Update in Hospital Medicine
DISCLOSURE

ACP national academic advisory board
Outline

Sepsis/Septic Shock..(yet another update)
IV Fluids
PE and Syncope
Treatment for VTE in Cancer patients
Aspirin use in patients with h/x of PCI undergoing surgery
Hip surgery and timing
C Diff update
Case Study

55 yr old female w/ PMH of HTN, DM, COPD presents with fever, shortness of breath and a productive cough. Her BP is 80/50, RR 24, T 102.5, O2 95% on 3L O2. CXR shows right lower lobe pneumonia. Lactate is 4. She’s given 30ml/kg of IV fluids.

Her Bp is still 80/55. Central line is placed and is admitted to ICU for further care. She’s started on Norepinephrine drip in the ICU
Which of these statements may apply to her plan of care?

A. Starting IV Hydrocortisone may help in weaning off her vasopressors
B. Hydrocortisone drip may improve mortality
C. Normal saline could reduce major adverse kidney events
D. Adding Positive inspiratory pressure will improve her blood pressure
E. Nothing can help her now- she needs a hospice consult!
Adjunctive Glucocorticoid Therapy in Patients with Septic Shock


Hydrocortisone plus Fludrocortisone for Adults with Septic Shock

Trials

AUSTRALIAN TRIAL

3658 patients
Randomized, pragmatic, double-blind, parallel-group controlled trial
1/3rd surgical patients
Pneumonia in 30%; abdominal infection 25%
All mechanically ventilated
Continuous infusion of hydrocortisone (200 mg/day)

FRENCH TRIAL

1241 patients
80% from medicine floor
>50% with pneumonia
Nearly all mechanically ventilated
Hydrocortisone (50 mg q6 hours) + fludrocortisone (50 mcg once daily) for 7 days

Venkatesh et al. NEJM. 2018; 378:797-808.
French Trial

Initially designed as a 2x2 factorial design with four parallel groups.

1. Placebo
2. Corticosteroids
3. Drotrecogin Alfa
4. Corticosteroids + Drotrecogin Alfa

Drotrecogin Alfa gets recalled in 2011, trial changes to 1 + 2.
Survival Curves

Venkatesh et al. NEJM. 2018; 378:797-808.

Additional outcome data

No. at Risk
Hydrocortisone 1843 104 34 9 6 3 3 2 1 0
Placebo 1854 213 53 19 8 6 4 0 0 0

Hazard ratio, 1.32 (95% CI, 1.23–1.41)
P<0.001

Figure 2. Cumulative Incidence Function of Time from Randomization to Resolution of Shock.
The cumulative incidence function plot was created by treating death as a competing risk.

Venkatesh et al. NEJM. 2018; 378:797-808.

Moral of the Story

Hydrocortisone shortens the duration of septic shock

Makes sense to treat patients with hydrocortisone (and probably fludro) in sicker patients.
Which of these statements may apply to her plan of care?

A. Starting IV Hydrocortisone may help in weaning off her vasopressors
B. Hydrocortisone drip may improve mortality
C. Normal saline could reduce major adverse kidney events
D. Adding Positive inspiratory pressure will improve her blood pressure
E. Nothing can help her now- she needs a hospice consult!
A 47 year-old woman presents with sepsis secondary to community acquired pneumonia. In addition to administration of early antibiotics, you consider several other interventions. Which of the following statements about those interventions is true?

A. RESUSCITATION WITH LACTATED RINGERS IS LESS LIKELY TO RESULT IN ADVERSE KIDNEY EVENTS.

B. GIVING NORMAL SALINE WILL REDUCE MY HOSPITAL FREE DAYS

C. GIVING 30ML/KG OF IV FLUIDS WILL IMPROVE MORTALITY

D. GIVING LACTATED RINGER WILL IMPROVE MORTALITY
Balanced Crystalloids versus Saline in Noncritically Ill Adults

Wesley H. Self, M.D., M.P.H., Matthew W. Semler, M.D.,
Jonathan P. Wanderer, M.D., Li Wang, M.S., Daniel W. Byrne, M.S.,
Sean P. Collins, M.D., Corey M. Slovis, M.D., Christopher J. Lindsell, Ph.D.,
Jesse M. Ehrenfeld, M.D., M.P.H., Edward D. Siew, M.D.,
Andrew D. Shaw, M.B., Gordon R. Bernard, M.D.,
and Todd W. Rice, M.D., for the SALT-ED Investigators*
SALT-ED Trial

