes in order to better risk stratify patients presenting to the ED with chest pain. Of note, the score was initially developed because people say TIMI score, GRACE score, etc. do not optimize use of troponin and ecg, which are ubiquitous tests that come back quickly and can play a large role in risk stratification. **It is important to remember that this score is a predictor of outcomes—not ACS.**

Design/Methods: HEART score incorporates history, ecg, age, risk and initial trop added up to form a composite score as high risk, intermediate risk, or low risk. The score is formed by:

- History (slightly suspicious=0, moderate=1, highly suspicious= 2)
- EKG (Normal=0, nonspecific repol disturbance= 1, significant ST deviation=2)
- Age (<45=0, 1-2 risks=1, > 3= 2)
- Initial trop (< normal limit= 0, 1-3x normal=1, >3x normal=2)

Add these together and this forms a score of 0-3 (low risk), 4-6 (intermediate), or 7 and higher, high risk.

The authors did get TIMI and GRACE scores on all of them. Also, of 2400 patients, 400 had bad things happened. Rest of them didn't, so ratio of positive to negative was 1:5 in whole population (basically this means it's a pretty sick group), but this is a good thing—we want high risk patient risk stratification. Troponins were regular old trops and done at 0 and 6 hours later—not new high sensitivity troponins.

Inclusion/Exclusion: Any patient admitted to the emergency department due to chest pain irrespective of age, pre-hospital suspicions and previous medical treatment was eligible. **Of note, patients presenting with only dyspnea or palpitations were not included** (interesting because that can be the exclusive presenting symptom for an MI), excluded STEMIs (because they went somewhere else).

Outcomes: Primary outcome was the occurrence of major adverse cardiac events (MACE) within six weeks. MACE consists of: AMI, PCI, CABG, coronary angiography revealing procedurally correctable stenosis managed conservatively, and death due to any cause.

Results: HEART score did pretty well.

- 0-3 is a very low risk of MACE (1.7% at 6 weeks). 4-6 (16.6% MACE) is middle and then greater than 6 (50% MACE). **HEART score worked to stratify well at the low and high end, which is important.**

Take homes: So you can identify fairly well a low risk (move to outpatient), also in greater than 6 group, you could stratify people where really bad things happen (better than TIMI and

GRACE). HEART worked well in problematic groups: diabetics (silent MI), women (well with proviso it excluded SOB, which old women present with), did well in old people (greater 75). Prospective validation of HEART score and its risk stratification role in the ED using just data that is immediately available.

Concerns: 1% miss rate but one percent of something that is super prevalent (1/10 ED visits), so math is going to be hard. Also, a third of the cases were low risk (which is perhaps too low to apply to the U.S), so we may need help defining a low risk population.

But, does seem to have independent discriminatory power vs. TIMI or GRACE because score at well end puts a lot of people into low risk than TIMMI or GRACE but also discriminates the high risk well, so it does have some independent validity even alone.

3. McCullough PA, Nowak RM, McCord J, Hollander JE, et al. B-type natriuretic peptide and clinical judgment in emergency diagnosis of heart failure: analysis from Breathing Not Properly (BNP) Multinational Study. Circulation. 2002 Jul 23;106(4):416-22. PMID: 12135939

Study Question: To evaluate the use of BNP as a diagnostic test for diagnosis of heart failure and compare BNP to physician assessment in patients presenting to ED with chief complaint of dyspnea. Basically, does BNP add anything to clinical judgement in making a diagnosis of CHF?

Study Design: 1,538 patients with mean age of 64 years old and 44% female presenting to the Emergency Department with acute dyspnea. Patients underwent routine care and had BNP measured in a blinded fashion. The gold standard for diagnosing CHF was 2 independent cardiologists who were also blinded to BNP results. The primary endpoint was the diagnostic accuracy at an optimal cutoff for BNP to estimate the clinical probability of CHF. **Inclusion criteria included all patients needing dyspnea on exertion, or at rest along with an initial suspicion for CHF due to accompanying symptoms.** Eighty patients were excluded from the study on the basis of the protocol exclusion criteria, which included the presence of advanced renal failure (calculated creatinine clearance <15 mL/min), acute myocardial infarction, and overt cause of dyspnea, including chest wall trauma or penetrating lung injury.

Principal findings: Diagnosis was Heart failure in 47% of patients. Using BNP cutoff of 100 had a sensitivity of 90% and specificity of 73% . BNP testing provided an accurate diagnosis in 81% of patients compared to 74% for clinical judgment. Overall, adding BNP to physician decision would have increased accuracy of diagnosis from 74% to 81.5%.

Take home: In patients presenting to ED with primary complaint of dyspnea, use of BNP added to clinical judgement diagnosis of CHF. BNP titers compare favorable in diagnostic accuracy to other HF diagnostic criteria. Supports BNP as a good rule-out test for Acute Decompensated Heart Failure (ADHF) with a sensitivity of 90% for BNP < 100 pg/mL when compared to the gold standard: blinded assessment of two independent cardiologists. The authors also argued that

BNP ruled-in 14 of the 19 patients that were erroneously diagnosed by clinicians as "CHF improbable," thereby reducing false negatives from 2% to 0.6%. The improved sensitivity, however, inevitably reduced specificity to near 74% for a cut-off of BNP ≥100 pg/mL.

4. Nichol G, Leroux B, Wang H, Callaway CW, et al; ROC Investigators. Trial of Continuous or Interrupted Chest Compressions during CPR. N Engl J Med. 2015 Dec 3;373(23):2203-14. PMID: 26550795

Study Question: To see if during CPR in patients with out of hospital cardiac arrest, outcomes after continuous compressions with positive pressure ventilation differed from those after compressions that were interrupted for ventilations ant a ratio of 30 compressions to two ventilations. Background here is important because ACLS guidelines from October 2015 stress the importance of high quality CPR and minimizing interruption (in theory increasing blood flow and survival) How does this fit in with those guidelines? This article attempted to investigate that by comparing interrupted and continuous CPR.

Demographics/Design: The authors performed cluster randomized trial across a bunch of EMS agencies and then randomized them so that different EMS groups switched protocols. The study involved 24,000 patients looking at the **primary outcome of survival at discharge**. Of note, survival at discharge may not be the best measure here—survival with good neurologic outcome, for example, may have been superior.

Take home points: Continuous CPR = 9% survival to discharge, in the interrupted 9.7% survival (p=.07). Good neuro outcome was **secondary outcome** with similarly little difference in outcomes (7% vs 7.7%) (p=.09).
In advanced prehospital systems who demonstrate excellent quality CPR, there is no difference in cardiac arrest outcomes. This is very interesting because we stress continuous CPR, but this study is questioning if there is a difference.

One problem is that differences were only measured until an advanced airway was placed (6 mins) and the compression fraction to measure good quality CPR in both is spectacular in both groups (it is supposed to be .75 and here it's .83 in continuous and .77 in interrupted).

So, if you have a spectacularly good EMS system where they are really compressing, it does not matter how you provide the breaths, but if you don't have this, it seems intuitively best to stay with a continuous approach. Also, compression only CPR is just simpler. (Emrap EMA).

Also, problematically, there are so many confounders and variables with patients in an EMS study and what really will always matter most is recognition and defibrillation.

5. Quinn J, McDermott D, Stiell I, Kohn M, Wells G. Prospective validation of the San Francisco Syncope Rule to predict patients with serious outcomes. Ann Emerg Med. 2006;47(5):448-54. PMID: 16631985

Clinical Question – Can SF Syncope Rule be used to risk stratify CC: syncope patients? High risk syncope?

- **1.2% of all US ED visits = syncope**

Design basics → **prospective cohort**, n = 760 patients with 791 visits of syncope/near syncope

SF Syncope Rule: 5 Y/N questions to predict risk for serious outcomes at 7 days in patients presenting with syncope or near syncope

- Works like PERC Rule → Yes to any question rules patient out of low risk group for serious outcome
- CHF, Hematocrit < 30, non sinus EKG or new changes/abnormalities, SOB symptoms, SBP < 90 at triage
    - **YES to any of these → High Risk for Serious Outcome Requiring Admission**
- Patients followed up within 30 days of ED visits for predefined serious outcome data
- Short Time Serious Outcomes requiring Admission:
    - Death
    - MI
        - Any trop bump or EKG change with clinical dx of MI on discharge, confirmed by Cardiology or Primary Care Team
    - Arrhythmia
    - PE
    - Stroke
    - SAH
    - Hemorrhage or anemia requiring transfusion
    - Procedural interventions to treat related cause of syncope or any condition causing a return ED visit
    - Hospitalization for related event
- Include → syncope, pre-syncope with no exclusion
- Exclude → trauma related LOC, EtOH/Drug related LOC, Definite Seizure, LOC with new AMS or persistent neuro deficits = does not meet definition of syncope

Outcomes

Primary → Performance of SF Syncope Rule

- Serious outcomes in cohort after ED visit → 54 (6.8%)
    - Arrythmia and MI most common
- 98% (95CI 89-100%) sensitive, 56% specific for predictive serious outcomes
    - SnOUT for serious adverse events from syncope, can't SpIN though

Secondary → 95% of physicians interpreted rule accurately

Criticisms → enrolled at one hospital, study performed at hospital where protocol is developed

- Validate tool at same center used to derive original rule

- Huge margin of error in sensitivity (CI of 89-100%)
- Lots of misses with extremely low sensitivity/specificity

Take Home

SF Syncope Rule is questionable at best with large margin of error in sensitivity, low specificity. It is easy to use but does not do a great job risk stratifying patients with syncope and severe illness, especially given exclusion criteria (trauma, drug/EtOH, etc) exclude large populations that present with syncope. Study also developed and validated clinical tool at same hospital, can we generalize this?

6. Sgarbossa EB, Pinski SL, Barbagelata A, Underwood DA, et al; GUSTO-1 (Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries) Investigators. Electrocardiographic diagnosis of evolving acute myocardial infarction in the presence of left bundle-branch block. N Engl J Med. 1996 Feb 22;334(8):481-7. PMID: 8559200

Clinical Question → Testing ECG criteria for diagnosis of acute MI in the presence of left-bundle branch block, developing the Sgarbossa criteria

Baseline ECG of patients in GUSTO-1 Trial (tPA and Streptokinase for occluded coronaries) who had left-bundle branch blocks **blindly** compared with ECGs of control patients with chronic CAD and LBBB

LBBB → QRS at least 0.125 seconds in presence of sinus of SVT, Qs or rS complex in V1, and peak R wave time of at least 0.06 seconds in lead I, V5 or V6, associated with no Q wave in same lead

Exclude → intermittent LBBB

145 t of 26,003 searched from GUSTO-1 had LBBB: AMI confirmed in 131 of these patients with elevated CKMB

Criteria/Outcomes

- ST elevation at least 1 mm and concordant with QRS → 73 sensitive, 92 specific, 9.54 positive likelihood ratio, 0.3 negative likelihood ratio
- ST segment depression at least 1 mm in V1, V2, or V3 → 25 sensitive, 96 specific, 6.58 positive likelihood ratio, 0.78 negative likelihood ratio
- ST segment elevation at least 5 mm and discordant with QRS → 31 sensitive, 92 specific, 3.63 positive likelihood ratio, 0.75 negative likelihood ratio
- Positive T wave in Lead V5 or V6 → 26 sensitive, 92 specific, 3.42 positive likelihood ratio, 0.8 negative likelihood ratio
- Left Axis deviation → 72 sensitive, 48 specific, 1.38 positive likelihood, 0.59 negative likelihood ratio
- All this to say → **ST segment deviation was the only ECG finding useful in AMI in the presence of LBBB**
    - **Previous usage of QRS complex not useful**
    - **At least 5 mm ST elevation with negative QRS identified evolving infarct**
    - **ST segment depression in V1, V2 or V3 useful as they should not be present in LBBB alone as these are typically QRS negative**

    - **ST segment of at least 1 mm concordant with QRS or ST depression of at least 1 mm in V1/V2/V3 is very specific for infarct even without any other changes**
- **Low sensitivities similar to sensitivity of ST segment changes in patients with normal conduction (ie no LBBB)**
- **Criticisms →small trial, no differentiation between previous and new LBBB, High interobserver agreement as all readers trained Cardiologists**

Take Home
ST changes best for identifying AMI in the setting of LBBB, QRS not that useful.

7. Wyse DG, Waldo AL, DiMarco JP, Domanski MJ, et al; Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) Investigators. A comparison of rate control and rhythm control in patients with atrial fibrillation. N Engl J Med. 2002 Dec 5;347(23):1825-33. PMID: 12466506

Clinical Question → Rate or Rhythm control in patients with Afib at high risk of stroke or death?

- First study to compare rate control vs. rhythm control in AF
- Multicenter, N = 4060, median follow-up = 3.5 years
- Include → age 65 or younger with likely recurrent AF, AF likely to cause morbidity/mortality for patient, long term AF treatment warranted, other RF for stroke or death
- Exclude → contraindications to AC therapy, ineligible for trials of 2 or more meds regardless of which strategy (rate vs. rhythm)
- Rate → HR < 80 at rest, <110 during activity (6 minute walking)
    - Drugs → Beta Blockers, Calcium Channel Blockers, Digoxin
        - AC with Warfarin (goal INR 2-3)
- Rhythm → agent chosen by physician, cardiovert as necessary for sinus rhythm
    - Drugs → quinidine, procainamide, disopyramide (Class Ia); flecainide, propafenone, morcizine (Class Ic); amiodarone, sotalol, dofetilide (Class III)
        - AC with Warfarin encouraged, but could be stopped if sinus for at least 4, preferably 12 consecutive weeks

Outcomes

- **Primary = 5 year mortality**
    - 25.9% in rate vs. 26.7% in rhythm (Hazard ratio 1.15, 95CI 0.99-1.34, **P = 0.08**)
- Secondary
    - Composite of death, disabling stroke, disabling anoxic brain injury, major bleeding or cardiac arrest → 32.7 % in rate vs. 32.0% in rhythm (**P = 0.33**)
    - Hospitalization → 73.0 % in rate vs. 80.1 % in rhythm (**P < 0.001)**
    - Several other secondary outcomes (ischemic stroke, primary intracerebral hemorrhage, subdural or SAH, disabling anoxic encephalopathy, torsades, PEA/bradycardia, hemorrhage not involving CNS)
        - **Only significant decreases in Torsades, PEA/Bradycardia for rate vs. rhythm control, all other secondary outcomes with P values greater than 0.44**

- Various therapy analyses comparing various agents, chronicity (rate first then rhythm, rhythm first then rate, etc), use of warfarin
  - **>85% use of warfarin in rate group, 70% in rhythm group**
- Subgroup stratification
  - Rhythm control with higher mortality than rate control amongst elderly, patients with CAD, patients without CHF
  - After adjusting for this → **Higher risk of death in rhythm control group than rate control**

Take Home → no survival benefit between rate and rhythm control in nonvalvular AF patients, rhythm trends toward increased mortality

GASTROENTEROLOGY

8. Palamidessi N, Sinert R, Falzon L, Zehtabchi S. Nasogastric aspiration and lavage in emergency department patients with hematochezia or melena without hematemesis. Acad Emerg Med. 2010 Feb;17(2):126-32.

Study Question/Background: Some people advocate for nasogastric aspiration and lavage in patients with melena or hematochezia because they claim it helps localize the bleed, leading to a focused work up. Critics of this practice state GI bleed patients will get upper and lower endoscopy regardless of what nasogastric lavage shows and that inserting a nasogastric tube carries risks including hemorrhage, aspiration, perforation, hemo/pneumothorax. This study aimed to see if nasogastric lavage in patients with either melena or hematochezia WITHOUT hematemesis could locate the bleed to the upper or lower GI tract

Demographics/Design:
- Review study looking at previous studies where researchers performed nasogastric aspiration (no lavage) followed by EGD in patients with melena or hematochezia.
- Exclusion criteria: hematemesis, coffee ground emesis, known or suspected esophageal varices
- Primarily looked at if UGIB was found and whether there were complications from the NG tube

Outcomes:
- Only 3 retrospective studies were found that met the authors criteria
- Authors concluded that nasogastric aspiration with or without lavage had low sensitivity and low negative likelihood ratio for correctly identifying UGIB

Limitations:
- The studies authors looked at had a wide variability in the rate of UGIB (32-74%) likely from the different patient populations (one paper only looked at pts with MIs who then developed melena)
- There was also a wide range of sensitivities among the studies reviewed in nasogastric aspiration for predicting UGIB (42-84%)
- There were different definitions of what a positive endoscopy for UGIB meant
- Only one of the 3 studies was blinded

Take Home: The variance among the 3 studies means the value of this procedure is unclear. The GI literature on this topic also remains controversial. Perhaps whne asked by GI to pursue this, ask them how it will change their management.

INFECTIOUS DISEASE

9. de Almeida JR, Al Khabori M, Guyatt GH, Witterick IJ, et al. Combined corticosteroid and antiviral treatment for Bell palsy: a systematic review and meta-analysis. JAMA. 2009 Sep 2;302(9):985-93. PMID: 19724046

Study Question/Background: Lifetime risk of 1/60 of Bell Palsy in all comers, with 20 to 30 per 100,000 incidence per year. 71% of untreated patients completely recover, 84% with complete or near normal recovery but remained with persistent moderate to severe weakness, facial contracture or synkinesis (involuntary muscle movements accompanying voluntary movement). Poor prognosis with initial severity: 61% of complete pareses recover fully while 94% of incomplete pareses recover fully within 4 months of presentation. This study attempted to estimate the association of corticosteroids and antiviral agents with the risk of unsatisfactory facial recovery in patients with Bell palsy.

Demographics/Design: Meta-analysis utilizing RCTs comparing treatment with either corticosteroids or antiviral agents with control, measuring at least 1 of following outcomes: unsatisfactory facial recovery at greater than or equal to 4 months from diagnosis; unsatisfactory short-term recovery at 6 weeks to less than 4 months; synkinesis and autonomic dysfunction; or adverse effects. 18 trials with 2786 pooled patients met this criteria.

Outcome: Regression analysis showed a synergistic effect with corticosteroids and antiviral agents in combination compared to either alone (0.54 Odds Ratio [OR] for interaction). Corticosteroids alone were associated with a reduced risk of unsatisfactory recovery (Relative Risk [RR] 0.69), a reduced risk of synkinesis and autonomic dysfunction (RR 0.48, Number needed to benefit 1 person = 7) and no increase in adverse effects. Antivirals alone were not associated with a reduced risk of unsatisfactory recovery. Corticosteroids had greater benefit when administered with antiviral drugs, although with borderline significance.

Take Home: Corticosteroids are associated with reduced risk of unsatisfactory recovery in the treatment of Bell palsy. The combination of corticosteroids and antiviral agents may have some additional benefit.

10. de Gans J, van de Beek D; European Dexamethasone in Adulthood Bacterial Meningitis Study Investigators. Dexamethasone in adults with bacterial meningitis. N Engl J Med. 2002 Nov 14;347(20):1549-56. PMID: 12432041

Study Question/Background: Bacterial meningitis, particularly pneumococcal, portends high mortality and morbidity rates in adults. Previous animal studies have shown adjuvant corticosteroid treatment have shown beneficial effects of adding corticosteroids to antibiotic therapy. The study aimed to determine if adjunctive therapy with dexamethasone improved outcomes compared to standard antibiotic therapy alone. Previous studies examining the same question yielded mixed results

Demographics/Design: Multicenter, double blind, placebo controlled RCT in Europe. 301 patients, 157 randomized to dexamethasone arm, 144 randomized to placebo. All patients received appropriate antibiotics at physician's discretion. Intention to treat analysis. Included adults with cloudy CSF, bacteria in CSF on gram stain or CSF WBC > 1000. Mean age 45 years, 57% male, mean duration of symptoms prior to admit of 24 hours. 36% with strep pneumo, 32.5% with Neisseria meningitidis, 22% with negative bacterial culture but other sign of meningitis. Blood and CSF culture taken, broad spectrum antibiotics started then tailored based on CSF gram stain. 77% received amoxicillin, 8% received third-gen cephalosporin, 8% received both. Adjunctive therapy of Dexamethasone 10 mg IV q6h for 4 days in treatment arm. Glasgow outcome scale at 8 weeks used as primary outcome. Death, focal neuro deficits, hearing loss, impaired consciousness, seizures and cardiorespiratory failure all at 8 weeks as secondary outcomes.

Outcomes: 15% of dexamethasone patients had unfavorable Glasgow outcome scales versus 25% in the placebo arm. Death, focal neuro deficits, impairment of consciousness, seizures and cardiorespiratory failure at 8 weeks. were significantly lower in the dexamethasone arm versus placebo arm.

Take home: Grade 1B recommendation for dexamethasone administration in patients in developed world with suspected or proven pneumococcal meningitis. Grade 1B recommendation against steroid administration in developing world with high prevalence of HIV, poor nutrition and delays in clinical presentation.

11. Marik PE, Flemmer M, Harrison W. The risk of catheter-related bloodstream infection with femoral venous catheters as compared to subclavian and internal jugular venous catheters: a systematic review of the literature and meta-analysis. Crit Care Med. 2012 Aug;40(8):2479-85. PMID: 22809915

Study Question/Background: High mortality and morbidity of patients with catheter-related blood stream infections. Guidelines at the time recommended avoidance of femoral venous access to avoid catheter-related blood stream infections. At the time risk of infections from femoral compared to subclavian and internal jugular venous catheterization had not been systematically reviewed. Study aimed to determine the rate of catheter related infections of the femoral vein site compared to subclavian and internal jugular sites. Mixed results in previous RCTs and cohort studies.

Demographics/Design: Systematic review and metanalysis of RCTs and Cohort studies that reported frequency of catheter related blood stream infections, infections per 1000 days of catheter placed, in patients with femoral site venous catheters versus subclavian or internal jugular catheters. 2 RCTs with 1006 catheters and 8 cohort studies with 16, 370 catheters pooled for analysis. 3250 catheters in subclavian vein, 10,958 in internal jugular vein, 3188 in femoral vein. Average catheter-bloodstream infections of 2.5 per 1000 catheter days.

Outcomes: No significant difference in risk between femoral and subclavian sites of catheter related blood stream infections. Lower risk for infection from internal jugular site versus femoral site. **But, two studies determined outliers, with removing these two studies no significant difference in risk of line infection between femoral and internal jugular sites. No significant difference in risk of line infection between subclavian and internal jugular sites. No difference in deep venous thrombosis between femoral site and subclavian and internal jugular sites.** Significant heterogeneity between studies.

Take home: Previous studies showed lower risk of line infections when comparing internal jugular and femoral sites. Recent studies now show no difference in rate of catheter related blood stream infections between the three sites.

12. Weiss EA, Oldham G, Lin M, Foster T, Quinn JV. Water is a safe and effective alternative to sterile normal saline for wound irrigation prior to suturing: a prospective, double-blind, randomised, controlled clinical trial. BMJ Open. 2013 Jan 16;3(1). PMID: 23325896

Study Question: The goal of the study was to determine if there is any significant difference in the infection rates of wounds irrigated with sterile normal saline (SS) versus tap water (TW) before primary wound closure. Traditional teaching recommends sterile saline over tap water as hypotonic water risks cell lysis and impaired wound healing, but studies preceding this had cofounders of not controlling for pressure and volume of irrigation.

Design: This was done at Stanford as a single center, prospective, randomized double blind trial. Wound irrigation solution type was computer randomized. Patients older than 1 who presented to the ED with a soft tissue laceration requiring closure were entered into the study with exclusion criteria including immunocompromised patients, puncture or bite wounds, underlying tendon or bone involvement or wounds older than 9 hours. **The primary outcome measured was the difference in wound infection rates between the two randomized groups.**

Outcomes: Of the 631 remaining patients, 318 were randomized into the TW group and 313 into the SS group. Six patients were lost to follow-up (5 SS, 1 TW). A total of 625 patients were included in the statistical analysis. There were no differences in the demographic and clinical characteristics of the two groups. There were 20 infections 6.4% (95% CI 9.1% to 3.7%) in the SS group compared with 11 infections 3.5% (95% CI 5.5% to 1.5%) in the TW group, a difference of 2.9% (95% CI -0.4% to 5.7%).

Take Home: No difference in the infection rate of wounds irrigated with either TW or SS solution with fewer wound infections in the TW group making it a safe and cost effective alternative.

13. Wong CH, Khin LW, Heng KS, Tan KC, Low CO. The LRINEC (Laboratory Risk Indicator for Necrotizing Fasciitis) score: a tool for distinguishing necrotizing fasciitis from other soft tissue infections. Crit Care Med. 2004 Jul;32(7):1535-41. PMID: 15241098

Study Question: Early debridement is the major determinant of outcome in necrotizing fasciitis, but early recognition has proven clinically difficult. The authors here wanted to develop a scoring system (LRINEC score) to differentiate necrotizing fasciitis from other soft tissue infections using common clinical lab tests performed in the setting of soft tissue infection.

Design: Retrospective observational study of patients divided into a developmental cohort (n = 314) and validation cohort (n = 140) at two teaching tertiary care hospitals with one hundred forty-five patients with necrotizing fasciitis and 309 patients with severe cellulitis or abscesses admitted to the participating hospitals. So, the study design was retrospective, and included 314 patients in a developmental cohort, from whom a scoring system was derived, and another 140 patients in a validation cohort to evaluate the performance of the score.

Outcomes: The developmental cohort consisted of 89 consecutive patients admitted for necrotizing fasciitis. Control patients (n = 225) were randomly selected from patients admitted with severe cellulitis or abscesses during the same period. Total white cell count, hemoglobin, sodium, glucose, serum creatinine, and C-reactive protein were selected as the best predictors based on analysis. The LRINEC score was constructed as including: CRP, WBC, hemoglobin, sodium creatinine, glucose with varying point assignments based on the authors retrospective analysis. The cutoff value for the LRINEC score was 6 points with a positive predictive value of 92.0% and negative predictive value of 96.0%.

Take Home: LRINEC showed good test characteristics, with a positive predictive value of 92% and negative predictive value of 96%. The area under the ROC curve was 0.976 in the validation cohort. The LRINEC score appears to be helpful in diagnosis of necrotizing fasciitis.

14. DECISION RULES FOR THE USE OF RADIOGRAPHY IN ACUTE ANKLE INJURIES Stiell, I.G., et al, JAMA 269(9):1127, March 3, 1993

Study Question: To examine the validity of a set of decision rules to establish if patients need a foot or ankle Xray. At the time of the study, about five million ankle xrays were ordered yearly but only about 15% are positive for fracture.

Design: The authors prospectively examined the validity of their previously formulated decision rules for obtaining ankle or foot x-rays in adults presenting with injuries due to blunt trauma. The decision rules were examined and refined in a total of 1,032 patients in the initial study phase, and the refined decision rules were validated in 453 additional patients. The refined decision rule calls for ankle x-rays only in patients with bone tenderness at the posterior edge or tip of the lateral or medial malleolus, or with inability to bear weight both immediately and in the emergency department (can look at MDCalc for photos).

Outcomes: Prospective application of these refined criteria identified all of the patients with clinically significant ankle fractures (sensitivity, 100%; specificity, 49%). The refined decision rule for midfoot injuries calls for x-rays in patients with bone tenderness at the base of the fifth metatarsal or the navicular, or with inability to bear weight immediately and in the ED. These refined criteria had a 100% sensitivity, and 79% specificity, for clinically significant midfoot fractures on prospective validation. Application of the criteria would have reduced the use of radiography in this study sample by 30%.

Take home: The Ottawa ankle rules are reliable predictors for clinically significant fractures in adults with acute blunt ankle trauma.