- 13,347 Non-ICU patients
- Single-center, pragmatic, multiple-crossover trial comparing (LR or Plasma-Lyte A) vs. Normal Saline
- Fluid given in ED was determined based on the month
- 16-month trial
- Primary outcome was hospital-free days
  - Secondary: Major Adverse Kidney events (MAKE)
<table>
<thead>
<tr>
<th>Outcome</th>
<th>Balanced Crystals (N=6708)</th>
<th>Saline (N=6639)</th>
<th>Adjusted Odds Ratio (95% CI)*</th>
<th>Adjusted P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median hospital-free days to day 28 (IQR)</td>
<td>25 (22–26)</td>
<td>25 (22–26)</td>
<td>0.98 (0.92–1.04)</td>
<td>0.41</td>
</tr>
<tr>
<td>Major adverse kidney event within 30 days — no. (%)</td>
<td>315 (4.7)</td>
<td>370 (5.6)</td>
<td>0.82 (0.70–0.95)</td>
<td><strong>0.01</strong></td>
</tr>
<tr>
<td>Death — no. (%)</td>
<td>94 (1.4)</td>
<td>102 (1.5)</td>
<td>0.89</td>
<td></td>
</tr>
<tr>
<td>New renal-replacement therapy — no./total no. (%) †</td>
<td>18/6582 (0.3)</td>
<td>31/6530 (0.5)</td>
<td>0.56</td>
<td></td>
</tr>
<tr>
<td>Final serum creatinine ≥200% of baseline — no./total no. (%) †</td>
<td>253/6582 (3.8)</td>
<td>293/6530 (4.5)</td>
<td>0.84</td>
<td></td>
</tr>
<tr>
<td>Stage 2 or higher acute kidney injury — no./total no. (%) †</td>
<td>528/6582 (8.0)</td>
<td>560/6530 (8.6)</td>
<td>0.91 (0.80–1.03)</td>
<td>0.14</td>
</tr>
<tr>
<td>In-hospital death — no. (%)</td>
<td>95 (1.4)</td>
<td>105 (1.6)</td>
<td>0.88 (0.66–1.16)</td>
<td>0.36</td>
</tr>
</tbody>
</table>

* Multivariable models were adjusted for age, sex, race, admitting service, and time (days since trial initiation).
† Patients with end-stage renal disease who were receiving long-term renal-replacement therapy at the time of emergency department arrival (126 in the balanced-crystalloids group and 109 in the saline group) were not eligible for the following outcomes: new renal-replacement therapy within 30 days, final serum creatinine concentration within 30 days at least 200% of the baseline value, and stage 2 or higher acute kidney injury.
Conclusion

Fluids were given in ED- post admission fluids administered were not controlled.

LR may have a role in reducing adverse kidney events.

https://www.reactiongifs.us/i-told-you-so-stephen-colbert/
A 47 year-old woman presents with sepsis secondary to community acquired pneumonia. In addition to administration of early antibiotics, you consider several other interventions. Which of the following statements about those interventions is true?

A. RESUSCITATION WITH LACTATED RINGERS IS LESS LIKELY TO RESULT IN ADVERSE KIDNEY EVENTS.

B. GIVING NORMAL SALINE WILL REDUCE MY HOSPITAL FREE DAYS

C. GIVING 30ML/KG OF IV FLUIDS WILL IMPROVE MORTALITY

D. GIVING LACTATED RINGER WILL IMPROVE MORTALITY
75 yr old male with history of HTN, DM, and HLD presents with syncope. He had no prodromal symptoms, no recent travel. He’s not had a previous history of syncope. You are considering a CTA Chest to rule out Pulmonary embolism. The patient asks you what are the chances that he has had a pulmonary embolism?