NEUROLOGY

15. Hacke W, Kaste M, Bluhmki E, Brozman M, et al; ECASS Investigators. Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke. N Engl J Med. 2008 Sep 25;359(13):1317-29. PMID: 18815396

Study Question/Background: Trial comparing IV alteplase (tPA) in the 3-4.5 hour window after onset of symptoms in an acute ischemic stroke vs. placebo. This is an extraordinarily important topic, as the value added of tPA has been hotly contested for a long time given what a dangerous drug it is. This is also important because this is an expanded window from the initial protocol for tPA in ischemic stroke. Initially, based on the NINDs trial, the window for tPA was < 3 hours, as that was the explanation given for why the NINDs trial protocol was superior to trials that did not support the same findings of benefit in giving tPA. This trial has not been able to be repeated at the < 3 hour window due to claims that it would be unethical to do so. Of note, before this trial, most trials showed increased mortality with tPA above 3 hours. Nonetheless, the study could be done.

**This is an area of literature that has an enormous amount of debate—some background is given in this write up, but it is worth investigating the primary literature further if you have interest.

Demographics/Design: A multinational, manufacturer sponsored study of IV alteplase (tPA) in 821 patients 3-4.5 hours after the onset of symptoms of an acute ischemic stroke. Exclusion criteria included age greater than 80, minor or rapidly improving symptoms, **"severe stroke"**

with NIHSS above 25 or on appropriate imaging, or a history of previous stroke and diabetes. It is important to note that the tPA group had slightly better baseline characteristics with less of a history of stroke and slightly less severe stroke.

Outcome: The primary outcome was patient disability at 1, 7, 30 and 90 days using different widely accepted scales including the modified Rankin and a global multi scale composite measure. The study found a 7.2% absolute benefit among patients receiving tPA in the number who achieved a modified Rankin Scale (mRS) score of 0-1 at 90 days (52.4% for tPA vs 45.2% for placebo) with a similar difference using the global composite measure. Intracranial hemorrhage (ICH) was identified in 27% of the tPA group and in 17.6% of the placebo group, but "symptomatic ICH" was reported for only 2.4% and 0.2% respectively. Three tPA patients did die from ICH, but overall 90-day mortality was statistically equal in both groups.

Take Home: This is a complicated topic and it is important to put this study into the cannon of the rest of the literature. That said, this study concluded that, contrary to previous randomized trials, tPA given 3-4.5 hours after the onset of an acute ischemic stroke resulted in slightly better 90 day clinical outcomes.

16. Hasbun R, Abrahams J, Jekel J, Quagliarello VJ. Computed tomography of the head before lumbar puncture in adults with suspected meningitis. N Engl J Med. 2001 Dec 13;345(24):1727-33. PMID: 11742046

Study Question/Background: A lot of clinicians perform a head CT in adults with suspected meningitis before doing an LP in order to identify possible intracranial masses and avoid brain herniation following LP. This study attempted to investigate macroscopically the validity of this approach as well as the consequences and if certain clinical features at baseline could be used to identify adults with suspected meningitis who were unlikely to have abnormal findings on CT head.

Demographics/Design: Prospective study investigating whether the absence of certain clinical features could identify patients with suspected bacterial meningitis who are low risk for abnormal head CT. During the 4-year study period, baseline information was collected before LP or CT head for 301 ED patients over the age of 16 with suspected meningitis. The Modified National Institutes of Health Stroke Scale was used to identify neurologic abnormalities.

Outcomes: Of the 301 patients with suspected meningitis, 235 (78%) patients underwent head CT scanning before LP; meningitis was diagnosed in 27%. In 56 of these 235 patients (24%), CT results were abnormal and 5% had a mass effect. Clinical features associated with head CT abnormalities included age > 60, immunocompromised, history of CNS disease, seizure within one week of presentation, an abnormal level of cognitive function and focal neurologic abnormalities. **Of the 96 patients with none of these findings who underwent CT scanning only three had an abnormal CT, each of whom underwent LP without herniation.**

Interestingly, when questioned about their reason for getting the CT, the majority of providers cited legal reasons.

Perhaps the most important outcome in this study, though, is that when they got the CT first, it took them two hours longer on average to give antibiotics.

Take home: In absence of the clinical features above, adults with suspected meningitis may be appropriate candidates for immediate LP because they appear to be at low risk of herniation. **If you are going to do the CT first, give the antibiotics now.**

17. Hypothermia After Cardiac Arrest Study Group. Mild Therapeutic Hypothermia to Improve the Neurologic Outcome after Cardiac Arrest. N Engl J Med. 2002 Feb 21;346(8):549-56. PMID: 11856793

Study Question: Does cooling (mild/moderate hypothermia) help mitigate brain damage and reperfusion injury following cardiac arrest? Before this, there was a little bit of data suggesting that after animal models go into full arrest and stop perfusing, they generate free radicals. Thus, in theory, rapid cooling may help to reduce these reperfusion injuries and improve outcomes.

Demographics/Design: Multinational European study with 275 patients who had return of circulation (ROSC) within 60 minutes after initiation of resuscitation from Vfib or non-perfusing ventricular tachycardia, with persistent absence of response to verbal commands. They were then randomized to either get hypothermic or normothermic post resuscitation care with the hypothermic patients cooled via blanket to a target bladder temperature of 32-34 C for 24 hours.

Outcomes: The main outcome was a favorable neurologic outcome (less than severe disability, assessed by blinded monitors) at six months. This was achieved in 55% of the hypothermia group and 39% of the controls, indicating a number needed to treat of 6 with hypothermia to prevent one unfavorable neurologic outcome. Also, the six-month mortality rates in the two groups were 41% (hypothermia group) and 55% for the control.

Secondary data included that the target temperature could not be achieved in 14% of the hypothermia group. The median interval from ROSC to the initiation of cooling was 105 minutes and the interval from ROSC to attaining target temp was eight hours.

Take home: Following full arrest after resuscitation from ventricular fibrillation, moderate hypothermia for 24 was associated with improved neurologic outcomes and reduced mortality. Early concerns included that this was a small study with little supporting literature at the time, but was very promising nonetheless.

18. Johnston SC, Rothwell PM, Nguyen-Huynh MN, Giles MF, et al. Validation and refinement of scores to predict very early stroke risk after transient ischaemic attack. Lancet. 2007;369(9558):283-92. PMID: 17258668

Background/Study Question: This paper was done by the same authors who developed previous scores (ABCD and California) to attempt to predict stroke risk following a TIA. Previously, the California score and the ABCD score were developed to assess the risk of stroke after TIA, but address the 90 day and 7-day risk (respectively), despite the fact that the risk of stroke following a TIA is highest in the first two days. This study attempted to use the same database as the ABCD score to **validate a unified score optimized for prediction of 2-day stroke risk following TIA to inform ED management.**

Methods: The two scores that previously existed (California and ABCD) were validated in four independent groups of patients diagnosed with TIA in the ED and clinics in defined populations in the US and UK. These two groups were then used to derive a new unified score based on logistic regression. The new score that ended up being derived and validated in this study (basically ABCD with addition of diabetes was):

- Age ≥ 60 (+1)
- BP>140/90 (+1)
- Clinical features of TIA with unilateral weakness (+2) or speech disturbance without weakness (+1)
- Duration of symptoms 10-50 mins (+1) or ≥ 60 minutes (+2)
- History of diabetes (+1)

Outcomes: Overall, of 4,809 TIA patients, 9.2% developed a stroke within 90 days, 5.5% within seven days and 3.9% within two days. The ABCD2 score was developed with the measures above. This score had a c statistic of .62-.83 and classified 21% of patients at high risk of developing a stroke within two days (with a score of 6-7 and an 8.1% stroke risk). The authors conclude that this score, ABCD(2), validated well (c statistics 0.62-0.83); overall, 1012 (21%) of patients were classified as high risk (score 6-7, 8.1% 2-day risk), 2169 (45%) as moderate risk (score 4-5, 4.1%), and 1628 (34%) as low risk (score 0-3, 1.0%).

Take Homes: The authors conclude that they validated the existing prognostic scores for stroke risk after TIA and developed **a new, unified score (ABCD(2)) that will be most predictive and useful for two day risk of stroke in TIA patients. That said,** it is hard to conclude how useful this truly is as a risk stratification tool since the risk is never 0% and it's also never really that high. At the highest risk, it is 8% and the moderate risk is 4%, so that raises a question of if this is really powerful enough to use as a tool to make clinical decisions—even the lowest risk is 1%. In reality, for a lot of these patients the management still consists of quickly ruling out reversible causes and doing the entire work up (**cite EMA).**

19. Kattah JC, Talkad AV, Wang DZ, Hsieh YH, Newman-Toker DE. HINTS to diagnose stroke in the acute vestibular syndrome: three-step bedside oculomotor examination more sensitive than early MRI diffusion-weighted imaging. Stroke. 2009 Nov;40(11):3504-10. PMID: 19762709

Clinical Question – Are there reliable bedside assessments to differentiate peripheral vertigo from central vertigo in patients presenting with acute vestibular syndrome (AVS)?

- Frequent misdiagnosis of central stroke vs. peripheral neuropathy in ED
- 2.6 million US ED visits for dizziness → 150K diagnosed with peripheral vestibulopathy
    - **Studies suggest up to 25% of acute vestibular syndrome presentations represent posterior circulation infarct**
        - **Small observational studies though**
- Oculomotor FNDs may identify strokes in AVS, but lacking prospective data
- CT bad at finding posterior stroke, MRI a pain in the ass depending where you work
- Why not typical neuro exam (ataxia, dysarthria)?
    - Less than 50% of AVS presentation have limb ataxia, long-tract signs or obvious cerebellar signs.
- Combine 3 validated exams that help with central vs. peripheral
    - Horizontal Head Impulse → tests VOR reflex
        - Unilateral saccade = peripheral
        - No unilateral saccade = equivocal
    - Nystagmus → changes with eccentric gaze
        - Horizontal, unidirection = peripheral
        - Vertical, Torsional or bidirectional = central
    - Skew Deviation → ocular misalignment from imbalance of input from R vs. L vestibules
        - Alternate eye cover testing
        - Positive for central if vertical skew deviation after uncovering

Design/Demographics/Exclude

- Single center, prospective, cross-sectional, N = 101, urban academic stroke center
- **Include** patients with acute vestibular syndrome (acute vertigo, N/V or gait changes) AND at least 1 vascular risk factor: smoking, HTN, DM, HLD, Afib, Eclampsia, Hypercoag, Recent cervical trauma or prior stroke/MI
- **Exclude** if history of recurrent vertigo
- 65% Men, Mean Age 62 yo, 70% with greater than 1 RF
- 25 with peripheral vertigo, 76 with central cause (69 strokes)
- HINTs exam performed by single neuro-opthomologists: Head Impulse, Nystagmus, Test of Skew
    - Followed up with imaging (98 MRI)
- **Benign HINTS** = abnormal Head Impulse, unidirectional horizontal Nystagmus, Test of Skew Negatiive
- **Dangerous HINTS** = normal/equivocal Head Impulse, direction changing Nystagmus (or vertical/rotary), present or untestable skew deviation

Outcomes/Results

Primary Outcome → Dangerous HINTS vs. MRI Findings (Gold Standard)

- 100% Sensitive, 96% Sensitive for stroke vs. MRI

- Criticisms
    - Examiner blind to imaging results but nothing else
    - Population with high rates of vascular risk factor, gen pop coming into ED likely closer to 1/3 of this

Take Home – HINTS exam is an easy 3-step bedside oculomotor examination that is useful for differentiating peripheral causes of vertigo from central causes. The study utilized a small sample, with heavy skew towards vascular risk factors. The HINTS exams were performed by neuro-ophthalmologists who were blind only to imaging results having full history and physical. The HINTS exam seems to be useful, possibly with staying power, but will require more research to gain favor amongst ED providers.

20. The National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. Tissue plasminogen activator for acute ischemic stroke. N Engl J Med. 1995 Dec 14;333(24):1581-7. PMID: 7477192

Clinical Question – Does tPA reduce morbidity and mortality in patients with ischemic stroke?

- Previous studies suggesting tPA beneficial within 3 hours of stroke onset.

Design/Demographics/Exclude

- Double blind, RCT, placebo-control
- Part 1 (n=291) tested if tPA had clinical activity via improvement of 4 points on NIHSS or resolution of FND within 24 hours of onset
- Part 2 (n = 333) assessed clinical outcomes at 3 months including GCS, modified Rankin, NIHSS, Barthel index
- Include ischemic stroke with clearly defined LKN, deficit measurable on NIHSS, baseline CTH with no signs of ICH
- Exclude
    - Brain → stroke, head trauma, ICH, SAH, seizure with stroke, improving symptoms
    - Other → major surgery within 2 weeks, elevated BP, recent GI/GU bleed, on AC, thrombocytopenia, hypo/hyperglycemia
- 41% female, 67 yo mean

Outcomes/Results

- **Primary** → Improvement by > 4 on NIHSS or complete resolution in 24 hours (*tpa vs. placebo)*
    - 47% tPA group vs. 39% placebo (P=0.21)
    - <u>Proportion after stroke with favorable outcomes at 90 days</u>
        - Barthel index: 50% vs. 38% (OR 1.6; 95% CI 1.1-2.5, P=0.026)
        - Modified Rankin scale: 39% vs. 26% (OR 1.7; 95% CI 1.1-2.6; P=0.019)
        - Glasgow outcome scale: 44% vs. 32% (OR 1.6; 95% CI 1.1-2.5; P=0.025)
        - NIHSS: 31% vs. 20% (OR 1.7; 95% CI 1.0-2.8; P=0.033)
    - **Major Adverse effects** → 10 fold incidence of ICH within 36 hours of stroke treatment in tPA group, 7 fold incidence of ICH within 3 months of stroke treatment in tPA group.
        - However similar moralities amongst ICH group and non-ICH group

Take Home → Significant improvement in NIHSS scores with tPA administration within 3 hours of stroke, but this does not provide a survival benefit as morality is similar amongst tPA and non-tPA. Significant increase in ICH in tPA patients, but no change in morality surprisingly.

21. Nielsen N, Wetterslev J, Cronberg T, Erlinge D, et al; TTM Trial Investigators. Targeted temperature management at 33°C versus 36°C after cardiac arrest. N Engl J Med. 2013 Dec 5;369(23):2197-206. PMID: 24237006

Clinical Question → Does hypothermia to a goal of 33 degrees Celsius reduce all-cause mortality when compared to a goal of 36 degrees Celsius for patients with out-of-hospital cardiac arrest?

- Previous trials in 2002 demonstrated survival and neurologic benefit with targeted temperature management, goal was 32-34 C in patients with out-of-hospital VF or pulseless VT.

Design/Demographics/Exclude

N = 939 with out of hospital arrest, 473 to 33 C arm; 466 to 36 C arm, ICUs in Europe and Australia

- **Include :** 18+ yo, out of hospital arrest of presumed cardiac origin with persistent ROSC, unconscious with GCS < 8 after sustained ROSC
- **Exclude**: Unwitnessed arrest with asystole as the initial rhythm, admit temp < 30 C, suspected or confirmed acute intracranial hemorrhage or stroke, obvious or suspected pregnancy, known bleeding diathesis,

83 % Male, mean age 64, 31% PMH of ischemic heart disease

Randomized to one of two body temperatures achieved via chilled fluids, ice packs, intravascular and/or surface temperature management devices for 36 hours. Both arms rewarmed to 37 C after 28 hours, in intervals of 0.5 C per hour.

Outcomes/Results

Primary Outcome → All cause mortality at end of trial (33 C vs. 36 C): 50% vs. 48% (P=0.51)

- **Secondary Outcomes**
  - **No significant difference in cerebral performance category score (scale of 3-5, 3 = severe disability, 4 = coma, 5 = brain death)**
  - **No significant difference in Modified Ranking score 4 to 6 (4 = moderate disability, 5 = severe disability, 6 = death)**
  - **No significant difference in all cause mortality at 180 days**
  - **No differences in subgroup when analyzed by age < 65 vs age >65, gender, time from arrest to ROSC, initial rhythm, shock on presentation**

Take Home

Target Temperature Management to 33 C was not associated with a reduction in all-cause mortality of improved neurologic outcomes compared to 36 C in patients with out-of-hospital cardiac arrest. Previous studies showing lower temperatures associated with decreased CO,

infection, need for sedation; therefore, less likely to have adverse effects, but same outcomes at 36 C vs. 33 C.

22. Perry JJ, Stiell IG, Sivilotti ML, Bullard MJ, et al. High risk clinical characteristics for subarachnoid haemorrhage in patients with acute headache: prospective cohort study. BMJ. 2010 Oct 28;341:c5204. PMID: 21030443

Clinical Question → Are there identifiable high risk clinical characteristics for SAH in neurologically intact patients presenting with headache?

- Pervasive problem, **ED doc's bane → is this HA normal or is this the SAH HA?**
- HA 2% of all ED visits, **SAH accounts for 1-3% of these Has**
- Classic teaching → sudden onset, severe with maximum at onset
    - Much harder to ID with FND, coma
- Missing this = **catastrophic morbidity or mortality**
- Better outcomes with early treatment, CT, LP
- Assessed clinical characteristics of neuro intact patients in EDs whom had a HA peaking within an hour → for variables predictive of SAH that are reliable between physicians

Design/Demographics/Exclude

- Prospective multicenter cohort at 6 teaching hospitals in Canada
- **Include:** alert (GCS = 15), >= 16 yo who presented to ED with CC of non-traumatic HA peaking within 1 hour or syncope associated with HA.
- **Exclude**: Hx of 3 or more recurrent HA of same character and intensity as presenting HA over period of 6 months, those referred with known SAH by CT or LP, return for HA after eval for SAH (CT/LP), papilledema, new FND, previous aneurysm or SAH, brain neoplasm or hydrocephalus
- Assessment performed by attending ED docs or ED residents supervised by ED attending
    - **Data forms to identify the presence or absence of 33 clinical findings in consecutive eligible patients**
        - **2nd physician asked to fill out same for same patient if available**
    - **Follow-up at 1 month and 6 months**
- **SAH = blood on CT head, xanthochromic in CSF or RBCs > 5 in final CSF sample, with aneurysm or AVM evident on CTA head**
    - **Established with consensus by 5 ed docs and 1 neurosurgeon**
    - **N = 1999, 130 with SAH**
        - **60.4 % female, Mean age 43.4 (SD 17.1), 18.7% HA woke from sleep, 78.5 % "Worse HA of life", 33.5 % with neck stiffness/pain, 5.3% LOC with 63.9% LOC witnessed**
    - **Procedures and Dispo**
        - 80.3 % got CTH, 45.3% got LP, 82.9% got CTH or LP, 42.7% got both, 10.2 % admitted to hospital, 12 (0.6%) Died
    - **Final Diagnosis**
        - 54.1 % Benign HA, 27.3 % Migraine, **6.5 % SAH**, 4.3% Viral illness, 1.8% TIA

Outcomes/Results

- Three Rules Tested

    - 1) Age >40, neck pain or stiffness, witnessed LOC, onset with exertion
    - 2) Arrive by EMS, Age > 45, at least 1 episode of emesis, DBP > 100
    - 3) Arrive by EMS, SBP > 160, neck pain or stiffness, Age 45-55
- **All the above rules with 100% sensitivity**
- **Specificity ranged from 28.4% to 39.8%**
- Utilized recursive partitioning algorithm for above **rule 1 = Ottawa SAH Rule** (arrival by ambulance validity questionable)
    - Start with N of 1999, 130 with SAH
    - ↓
    - Age > 40 → yes: n=1098, 117 with SAH
    - No ? ↓
    - Neck Pain? → yes: n = 278, 11 with SAH
    - No ? ↓
    - Witnessed LOC? → yes: n = 15, 1 with SAH
    - No ? ↓
    - Exertion → yes: n = 78, 1 with SAH
    - ↓
    - No still? → n = 530, no SAH in this group
- Criticism and Limitations
    - HA timing up to 1 hour could dilute HA sample
    - Lack of standard definition of positive SAH at the time
    - 1/3 of eligible patients may not have been enrolled
        - Patients coded as missed if they could not meet eligibility
            - Poor recording meant difficulty in how rapidly HA peaked
    - Rules need to be validated
        - Validated in 2013 by same authors (Perry et. Al September 2013, JAMA)
        - **On MD Calc with First author Perry providing commentary and caveats: Ottawa SAH Rule**
    - Rule misinterpreted by Physicians 4% of time → none lead to not working up SAH, more overkill in labs/diagnostics for these 4% misses

Take Home → Arrival by EMS, age >= 40, neck stiffness or pain, onset with exertion, vomiting, witness LOC and elevated SBP strongly and reliably associated with SAH, useful for identifying high risk patients. Presence of one or more of these findings in non-traumatic headache reaching maximum intensity for 1 hour and unlike previous headaches should set off SAH red-flag. Use MD Calc Ottawa SAH rule with clinical gestalt in mind.

PEDIATRICS

23. Bjornson CL, Klassen TP, Williamson J, Brant R, et al; Pediatric Emergency Research Canada Network. A randomized trial of a single dose of oral dexamethasone for mild croup. N Engl J Med. 2004 Sep 23;351(13):1306-13

Study Question/Background: Prior to this study, steroids were an established treatment for severe croup but studies looking at steroids for mild croup were weak, even though most children presenting with croup have mild symptoms. These children were routinely sent home without treatment and did fine but the authors of this study wanted to see if steroids could be of some benefit to these children.

Demographics/Design:

- Multicenter, double blind, placebo controlled, RCT across 4 pediatric EDs
- Using Westley Croup Score, 720 children were characterized as having mild croup→these children were then randomized to 1 dose of dexamethasone or placebo

Outcomes:

- Primary outcome measured: return to PCP in 7 days for croup → 15.3% of placebo group vs 7.3% dex group (statistically significant)
- Secondary outcome measured: persistent symptoms at days 1, 2, and 3 post treatment→1st 24 hours post-treatment, placebo group had more severe symptoms with an odds ratio of 3.2 but differences between both groups disappeared by day 3 when over 75% of both groups had resolution of symptoms
- Other outcomes included less sleep lost by children in the dex group compared to placebo and less parental stress in the dex group compared to placebo

Limitations:

- Symptom severity on days 1, 2, 3, 7, and 21 were reported by parents over the phone which researchers used to calculate Westley severity score. This is problematic as self-reporting is unreliable and parents had to be able to identify things such as stridor
- The study allowed attendings to use additional treatments such as mist, antibiotics, epi, beta agonists because the researchers posited that these would only alter symptoms for 2 hours and not interfere with the dexamethasone. However, this confounds the study with other variables.

Take Home: While most children with mild croup symptoms will improve on their own, a 1 time dose of dexamethasone can lead to decreased symptoms in the first 24 hours, less bounce backs, more sleep for the child, and less stress for the parents.

24. Holmes JF, Mao A, Awasthi S, McGahan JP, et al. Validation of a prediction rule for the identification of children with intra-abdominal injuries after blunt torso trauma. Ann Emerg Med. 2009 Oct;54(4):528-33.

Study Question/Background: Trauma is a leading cause of morbidity and mortality in children over 1 year of age, with abdominal trauma being the 3rd leading cause of death. However, we do not want to CT every child that comes in with trauma given the increased risk of radiation to this age group. Prior to this study, there was no externally validated decision making tool on which children presenting with abdominal trauma needed CT. Researchers wanted to develop a

prediction rule using 6 high risk variables on physical exam and initial lab tests. These included: low age adjusted systolic bp, abdominal pain, femur fracture, AST >200 and ALT >125, hematuria > 5 RBCs, and HCT <30%. The study authors basically took an already internally validated tool which identified children in whom a CT would not be of benefit and aimed to externally validate it.

Demographics/Design:

- Prospective, observational, cohort
- Study looked at children <18 years old, presenting with blunt abdominal trauma and underwent a definitive diagnostic test (CT, DPL, laparoscopy, laparotomy) looking for intraabdominal injury
- Children without any of the 6 risk factors were deemed low risk and that CT would be of no benefit

Outcomes:

- Of 1,324 cases of children presenting with intraabdominal trauma, 1,119 (85%) met the variables needed for the prediction tool to be applied and made up the sample size
- 754 children met criteria using the prediction tool to warrant further testing, 365 tested negative
- Of the 365 testing negative for the tool, 8 were later found to have intraabdominal injury
- Authors concluded the tool had a 94.9% sensitivity and applying it could reduce abdominal CTs by a third

Limitations:

- FAST exam was not included in this study as either part of the prediction rule or part of definitive testing even though use of FAST for trauma is widespread and spares children radiation while identifying intraabdominal trauma. This is likely because in 2009, FAST for trauma was not the standard of care.
- Authors identified other variables not included in their prediction tool that are even higher risk if present, thus adding them into the prediction tool would further increase the sensitivity
- Study was only done at 1 urban trauma center so unclear if it can be applied to other populations

Take Home: In settings where FAST is not available, this article may provide a clinical prediction tool for which children would benefit from a CT scan when presenting with abdominal trauma. It is difficult to say however as it was only conducted at one center so it needs more external validity prior to widespread use.

25. *Kocher MS, Mandiga R, Zurakowski D, Barnewolt C, Kasser JR. Validation of a clinical prediction rule for the differentiation between septic arthritis and transient synovitis of the hip in children. J Bone Joint Surg Am. 2004 Aug;86-A(8):1629-35.*

Study Question/Background: Sometimes it can be difficult to distinguish between septic and transient synovitis as they present similarly. Delayed diagnosis of septic joint leads to poor

outcomes. This study took a previous internally validated clinical prediction tool for septic arthritis that looked at 4 parameters (fever, ESR, WBC, non-weight bearing) and tried to apply it to a new patient population.

Demographics/Design:

- Prospective study at 1 major children's hospital
- Looked at 213 children presenting with hip pain
- 59 children of the 213 were excluded using the following criteria: immune compromised, renal failure, neonatal sepsis, post op infection, rheumatologic disease, Legg-Calves-Perth, joint fluid insufficiency

Outcomes:

- Using WBC and blood cultures, 24 patients were diagnosed with true septic arthritis (positive cultures, fluid WBC >50k) ; 27 with presumed (negative blood cultures), 103 with transient synovitis (negative fluid WBC and blood cultures)
- The original study from which the tool was derived had an ROC of 0.96, this study had an ROC 0.86 (side note: ROC is receiver operating characteristic and is a way of measuring diagnostic accuracy of a test using an ROC curve)
- Authors concluded that although the ROC was lower aka less accurate than in the original population, the tool still had good diagnostic performance

Limitations:

- This study was had a small size and was conducted at 1 center
- They used 4 independent factors but did not look at if any of these factors in combination i.e. fever and elevated WBC led to increased likelihood of septic joint which may have increased the predictive power and ROC of this study.

Take Home: While this tool was applied to a small population at one center, it may be helpful in identifying early septic arthritis compared to transient synovitis.

26. Kuppermann N, Holmes JF, Dayan PS, Hoyle JD Jr, et al; Pediatric Emergency Care Applied Research Network (PECARN). Identification of children at very low risk of clinically-important brain injuries after head trauma: a prospective cohort study. Lancet. 2009 Oct 3;374(9696):1160-70. PMID: 19758692

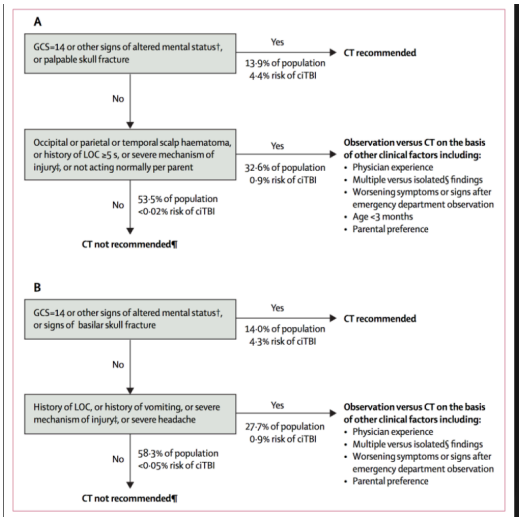
Study Question: The study attempts to validate decision rules to guide CT imaging following head trauma to identify children at very low risk of clinically important brain injury where CT can be avoided.

Methods: Prospective multicenter study with 42,412 patients under 18 years old with minor blunt head trauma and a GCS of 14-15. The goal was to validate two different decision criteria in order to predict traumatic brain injury (which they actually don't define clearly): one for children younger than two (10,718 patients) and one for older children.

Outcomes: Head CT was performed in 1/3 of children and identified a “clinically important head injury” in .9% of patients. Surgery was performed in .14% of the patients. The independent predictors of clinically important injury in children over two were: abnormal mental status, vomiting, any loss of consciousness, severe mechanism of injury, signs of basilar skull fracture and severe injury. With the assumption that no injuries were missed in the kids who never even got a CT (a reasonable assumption) the sensitivity and specificity of these predictors in this age group were 97% and 59% respectively.

Predictors in children below two were "not acting normally" according to parents, loss of consciousness for more than 5 seconds, severe mechanism of injury, non-frontal scalp hematoma and a palpable skull fracture. Assuming no missed injuries, the sensitivity and specificity of this rule were about 99% and 54%, respectively. Nearly 60% of children in the series had none of the aforementioned predictors, and the predictor variables identified all children undergoing neurosurgery.

Take home: Famous “PECARN” study where authors conclude that children with none of the predictors listed above seem to be at very low risk for clinically important head injury. ** Highly recommend looking this up on MDCALC when needed, but the algorithm is below:



One concern with this study is that this is a rather large amount of head CTs with very few findings, particularly given that no definition for TBI in this study was offered. It is important to keep in mind that essentially 1/1,000 head CTs here had a finding that changed the management of the patient even though the sensitivity of the test was close to 100% (although dipped all the way to 85% on confidence intervals). It is highly plausible that a similarly small percentage of kids had some type of negative consequence from their head CTs (cancer, etc) making the marginal benefits of CT here very small. Also, these decision tools are difficult to interpret even with MDCALC. It can be very hard for even an experienced physician to define

elements like “LOC for 5 secs or more,” “a non-severe mechanism,” “a severe headache” and “if the parent thinks the child is OK.”

While this study is important and the sensitivities these tests offer are spectacular, it seems prudent to really take a step back and determine if this algorithm is adding a marginal benefit in finding occult head trauma that otherwise would have been missed? This study, though, is still spectacularly useful, particularly for medical students and residents unfamiliar with caring for kids to establish red flags to look out for.

27. Pieretti-Vanmarcke R, Velmahos GC, Nance ML, Islam S, et al. Clinical clearance of the cervical spine in blunt trauma patients younger than 3 years: a multi-center study of the american association for the surgery of trauma. J Trauma. 2009 Sep;67(3):543-9; discussion 549-50. PMID: 19741398

Clinical Question: Similar to the article above, these authors wanted to see if simple clinical criteria can be used to safely rule out CSI in patients younger than 3 years. This is (again) relevant as working up cervical spine clearance in a young child is problematic as one should be weary of radiation exposure and related complications.

Methods: The authors reviewed trauma registries from 22 trauma centers for a ten-year period to identify blunt trauma patients younger than 3 in order to search for cervical spine injury as the primary outcome (12,537 patients). The authors then used millions of variables in a multivariate analysis to identify independent predictors of cervical spine injury and each’s magnitude of effect.

Outcomes: The study found a c-spine injury in 83 children (.66%). For every one child that a CSI was found in, a CT was performed on 40 patients without a C-spine injury. Based on their massive multivariate analysis, the authors developed an instrument that assigned 3 points to GCS less than 14, 2 points each to GCS[eye] of 1 or involvement in a MVA, and 1 point to age 2-3 years. The prevalence of CSI was .07% in children with a score of 0-1, compared to 21% among those with a score of 7 or 8. If you take this cut off, the instrument had a sensitivity and specificity for CSI of 93% and 70% respectively and the authors calculate a negative predictive value of 99.9%.

Take Home: The biggest take home point seems to be that c-spine fracture was extremely uncommon in children under 3 in this cohort. The authors state that this prediction instrument should be used to identify a subgroup of children who may not need imaging.

That said, major concerns with this study include that with a sensitivity of 93%, you would miss 1/6 with CSI. Also, there was no follow up after imaging review in this study, so we are not totally aware of the number of CSI the study truly missed. As with the study above, this is a lot of kids getting CTs to get one positive finding. The main take away seems to be that c-spine injury is very rare. The authors spend a lot of time discussing the 99.9% negative predictive

value of this study, but it was 99% before they even did anything because such a small percentage of the cohort even had the disease.

28. Spiro DM, Tay KY, Arnold DH, Dziura JD, et al. Wait-and-see prescription for the treatment of acute otitis media: a randomized controlled trial. JAMA. 2006 Sep 13;296(10):1235-41. PMID: 16968847

Clinical question: Acute otitis media (AOM) is the most common diagnosis for which children get antibiotics. Some previous trails attempted to evaluate the utility of these antibiotics, but were found to be methodologically flawed and none took place in the ED. This study evaluated if treating AOM with a standard prescription was any better than using a "wait and see approach" (WASP) where parents were instructed to wait a few days before filling the prescription to see if symptoms improved. Thus, the goal was to see if a WASP approach could reduce antibiotic use, decreasing the side adverse outcomes related to antibiotic use.

Methods: 283 immunocompetent and nontoxic-appearing children aged six months to twelve years with a diagnosis of AOM were randomized at the Yale ED to immediate prescription of an antibiotic or to a wait- and-see strategy (instructions to fill the prescription if the child did not improve, or worsened, over the following three days). All antibiotic prescriptions expired within three days after the visit. Discharge instructions also included the use of ibuprofen for pain and fever, and analgesic drops. The study **excluded** children with myringotomy tubes or a perforated tympanic membrane, and those with uncertain access to medical care. Of note, **the WASP** approach did not require the parents to return back to the ED, but gave the parents the prescription and just asked them to wait to fill it.

Outcomes:: The antibiotic prescription was filled for 38% of the wait-and-see group compared with 87% of the standard care group with no significant difference in the outcomes of fever, otalgia, or follow up medical visits for the same problem 30-40 days after presentation.

Among children with otalgia at baseline, there was a statistically significant decrease (of uncertain clinical significance) in the duration of otalgia in the immediate antibiotic group (2.0 vs. 2.4 days). Diarrhea was more frequent in the immediate antibiotic group (23% vs. 8%).

Take Home: Important study further confirming that even though only 40% of the WASP group filled their antibiotic prescription for AOM vs. 90% of the immediate group, the adverse outcomes of AOM (otalgia, fever, etc.) were the exact same in both groups. We can avoid giving antibiotics to a lot of these kids and avoid the adverse effects of these antibiotics.

PULMONOLOGY

29. The Acute Respiratory Distress Syndrome Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. N Engl J Med. 2000 May 4;342(18):1301-8. PMID: 10793162

Study Question/Background: Prior to this study, pts with lung injury or ARDS would get higher tidal volumes compared to other pts to avoid acidosis and achieve normal pH and pCO2. The researchers thought these high tidal volumes may worsen lung injury by stretching the lungs and causing release of inflammatory mediators. This study aimed to find out if lower tidal volumes in ARDS pts resulted in better outcomes.

Demographics/Design:

- Large multicenter (10 different hospitals) randomized controlled trial
- 861 patients with acute lung injury or ARDS and no other major medical problems were randomized to either traditional tidal volumes of 12 cc/kg or low tidal volumes of 6cc/kg

Outcomes:

- Primary outcome measured: Death before a patient was discharged home →31% in low tidal volume group vs 39.8% in the large tidal volume group→ this caused researchers to stop the study early
- Second outcome measured: Number of days without ventilator use in the first 28 days after randomization → 12 days off the ventilator in the low tidal volume group vs 10 days in the high tidal volume group

Limitations:

- Researchers used respiratory rates and bicarb to correct acidosis in the low tidal volume group which confounds whether their results are from lower tidal volumes or avoidance of acidosis
- The researchers basically excluded anyone with medical problems other than ARDS which probably meant they had improved outcomes to begin with. Additionally, people with more medical problems are more likely to have complications like ARDS so unclear if this study applies to most patients we see.

Take Home: In patients with ARDS, lower tidal volumes along with avoidance of acidosis may improve mortality and reduce the number of days intubated.

30. Bauer TT, Ewig S, Marre R, Suttorp N, Welte T; CAPNETZ Study Group. CRB-65 predicts death from community-acquired pneumonia. J Intern Med. 2006 Jul;260(1):93-101. PMID: 16789984

Study Question/Background: CURB score was already a validated tool in predicting CAP severity. This study aimed to validate CURB, CRB, CRB-65 as inpatient and outpatient CAP severity markers.

Demographics/Design:

- Large multicenter prospective study across 670 clinics and 10 hospitals

- 1343 pts evaluated using CRUB and 1967 using CRB and CRB-65

Outcomes:
- Overall 30 day mortality was 4.3% and all 3 scores were comparable in predicting mortality
- CRB misclassified more of the mortality patients as low risk
- CURB was harder to compute in some cases due to lack of BUN in dataset

Limitations:
- Selection bias from physicians interested in joining the study
- Study conducted in Germany may not be applicable to the US population

Take Home: CURB and CRB-65 are good tools for predicting pneumonia severity and mortality. CRB-65 may be easier to use in practice as it does not require a BUN

31. Brochard L, Mancebo J, Wysocki M, Lofaso F, et al. Noninvasive ventilation for acute exacerbations of chronic obstructive pulmonary disease. N Engl J Med. 1995 Sep 28;333(13):817-22. PMID: 7651472

Study Question/Background: While non-invasive ventilation was starting to be used to treat COPD, prior to this study, it was unclear if non-invasive ventilation actually lowered the risk of intubation, length of hospital stay, or mortality for these patients.

Demographics/Design:
- Multicenter, random, prospective study
- 85 pts across 5 centers who came in with a COPD exacerbation form known COPD or based on xrays, exam, and history
- Pts were randomized to either 5L NC (42 pts) vs non-invasive ventilation (43 pts) for at least 6 hours a day
- Researchers established pre-determined criteria for intubation for both groups

Outcomes:
- 31 pts (73.8%) in standard group vs 11 (25.6%)in non-invasive group required intubation
- Hospital stay was significantly longer in the standard group
- In hospital mortality was higher in the standard group (28.5%) vs the non-invasive group (9%)

Limitations:
- Small sample size
- Most of the intubations happened in the first 12 hours indicating that pts may have been too unstable and should have been excluded. However, even if these pts had been excluded, it likely wouldn't have affected the results

Take home: Use non-invasive ventilation for pts with COPD exacerbation to lower risk of intubation, length of stay, and mortality.

32. Konstantinides S, Geibel A, Heusel G, Heinrich F, Kasper W; Management Strategies and Prognosis of Pulmonary Embolism-3 Trial Investigators. Heparin plus alteplase compared with heparin alone in patients with submassive pulmonary embolism. N Engl J Med. 2002 Oct 10;347(15):1143-50. PMID: 12374874

Study Question: This study investigated to see if using thrombolytic agents in treating hemodynamically stable patients with acute submissive pulmonary embolism improved outcomes. Thrombolytic therapy is used for PE in patients with hemodynamic instability or cardiogenic shock, but had not been investigated in patients with acute submassive PE.

Design: Randomized, placebo-controlled trial to compare the effects of treatment with heparin plus alteplase with the effects of heparin plus placebo on the outcome of patients with acute submassive pulmonary embolism. The study focused on patients with pulmonary hypertension, right ventricular dysfunction, or both, **but excluded those with hemodynamic instability.**

Outcomes: Patients were evaluated at the end of their hospital stay or on day 30 after randomization, whichever occurred first. The primary end point was in-hospital death or clinical deterioration that required an escalation of treatment after the infusion of alteplase or placebo was terminated (escalation therapy= need for catecholamines, rescue thrombolysis, intubation, CPR or emergency surgical embolectomy or thrombus fragmentation)

The study had 256 patients enrolled—118 were assigned to get heparin plus alteplase and 138 received heparin plus the placebo. The incidence of the primary end point discussed above was significantly higher in the heparin plus placebo group vs. the heparin plus alteplase group (p=.0006) and the probability of 30 day event free survival was higher in the heparin plus alteplase group. This was mostly due to the increase in treatment escalation (25% vs. 10%) in the heparin plus placebo group because there was no mortality differences between the two groups. Within the treatment escalation group, the majority of the difference was due to the need for rescue thrombolysis (7.6% vs 23.2%).

Take home: Even though there were no mortality differences, when given in conjunction with heparin, alteplase can improve the clinical course of stable patients who have acute sub-massive pulmonary embolism and can prevent clinical deterioration requiring the escalation of treatment during the hospital stay. Particularly, the take away is that giving thrombolysis for a sub-massive PE decreased the need for rescue thrombolysis later but did not affect mortality or adverse events.

33. Kline JA, Courtney DM, Kabrhel C, Moore CL, et al. Prospective multicenter evaluation of the pulmonary embolism rule-out criteria. J Thromb Haemost. 2008 May;6(5):772-80. PMID: 18318689

Clinical Question: Pulmonary embolism (PE) is the second most common cause of sudden unexpected death in outpatients. It has been reported that the diagnosis of PE is often missed by physicians, but also that there is a high rate of testing for PE in patients at very low risk. This study evaluated the PERC rule at identifying patients who are low risk for PE in evaluating if you need to do a PE workup, or not.

Design: These multicentered authors, coordinated at Carolinas Medical Center, evaluated the performance of the eight-item pulmonary embolism rule-out criteria (PERC) in supporting the decision to avoid unnecessary testing for PE in patients with a low clinical suspicion of PE. The study involved 8,138 patients (the chief complaint was chest pain and/or dyspnea in 85%) seen in 13 EDs for whom a test for PE was ordered. The PERC rules were:

- Age ≥ 50
- HR ≥ 100
- SaO2 on room air < 95%
- Unilateral leg swelling
- Hempoptysis
- Recent surgery or trauma
- Prior PE or DVT
- Hormone use

One must be a "no" to all of these questions to be considered "low risk."

Outcomes:
The clinical suspicion for PE was low and the PERC was negative in 20% of the patients. Outcomes assessment at 45 days in these 1,666 very low risk patients indicated that image-confirmed PE was diagnosed in 0.9%, any venous thromboembolism (VTE) was diagnosed in 0.9%, and VTE or death occurred in 1%. In the subset with a negative PERC alone, 1.0% had a PE diagnosed, 1.2% had any VTE and 1.3% experienced VTE or death. The sensitivity and specificity of the PERC instrument as an independent diagnostic test were 95.7% and 25.4%.

Take home: These findings suggest that the incidence of VTE appears to be below 2% in patients with a low clinical suspicion for PE and a negative PERC. They also, though, suggest that PERC preforms pretty much exactly as well even without the clinical suspicion, which makes it an independently useful tool. This independent validity even without the confusing aspect of clinical suspicion, etc is very nice in comparison with some of the other decision tools. As always, it's extraordinarily important to use the rules as validated (can confirm via MDcalc, etc) in order for them to have the best possible external validity and the list is so long that one will probably have to look them up.

As discussed at other parts in this guide, it is also important to note that we are already starting with a very low probability event (about 3% in the low risk group here), so the high sensitivity here is nice, but means that a lot of unnecessary people are going to be positive.

34. Masip J, Roque M, Sánchez B, Fernández R, et al. Noninvasive ventilation in acute cardiogenic pulmonary edema: systematic review and meta-analysis. JAMA. 2005 Dec 28;294(24):3124-30. PMID: 16380593

Study Question: Review to investigate if noninvasive ventilation (NIV) like CPAP and BIPAP in patients with acute pulmonary edema is more effective than conventional oxygen therapy in preventing intubation and decreasing mortality.

Design: A composite of 15 randomized, controlled trials of noninvasive ventilation (NIV) in 843 total patients with acute pulmonary edema to determine if NIV is more effective than conventional oxygen therapy in preventing intubation and decreasing mortality.

Outcomes: All together, there were 15 randomized, controlled trials of NIV. Nine of these studies compared conventional oxygenation and continuous positive airway pressure (CPAP). These found a statistical reduction in the need for intubation with NIV (risk ratio [RR] 0.40, 95% CI 0.27-0.58). The corresponding pooled RR in the six studies of noninvasive pressure support ventilation (NIPSV, or BIPAP) was455 0.48 (95% CI 0.30-0.76). Mortality in the active treatment groups was decreased overall (RR 0.55) although it was statistically different only for CPAP (RR 0.53, 95% 0.35-0.81), while for BIPAP there was insufficient power despite a similar trend toward benefit (RR 0.60, 95% CI 0.34-1.05). In six studies that also compared CPAP and BIPAP (219 patients), there were no statistical differences between the two treatment modalities in the need for intubation (RR 1.45, slightly favoring NIPSV) or mortality (RR 0.90).

Take home: NIV should be strongly considered as a first-line treatment modality in patients with acute cardiogenic pulmonary edema. It's also worth remembering, as the authors of the study point out, that it does not seem worthwhile to differentiate the effects of these studies between BIPAP and CPAP as the sample sizes were so small and the effects were not statistically significant.

35. Wells PS, Anderson DR, Rodger M, Stiell I, et al. Excluding pulmonary embolism at the bedside without diagnostic imaging: Management of patients with suspected pulmonary embolism presenting to the emergency department by using a simple clinical model and D-dimer. Annals Intern Med 2001;135:98-107. PMID: 11453709

Study Question: Can the D-dimer assay be used with Wells' clinical criteria to safely manage patients in the emergency department (ED) with suspected pulmonary embolism (PE)?

Design: Prospective cohort study with adults > 18 who presented to four EDs in Canada with suspicion for PE based on acute onset of new or worsening shortness of breath or chest pain with symptoms for less than 3 days. Patients were **excluded** with suspected DVT in upper extremity as likely source of PE, no symptoms of PE in the last 3 days, on anticoagulation for over 24 hours, expected survival less than 3 months, contrast media is contraindicated, pregnant, or geographically inaccessible (unable to follow-up).

EM doctors then used the Wells' criteria to determine High, Moderate or Low risk for PE and all patients had a D-dimer test done. Those patients that had a low pre-test probability and a negative D-dimer, did not undergo any further testing and PE was considered excluded.

Patients in whom PE was excluded, were followed for three months for venous thromboembolism (VTE) events.

Outcomes: The primary outcome was proportion of patients who had a VTE during 3 month follow up among patients in whom the diagnosis of PE had been excluded. The secondary outcome was the safety of combined clinical model and D-dimer when the algorithm the authors used was followed correctly.

There were 930 patients included in the study and 86 people were diagnosed with PE (81 during initial evaluation and 5 during follow up.

So the primary outcome of VTE at 3 month follow up after initial negative workup yielded 437 patients that were excluded by low probability Wells and negative D-dimer with 1 patient having a PE during follow up (.2%). The D-dimer performance improved from a negative predictive value of 97.3% in the overall population to 99.5% in the low probability group.

Take home: Combined low PE pretest probability (Wells' criteria) and negative D-dimer has a very high NPV in excluding PE. Wells' criteria and D-dimer can be used to safely exclude PE in patients with a low pretest probability and a negative d-dimer.
Of note, since these studies, PERC developed which allows clinicians to "rule-out" PE in patients with a low pre-test probability for PE (by gestalt, low Wells score, low Geneva or low simplified Wells) without obtaining a D-dimer (Rebel EM).

Resuscitation

36. *De Backer D, Biston P, Devriendt J, Madl C, et al; SOAP II Investigators. Comparison of dopamine and norepinephrine in the treatment of shock. N Engl J Med. 2010 Mar 4;362(9):779-89.*

Study Question/Background: The 2016 Surviving Sepsis Campaign Guidelines strongly encouraged use of norepi as a first line pressor in septic shock. Dopamine is now only recommended in certain patients that are at a low risk for dysrhythmias. This is the study upon which the Surviving Sepsis Guidelines based their choice of norepi over dopamine as a first line shock pressor. It was later used as one of the larger studies in a meta-analysis proving arrhythmia and mortality risks with dopamine.

Demographics/Design:

- Multicenter RCT
- 1,679 patients with shock assigned to either dopamine or norepi
- Primary outcome measured = death rate at 28 days post randomization
- Secondary outcomes measured = number of days without organ support and other adverse events

Outcomes:

- No significant difference between death rates of groups at 28 days (52.2% dopamine vs 48.5% norepi)
- Significantly more arrhythmias in the dopa group (24.1%) vs norepi (12.4%)
- Subgroup analysis showed increased death rate in the dopamine group vs norepi in patients specifically with cardiogenic shock, this difference was not seen with septic shock or hypovolemic shock

Limitations:

- Open label norepi, epi, or vasopressin were used after patients were maxed out on norepi or dopamine dose which is a confounder

Take home points: While there is no difference in mortality rates when comparing dopamine and norepinephrine, dopamine is associated with greater adverse effects particularly arrhythmias. Furthermore, dopamine may have an effect on mortality rates in patients with cardiogenic shock though more studies need to be done before we can say this definitively.

37. Jones AE, Shapiro NI, Trzeciak S, Arnold RC, et al; Emergency Medicine Shock Research Network (EMShockNet) Investigators. Lactate clearance vs central venous oxygen saturation as goals of early sepsis therapy: a randomized clinical trial. JAMA. 2010 Feb 24;303(8):739-46. PMID: 20179283

Study Question/Background: Goal directed resuscitation for severe sepsis and septic shock already established, shown to reduce mortality in emergency department. Rate of severe sepsis doubled from 2000 to 2010, 500,000 patients with severe sepsis annually at the time of manuscript. Quantitative resuscitation previously established, with predefined physiologic or laboratory goals to be achieved in first few hours. Unclear optimal goals at the time of manuscript, especially determining tissue oxygen delivery. At the time surviving sepsis guidelines dictated use of central venous O2 sat (ScvO2) or mixed venous oxygen to determine

oxygen delivery and consumption, but from very controversial single RCT. Difficult to measure ScvO2 as it requires significant expertise and specialized equipment. Lactate is much easier to draw, and could serve as proxy for ScVO2. This study compared lactate clearance and ScVO2 as measures of oxygen delivery to tissues in severe sepsis and septic shock patients.

Demographics/Design: Multicenter RCT testing noninferiority of lactate compared to ScVO2 of in patients with severe sepsis or septic shock. 3 sites, patients randomized to ScVO2 group where resuscitation to normalized (8 mm Hg) central venous pressure (CVP), mean arterial pressure (MAP) and ScVO2 of at least 70%. Lactate arm patients resuscitated to normalized CVP, MAP, and lactate clearance of 10% or greater. Protocol performed until goals achieved or up to 6 hours. 300 patients, 150 assigned to each group. No differences in treatment during initial 72 hours of resuscitation. Primary outcome of absolute in-hospital mortality rate. Secondary outcomes included ICU length of stay, hospital length of stay, ventilator free days and new onset of multiple organ failure.

Outcomes: 23% of ScVO2 patients died while in hospital compared to 17% in lactate group, did not meat predefined 10% difference goal between study arms per intention to treat analysis. No significant difference in ICU length of stay, hospital length of stay, ventilator free days, or new onset of multiple organ failure between study arms.

Take home: No significant difference in hospital admitted mortality between patients normalized to ScVO2 versus patients normalized to lactate. Lactate non-inferior to ScVO2 as measurement of oxygen delivery in severe sepsis or septic shock, can be used as marker of tissue delivery, and is less complicated than ScVO2 determination.

38. ProCESS Investigators, Yealy DM, Kellum JA, Huang DT, et al. A randomized trial of protocol-based care for early septic shock. N Engl J Med. 2014 May 1;370(18):1683-93. PMID: 24635773.

Study Question: To evaluate the necessity of all the aggressive components of early goal directed treatment protocol for sepsis.

Design: 1,341 adults presenting to 31 U.S. hospitals with suspected sepsis and elements of systemic inflammatory response syndrome were randomized to initial treatment according to protocol-based early goal directed therapy (EGDT) or protocol-based standard therapy, or to usual care at the discretion of managing physicians. The aggressive EGDT protocol included central line placement and monitoring of SVC oxygen saturation, and prompted administration of IV fluids, vasopressors, dobutamine and packed red blood cells (RBCs). The less aggressive standard therapy protocol required central line placement only if peripheral access was inadequate and specified blood pressure goals and shock indices to be achieved, but recommended transfusion only if the hemoglobin was less than 7.5g/dL.

Outcomes: More than half of the patients in the protocol-based standard therapy and usual care groups underwent central line placement, which was performed later in the course of care than in the EGDT group. During the first six hours, the standard therapy group received the greatest volume of IV fluids, and there were differences between the groups in the use of vasopressors and RBC transfusion. There was no significant difference between the groups in 60-day in-hospital mortality (18.2-21.0%), which was highest in the protocol-based EGDT group, or in 90-day or one-year mortality. Acute renal failure was significantly more common in the protocol-based EGDT group than in the other two groups.

Take Home: Adherence to more or less aggressive early treatment protocols rather than provision of usual care was not associated with a significant improvement in outcomes among patients with septic shock.

39. Rivers E, Nguyen B, Havstad S, Ressler J, et al; Early Goal-Directed Therapy Collaborative Group. Early goal-directed therapy in the treatment of severe sepsis and septic shock. N Engl J Med. 2001 Nov 8;345(19):1368-77. PMID: 11794169.

Study Question/Background: Goal directed therapy has been used for severe sepsis and sepsis shock in the ICU, monitoring and adjusting cardiac preload, afterload and contractility to balance oxygen delivery with oxygen demand. This study wanted to evaluate the efficacy of early goal-directed therapy (EGDT) before admitting patients to the ICU.

Design: 263 adults presenting with severe sepsis were randomized to receive standard care in the ED guided by measurement of central venous pressure (CVP), mean arterial pressure (MAP) and urine output with early transfer to the ICU, or early goal-directed therapy initiated by the emergency physician and **continued for at least six hours in the ED**. In addition to CVP, MAP and urine output measurement, the latter group also had continuous monitoring of central venous oxygen saturation. The intervention protocol specified the amounts and indications for drugs, fluids and blood transfusion based on monitored parameters.

RESULTS: During the initial six hours, the intervention group was significantly more likely than controls to achieve combined hemodynamic goals for CVP, MAP and urine output (99.2% vs. 86.1%). In-hospital mortality was 30.5 percent in the group assigned to early goal-directed therapy, as compared with 46.5 percent in the group assigned to standard therapy (P=0.009).

Take Home: Impressive results supporting protocol driven treatment of septic shock in the ED—they found differences not just in

TOXICOLOGY

40. Weaver LK, Hopkins RO, Chan KJ, Churchill S, et al. Hyperbaric oxygen for acute carbon monoxide poisoning. N Engl J Med. 2002 Oct 3;347(14):1057-67. PMID: 12362006

Study Question: Prolonged cognitive sequelae have been reported in up to 50% of patients losing consciousness as a result of carbon monoxide (CO) poisoning, or those with a carboxyhemoglobin level above 25%. Hyperbaric oxygen (HBO) has been recommended for such patients with severe CO poisoning, but the research evidence that this intervention is beneficial is limited. This study hoped to evaluate the benefit of using hyperbaric oxygen for patients with severe CO poisoning.

Design: Double-blind study with 152 patients with acute CO poisoning (95% with a carboxyhemoglobin level above 10%) were randomized to either three HBO treatments (initiated within 24 hours after exposure and performed at intervals of 6-12 hours) or one normobaric oxygen (NBO) treatment and two normobaric room air sessions.

Results: The rate of cognitive sequelae was statistically reduced in the hyperbaric oxygen group at six weeks (25% vs. 46% in the normobaric oxygen group, odds ratio [OR] after adjustment for cerebellar dysfunction and other potential confounders, 0.45) and twelve months (18% vs. 33%). Patients with cerebellar dysfunction at baseline had an increased overall rate of cognitive sequelae when compared with those without cerebellar dysfunction (OR 5.7). Although cerebellar dysfunction was more common, prior to randomization, in the NBO group, there was still an advantage to HBO among patients with and without this problem. There were no differences between the treatment groups in several other important outcomes, however.

Take home: In this study, three hyperbaric oxygen treatments initiated within 24 hours after acute CO poisoning was associated with a reduction in cognitive sequelae compared to the control treatment

TRAUMA

41. Bickell WH, Wall MJ Jr, Pepe PE, Martin RR, et al. Immediate versus delayed fluid resuscitation for hypotensive patients with penetrating torso injuries. N Engl J Med. 1994 Oct 27;331(17):1105-9. PMID: 7935634

Study Question: Does immediate fluid resuscitation improve mortality outcomes in hypotensive patients with penetrating torso injuries? Classically, hypotensive trauma patients are managed with early fluid resuscitation, but literature preceding this study was beginning to suggest that this practice may be less beneficial than fluid restriction.

Design: Prospective study comparing the effects of immediate prehospital and ED fluid resuscitation with those achieved with restriction of fluid resuscitation until the time of surgical

intervention in **598 patients following penetrating torso trauma and pre-hospital hypotension (systolic BP≤90).**

Outcomes: 309 patients were in the immediate fluid group and received an average of 870 ccs lactated ringers in the prehospital setting and 1,608 ccs in the trauma center. For the fluid restriction group, they received an average of 92ccs in the prehospital setting and 283ccs in the trauma center. Predictably, upon arrival to the ED, patients in the fluid resuscitation group had higher systolic BPs (79 vs 72), but lower Hgbs and platelet counts. Importantly, there was no difference in fluid volume or blood products administered once the patients went to the OR.

For the primary outcome, patients in the delayed fluid group (basically fluid restriction) had a higher survival rate (70% vs 62%, p=.04) and tended to have fewer complications in the O.R. (23% vs 30%).

Of note, even though the pre hospital fluids group arrived to the ED with a higher blood pressure, the two groups ended up going to the OR with very similar blood pressures. So, even if the no fluids group did not get fluids, something happened to change their blood pressure while they were in the trauma bay (112 systolic BP in the immediate fluid group and 113 in the delayed).

Take home: **Very important paper showing evidence that delayed fluid resuscitation until operative intervention improves clinical outcomes in hypotensive adults with penetrating torso injuries**. Some concerns, though, include the point above that the BPs ended up being equal once they went to the OR. This raises some mechanistic questions about why keeping the BP low is good because, based on the equal BPs in the OR, it cannot be to minimize bleeding. Also, it seems important to note that even though the p-value for the two groups is statistically significant at .04, the 95% confidence intervals overlap, which is quantitatively confusing.

42. CRASH-2 trial collaborators, Shakur H, Roberts I, Bautista R, et al. Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant haemorrhage (CRASH-2): a randomised, placebo-controlled trial. Lancet. 2010 Jul 3;376(9734):23-32. PMID: 20554319

Study Question: Will administering tranexamic acid (which inhibits fibrinolysis) decrease bleeding and death in trauma patients with significant hemorrhage? For brief background, 1/3 of trauma patients' deaths are due to hemorrhage, so a drug that prevents clot breakdown (so is pro-thrombotic) should, in theory, help.

Methods: Absolutely massive study, with 20,211 trauma patients and 274 hospitals in 40 countries. Patients were randomized to get tranexamic acid (1g given over 10 minutes and then infusion of 1g over 8 hours) or a saline placebo. The study **included** only patients with significant bleeding (systolic bp ≤90 or pulse > 110), or at risk for significant bleeding (as they determined) who were treated within eight hours after injury.

Outcomes: All-cause mortality was 14.5% in the tranexamic acid group vs. 16.0% in controls (95% CI 0.85-0.97, relative risk [RR] 0.91, p=0.0035) and corresponding rates of death due to bleeding were 4.9% vs. 5.7%, respectively (RR 0.85, p=0.0077). There was **no significant difference** between the groups in the percentage of patients receiving blood product transfusions (50.4% in the tranexamic acid group [mean 6.06 units] and 51.3% in controls [mean, 6.29 units]), **the occurrence of vascular occlusive events (1.7% vs. 2.0%)**, **or death due to vascular occlusive events** (0.3% vs. 0.5%). **So, the number needed to treat for all-cause mortality is 67.**

It also seems worth noting this is a very sick population (1/6 dying), which makes it a good baseline population for the study.

Take home: Huge, well done study demonstrating that treatment with tranexamic acid (a cheap, widely available drug) in trauma patients with, or at risk for, significant bleeding reduces risk of hemorrhagic mortality with no increased risk of vascular occlusion. This is a very well done study, but some **concerns** include that it makes little intuitive sense that a drug can both stop bleeding and not cause more vascular events—these two are normally a tradeoff. Also, even though it is great how large this study was and that it was multi-national, that means it was more difficult to control for operative management and surgical control of hemorrhage across all these sites.

43. Hendey GW, Wolfson AB, Mower WR, Hoffman JR; National Emergency X-Radiography Utilization Study Group. Spinal cord injury without radiographic abnormality: results of the National Emergency X-Radiography Utilization Study in blunt cervical trauma. Lancet J Trauma. 2002 Jul;53(1):1-4. PMID: 12131380

Study Question: To define the incidence and characteristics of patients with spinal cord injury without radiographic abnormalities (SCIWORA). SCIWORA is a fear for ED physicians due to a series of early case reports that reported high rates of SCIWORA particularly in children—obviously raising concerns for missing spinal injuries in kids.

Methods: Prospective, observational study of blunt trauma patients in 21 U.S medical centers undergoing plain cervical radiography.

Spinal cord injury without radiographic abnormality (SCIWORA) defined as spinal cord injury demonstrated by MRI when a complete technically adequate plain radiographic series revealed no injuries.

Outcomes: With 34, 069 patients, 2.4% had cervical spine injury and .08% (27) had SCIWORA. There were also 3,000 children enrolled (30 had cervical spine injury), but none had SCIWORA. The findings on MRI were interesting—all had edema, contusion or hemorrhage around spinal

cord. Half had central disc herniation (would not have seen this before MR)—40% had spinal stenosis which put them at risk of SCIWORA.

Take home/ Background discussion: SCIWORA is very rare and only occurs in adults. SCIWORA was probably initially a misnomer because no one was really getting MRIs when this was diagnosed originally, so most people would have had something on MRI. Initially described as a pediatric disease, but probably more common in adults than it is with kids. It is, though, probably overrepresented in kids proportionally speaking, because the absolute number of spinal cord injuries is just so much higher in adults. It does seem to make some intuitive sense that SCIWORA would be overrepresented in children as it is easier for a child to injure cords without breaking bone.

One important thing to note about this study is the strict definition of seeing something on MRI in order to classify it as SCIWORA. This data was eventually used for the NEXUS study (below), where you had to have findings on MRI with a neuro deficit, negative x-ray, negative CT to be classified as having SCIWORA; the authors repeatedly stress that it is reasonable to diagnose SCIWORA even without findings on MRI.

The authors also make an interesting point that we do not think about SCIWORA in adults because we cause it something else—we end up calling it central cord syndrome. Different terms, but essentially the same thing when you look at the findings on MRI.

In summary, the fear of SCIWORA in kids came from original case reports where some kids came in days later with devastating injury. This data, though, was collected retrospectively and it seems most likely that the injury was there originally on presentation, but because we were not MRIing these kids, we missed ligamentous injurious, or even bone injury because they weren't getting CT. So the working theory now is that these kids had the injury on presentation, but it wasn't defined properly and then got exacerbated later.

44. Hoffman JR, Wolfson AB, Todd K, Mower WR. Selective cervical spine radiography in blunt trauma: methodology of the National Emergency X-Radiography Utilization Study (NEXUS). Ann Emerg Med. 1998 Oct;32(4):461-9. PMID: 9774931
VALIDITY OF A SET OF CLINICAL CRITERIA TO RULE OUT INJURY TO THE CERVICAL SPINE IN PATIENTS WITH BLUNT TRAUMA Hoffman, J.R., et al, N Engl J Med 343(2):94, July 13, 2000

Study Question: *Note: This is a combination review of the AliEM article that is listed first and the eventual NEXUS validation study in NEJM listed second.

The NEXUS criteria and group was organized to evaluate a set of five simple criteria that can identify patients at low to no risk of cervical spine injury who therefore do not need further imaging.

Methods: A prospective, multicenter, observational study designed to validate the ability of this five item decision instrument to identify patients at low risk of cervical spine injury (CSI) following blunt trauma. Huge, 34,069 subjects aged 1-101 managed at a cross sectional representation of 21 EDs in the U.S, where C-spine imaging was ordered by the physician. Criteria patients needed to meet were (aka NEXUS criteria):

- Absence of posterior midline neck tenderness
- Absence of focal neurological findings
- Normal level of alertness
- No evidence of intoxication
- Absence of another painful injury that may distract the patient from CSI

The five criteria were recorded in the validation portion before x-ray findings were known.

Outcomes: CSI was identified on x-ray in 2.4% of patients (818 patients). NEXUS criteria identified all but eight of these patients (sensitivity 99%) and two of these 8 patients met the pre-defined criteria for "clinically significant" (meaning they required action). One of the two had paresthesias and may, therefore, represent misapplication of the instrument, and the other refused treatment and remained asymptomatic at a six-week follow-up visit.

Take home:: This study validates the safety of the NEXUS decision instrument in guiding selective ordering of C-spine x-rays in blunt trauma patients. The authors are aware of the omnipresent concern that clinical judgement should always be used in decision making and that the user should make sure she is using to tool correctly as designed. Even though the rules are not 100% sensitive, the study authors calculate that ordering physicians can expect to miss an occult C-spine injury using these rules approximately once every 125 years of practice and that these rules would reduce c-spine imaging ordering by approximately 15%.

45. Karounis H, Gouin S, Eisman H, Chalut D, et al. A randomized, controlled trial comparing long-term cosmetic outcomes of traumatic pediatric lacerations repaired with absorbable plain gut versus nonabsorbable nylon sutures. Acad Emerg Med. 2004 Jul;11(7):730-5. PMID: 15231459

Study Question/Background: Traumatic lacerations amongst the most common reason for Peds ED visits. More than 2 million traumatic wounds treated yearly in EDs as of 2004. More and more ED providers shifting towards adhesives for children given comfort and ease, however many types of wounds exist which can not be managed with adhesive, and require suture. No universal agreement in choosing ideal type of suture for repairs, particularly controversial when discussing absorbable vs. non-absorbable sutures usage in children. Traditionally, non-absorbable used for outer most layer, new studies from surgery pointing surgeons more towards absorbable suture for outer most layer closure. Absorbable means less hospital visits and less burden on patient.

Demographics/Design: RCT in tertiary peds referral center comparing good long term cosmesis and rate of complications between absorbable plain catgut sutures and nonabsorbable nylon

sutures for traumatic lacerations. 5.0 or 6.0 used for face, 4.0 or 5.0 for extremities or torso, all patients received topical Abx and dry dressing. PO abx, steri-strips at physician discretion. Patients block randomized into plain catgut or nylon suture groups. All children younger than 18 yo with lacerations less than 12 hours old required suture repair per recruiting ED physician were enrolled.. **Adhesive amenable lacerations excluded, amongst many other exclusion criteria**. 1% Lidocaine used for local anesthesia amongst all study participants. Simple uninterrupted technique using cutting needles used in both groups as well. Patients 1-18 years old with lacerations less than 12 hours old were all recruited, of 147 eligible patients 95 enrolled. 50 randomized to absorbable, 45 randomized to non-absorbable.

Outcome: The primary outcome was visual analog scale of cosmesis (VAS), a validated tool utilized by a single blinded plastic surgeon 4 months after repair. VAS was 79mm for absorbable suture and 66 mm for non-absorbable suture, no difference in significance. Secondary outcomes included the validated Wound Evaluation Score (WES), which was utilized by a single research nurse at 5-10 days and 4 months. At 5-10 days there was no difference between groups in WES, however optimal WES was found in absorbable vs. nonabsorbable sutures (36% vs. 28%). Additional secondary outcomes included complications such as infection and dehiscence, with no difference between absorbable and non-absorbable suture, and need for surgical scar revision: 2 patients in the absorbable group and 1 patient in the nonabsorbable group. All 3 patients declined revision.

Take Home: Absorbable suture provides long-term cosmesis and similar complication rates in wound repairs compared to non-absorbable suture. Study **with low power, broad exclusion criteria,** may have some difficulty generalizing across all laceration repair populations.

46. Moore EE, Knudson MM, Burlew CC, Inaba K, et al; WTA Study Group. Defining the limits of resuscitative emergency department thoracotomy: a contemporary Western Trauma Association perspective. J Trauma. 2011 Feb;70(2):334-9. PMID: 21307731

Study Question/Background: In the 40-plus years since the spread of the ED thoracotomy researchers have attempted to discern when the procedure is futile. Health care reform provided a new avenue of data to develop guidelines for ED thoracotomy. This was a prospective multicenter study to identify patterns of injury and physiologic profiles at arrival of patients that were conducive to survival after ED thoracotomy.

Demographics/Design: 18 institutions in the Western Trauma Association recruited all patients meeting each institution's guidelines for ED thoracotomy. Criteria included certain injury patterns, and physiologic status: including duration of prehospital CPR and presenting cardiac rhythm. At the time specific indications for ED thoracotomy were not defined. All centers used left anterior thoracotomy with selective transsternal extension if further exposure was needed..

Outcomes: 56 patients survived ED thoracotomy to hospital discharge: of these 93% were male, 30 had a stab wound, 21 had a gunshot wound and 5 had blunt trauma. 30% involved a ventricular stab wound, 16% involved a GSW to the lung. 34% of patients had prehospital CPR.

For futile care, **survivors of blunt torso injuries had CPR up to 9 minutes, and penetrating torso wound with CPR up to 15 minutes. 7 patients had Asystole on arrival at the ED, all with pericardial tamponade, and only 3 had appropriate neurological recovery at discharge.**

Take home: ED thoracotomy is **futile when prehospital CPR is greater than 10 minutes with no response after blunt trauma, futile after 15 minutes of CPR after penetrating trauma with no response, and when asystole is the presenting rhythm and there is no pericardial tamponade.**

47. Stiell IG, Wells GA, Vandemheen KL, Clement CM, et al. The Canadian C-spine rule for radiography in alert and stable trauma patients. JAMA. 2001 Oct 17;286(15):1841-8. PMID: 11597285

Study Question/Background: Can we utilize a clinical decision rule to evaluate the cervical spine in alert and stable patients with trauma? Further questions included: are there high-risk factors that require imaging? Are there low-risk factors that allow for safe assessment of ROM of the cervical spine? Are these patients able to actively rotate the neck 45 degrees to the left and right? Prior to this study there was a high level of variation and ineffectiveness in usage of imaging of the C-spine in alert and stable trauma patients.

Demographics/Design: Multicenter prospective Canadian study (10 EDs), patients evaluated for 20 clinical findings before 3 view radiographs with Flexion/Extension views and CT of C-Spine at discretion of physician. 8924 adults enrolled: mean age of 37 year old, 51.5% male, 91.5% with neck pain. Patients had to **alert with GCS of 15 and stable with SBP > 90 and RR 10-24/min.** Mechanism of injury: 67% with MVA, 14.3% with falls. 68.9% received radiographs, 4.9% received CT C-Spine. 1.6% with C-spine fracture, 0.3% with dislocation, 0.1% with ligamentous instability. 0.7% stabilized with rigid collar, 0.6% stabilized with Halo, 0.3% stabilized with internal fixation, 0.2% with brace. 8.1% of patients were admitted. 20 clinical findings were reduced to clinical rule utilizing advanced statistical modeling. 3 parameters utilized: Age >65 years, extremity paresthesias or dangerous mechanism (rule out, if yes = high risk); low risk factor present (sitting in ED, ambulatory at any point, delayed neck pain, no mid-line tenderness, simple rear-end MVC = rule in for low risk); Able to actively rotate neck 45 degrees left and right (rule in for low risk)

Outcomes: Of 8294 enrolled, **151 (1.7%) found to have clinical important C-spine injury.** Determined clinically **unimportant injuries**: isolated avulsion fracture of osteophyte, isolated transverse process fracture involving facet joint, isolated spinous process fracture not involving lamina, and simple compression fracture less than 25% of vertebral body height. **Rule is 100% sensitive and 42.5% specific for identifying the 151 clinically important C-spine injuries.**

Take home: Canadian C-Spine rule is incredibly sensitive for identifying clinically important C-spine injuries in alert and stable patients. The rule can be easily utilized using MD Calc and other online applications.

48. Stiell IG, Wells GA, Vandemheen K, Clement C, et al. The Canadian CT Head Rule for patients with minor head injury. Lancet. 2001 May 5;357(9266):1391-6. PMID: 11356436

Background/Study Question: Performed by the same authors of the Canadian C-Spine rule, this paper similarly sought to reduce variability in practice regarding head CTs for patients presenting to the ED with head trauma. Specifically they sough to develop a tool that is sensitive and specific to determine whether a head CT is necessary.

Demographics/Design: A prospective cohort derivation study, similar to the Canadian C-Spine study, with 3121 patients from the same 10 Canadian EDs from the C-Spine study. The study excluded for both low risk criteria (minimal trauma with no LOC, amnesia or disorientation, absence of clear trauma [seizure, syncope]) and high risk criteria (age <16, penetrating skull injury, depressed skull fracture, acute focal neuro deficit, unstable VS, seizure prior to ED eval, bleeding disorder, on oral anticoagulation, return for assessment of same head injury, pregnancy). Mean age of 39, 69% mean, 3.1 hours after injury, 46% with witnessed LOC, 87% with amnesia, 80% with GCS = 15, 17% GCS = 14, 3% GCS = 13. Mechanisms of injury included 31% falls, 26% MVAs, 11% Assault, and 10% or less of sports injury, bicycle injury, pedestrian struck, hit by object/head strike, motorcycle injury. 22 parameters were assessed for each patient in a 1 hour review, treating physician determined whether or not to obtain CT (not the investigators). Follow up was performed via phone at 14 days to evaluate for memory loss, concentration difficulty, seizure or neuro deficits and a validated orientation-memory-concentration test. Patients receiving CT were compared to those who did not, and advanced statistical modeling was utilized to determine risk factors for clinically important brain injury.

Outcomes: 7 criteria were determined for high-risk patients requiring neurological intervention and moderate-risk patients with clinically important injury. High risk includes GCS <15 at 2 hours after injury, suspected open or depressed skull fracture, signs of basilar skull fracture, 2 or more episodes of vomiting and age > 65. Moderate risk includes retrograde amnesia to the event for 30 or more minutes, and a dangerous mechanism (pedestrian struck, ejected from motor vehicle or fall greater than 3 feet or greater than 5 stairs). The rule is incredible sensitive (100% for high risk injury, 98.4% for moderate risk) for factors necessitating head CT, although not very specific (high risk 68.7%, moderate risk 49.6%)

Take Homes: The Canadian CT Head rule is a powerful, sensitive tool for determining high risk and moderate risk patients who warrant a head CT after head trauma. It is relatively easy to use with an online application such as MD Calc. It is not particularly specific for head CT however.

ULTRASOUND

49. Melniker LA, Leibner E, McKenney MG, Lopez P, Briggs WM, Mancuso CA. Randomized controlled clinical trial of point-of-care, limited ultrasonography for trauma in the emergency department: the first sonography outcomes assessment program trial. Ann Emerg Med. 2006 Sep;48(3):227-35. PMID: 16934640

Study Question/Background: 38 million people (at the time of this article) evaluated for trauma annually, leading cause of death of those younger than 45. The longer it takes to get definitive operative treatment for trauma patients the greater the risk of more serious morbidity and mortality. Point of care, limited ultrasound evaluations (PLUS), also known as focused assessment with sonography in trauma (FAST), are rapid exams that are quicker than traditional CT and other traumatic evaluations, and do not require leaving the trauma bay to perform. If PLUS/FAST can assist in making operative decision making quicker than traditional methods, then perhaps outcomes in trauma patients could be improved. This study examined whether the PLUS/FAST could reduce time to operating room for trauma patients.

Demographics/Design: RCT at two level 1 trauma centers testing any diagnostic intervention the treating physician chose vs. any diagnostic intervention the treating physician chose with FAST/PLUS in patients with suspected torso trauma. 111 patients received FAST/PLUS in addition to standard measures at the treating physician's discretion, while 106 control patients received only standard measures. Mean age of 27, primarily male (69%), approximately 1 hour since injury, majority with torso trauma. 26% of PLUS/FAST patients required operations, while 32% of control patients required operations.

Outcome: The primary outcome was time from ED arrival to operation between the group receiving PLUS/FAST and the control group**. Of the 29 PLUS/FAST patients needing operations, their mean time to OR from ED was 57 minutes versus 166 minutes in patients in the control group needing operations.** Secondary measures included CTs performed, with 53% of all 111 PLUS/FAST patients receiving CT vs. 85% of all 106 control patients receiving CT. Other secondary outcomes showed no significant difference in hospital length of stay. A significant difference in total hospital charges was shown between the two groups for patients who received operations: $28,400 total cost for PLUS/FAST patients versus $47,600 for control patients.

Take Home: FAST/PLUS exams undoubtedly reduce the time to operation for torso trauma patients who need operative management. FAST/PLUS exams also reduced the number of CT scans performed, and reduced total hospital charges to patients.

50. Nagdev AD, Merchant RC, Tirado-Gonzalez A, Sisson CA, Murphy MC. Emergency department bedside ultrasonographic measurement of the caval index for noninvasive determination of low central venous pressure. Ann Emerg Med. 2010 Mar;55(3):290-5. PMID: 19556029

Study Question/Background: Intravascular volume assessment is sometimes challenging in ED patients. Invasive monitoring of central venous pressure (CVP) is certainly a useful guide, but comes with a slew of complications (bleeding, thrombosis, infection, amongst others), takes time and often comes after IV fluid boluses have been used to increase blood pressure. This study aimed to determine whether non-invasive ultrasound assessment of the inferior vena cava can predict central venous pressure.

Demographics/Design: Prospective observational study assessing correlation between CVP and Caval index (the relative decrease of inferior vena cava diameter during 1 respiratory cycle) in patients requiring ultrasound-guided central venous line placement. Inspiratory and expiratory diameters of the inferior vena cava (2 dimensions of each measurement) were performed in 73 ED patients requiring central line placement per ED physician evaluation. **The study specifically hypothesized that a caval index greater than or equal to 50% (50% collapse of IVC with respiratory variation) was associated with a CVP less than 8 mm Hg.** Median age 63, 60% women. Mean time from US assessment to CVP determination was 6.5 minutes, with 45 mL of fluid administered on average between US assessment and CVP determination. CVP determined utilizing invasive pressure measurement.

Outcomes: 32% of the 73 patients had CVP less than 8 mm Hg. Correlation between caval index and CVP was -0.74 (strongly negative correlation). The sensitivity of caval index greater than or equal to 50% in predicting a CVP less than 8 mm Hg was 91%, specificity of 94%, positive predictive value of 87% and negative predictive value of 96%

Take home: Strong correlation between caval index greater than or equal to 50% and low CVP. Bedside measurements utilizing POCUS can be used as a useful non-invasive tool to determine CVP during ED evaluation of patients.

UROLOGY

51. Smith-Bindman R, Aubin C, Bailitz J, Bengiamin RN, et al. Ultrasonography versus computed tomography for suspected nephrolithiasis. N Engl J Med. 2014 Sep 18;371(12):1100-10. PMID: 25229916

Study Question: Is ultrasound or abdominal CT a better diagnostic imaging test for nephrolithiasis?

Design: Prospective, randomized trial comparing US with CT in 2,759 patients aged 18-76 (mean 40.4) presenting to 15 different types of EDs with possible nephrolithiasis in the absence of high risk for other serious diagnoses. The patients were randomized to undergo point-of-care US performed by an emergency physician, US performed by a radiologist or abdominal CT scanning. They were followed for up to 180 days for the **primary outcomes** of high-risk conditions related to a missed or delayed diagnosis and cumulative radiation exposure.

Outcomes: Rates of high-risk diagnoses with complications during the first 30 days were low (0.2% to 0.7%) and did not differ significantly between the groups. Cumulative radiation exposure was significantly lower in the groups evaluated with US rather than CT scanning.

Take Home: Ultrasound performed just as well as CT in evaluating suspected nephrolithiasis without the radiation exposure of CT. One note, though, is that the study is talking about the first diagnostic imaging test that patients received—41% of patients who were in the ultrasound group got a CT while in the ER, so maybe the it was not ultrasound that was doing equally well, but really CTs combined with ultrasound.

VASCULAR

52. Hagan PG, Nienaber CA, Isselbacher EM, Bruckman D, et al. The International Registry of Acute Aortic Dissection (IRAD): new insights into an old disease. JAMA. 2000 Feb 16;283(7):897-903.

Study Question: Looking at international registry to see if people presented with classic symptoms of aortic dissection.

Design: The authors reviewed findings in 464 patients with acute aortic dissection (AAD) treated at one of twelve large referral centers in six countries from 1996 through 1998. The data were obtained prospectively or through retrospective chart review.

Outcomes: The patients had a mean age of 63 years and were most commonly male (65%) and Caucasian (83%) with a history of hypertension (72%). Type A dissections (which are the ones involving the ascending aorta) accounted for 62% of the cases. Severe pain was reported by 91% of the patients and was most often abrupt in onset (85%).

Chest pain was most common in patients with type A dissections (79% vs. 63% with type B dissections), while back pain was reported by 64% of patients with type B dissections but only 47% of those with type A dissections. Pain was often described as sharp (64%), and less commonly as tearing or ripping (51%), radiating (28%) or migrating (17%). Syncope was the presenting symptom in 9% of the patients. Hypertension was present on admission in 36% of type A dissections compared with 70% of type B dissections. Few patients exhibited pulse

deficits (15%) or murmurs of aortic insufficiency (32%). About one-fifth of initial chest x-rays (21%) showed no mediastinal widening or abnormalities of the aortic contour and 12% demonstrated no abnormalities. EKGs most commonly showed nonspecific abnormalities and were normal in 31% of the patients. The in-hospital mortality rate was 27%.

Take homes: Aortic dissection remains a very difficult diagnosis to make and the symptoms that we view as classic are not always there. Moreover, this is a retrospective paper, so the most confusing presentations of dissection were probably missed and never even ended up in the registry. It is important to maintain a high index of suspension to make this diagnosis.