A. 1 in 6 (16.6%)
B. 1 in 26 (3.8 %)
C. 1 in 16 (6.2%)
D. 1 in 50 (2%)
Prevalence of PE by International Classification of Diseases codes < 1% in all patients with syncope and < 3% in patients hospitalized for syncope

Cross-sectional study

1,671,944 adults from Canada, Denmark, Italy, and United States presenting to emergency department for syncope were evaluated for PE using International Classification of Diseases codes
Prevalence of PE at first evaluation ranged from
- 0.06% to 0.55% in all patients
- 0.15% to 2.1% in patients hospitalized for syncope after first evaluation

Prevalence of PE at 90-day follow-up ranged from
- 0.14% to 0.83% in all patients
- 0.35% to 2.63% in patients hospitalized for syncope after first evaluation

Prevalence of venous thromboembolism at 90-day follow-up ranged from
- 0.3% to 1.37% in all patients
- 0.75% to 3.86% in patients hospitalized for syncope after first evaluation

JAMA study continued
Conclusion

PE may not be as high as prevalent as the PESIT trial showed.

PE should still be part of the ddx as a cause of syncope.
75 yr old male with history of HTN, DM, and HLD presents with syncope. He had no prodromal symptoms, no recent travel. He’s not had a previous history of syncope. You are considering a CTA Chest to rule out Pulmonary embolism. The patient asks you what are the chances that he has had a pulmonary embolism?

A. 1 in 6 (16.6%)
B. 1 in 26 (3.8 %)
C. 1 in 16 (6.2%)
D. 1 in 50 (2%)
58 year old female with history of ovarian cancer presents with shortness of breath and pleuritic chest pain. Her oxygen saturation is 85% on room air, blood pressure is stable, HR is 115. CTA Chest shows pulmonary embolism. You start her on enoxaparin and admit her as an inpatient. She’s afraid of needles and wants to avoid giving herself shots if possible. What are the options for her anticoagulation at discharge?

A. Daily warfarin

B. Tell her to get over the fear of needles and you start Enoxaparin Daily

C. Fondaparinux

D. Edoxaban daily.
Edoxaban for the Treatment of Cancer-Associated Venous Thromboembolism

Gary E. Raskob, Ph.D., Nick van Es, M.D., Peter Verhamme, M.D.,
Marc Carrier, M.D., Marcello Di Nisio, M.D., David Garcia, M.D.,
Michael A. Grosso, M.D., Ajay K. Kakkar, M.B., B.S., Michael J. Kovacs, M.D.,
Michele F. Mercuri, M.D., Guy Meyer, M.D., Annelise Segers, M.D.,
Minggao Shi, Ph.D., Tzu-Fei Wang, M.D., Erik Yeo, M.D., George Zhang, Ph.D.,
Jeffrey I. Zwicker, M.D., Jeffrey I. Weitz, M.D., and Harry R. Büller, M.D.,
for the Hokusai VTE Cancer Investigators*
Study design

Open-label, noninferiority trial

1050 patients, intention-to-treat analysis

Patients with acute symptomatic or incidental VTE
Intervention

Patients

- Treated for at least 6 months and up to 12 months
- LMWH for 5 days then oral edoxaban at 60mg once daily
- SubQ Dalteperin
### Table 2. Clinical Outcomes during the Overall Trial Period.*

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Edoxaban (N = 522)</th>
<th>Dalteparin (N = 524)</th>
<th>Hazard Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary outcome</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Recurrent venous thromboembolism or major bleeding — no. (%)</td>
<td>67 (12.8)</td>
<td>71 (13.5)</td>
<td>0.97 (0.70–1.36)</td>
<td>0.006 for noninferiority; 0.87 for superiority</td>
</tr>
<tr>
<td><strong>Secondary outcomes</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Recurrent venous thromboembolism — no. (%)</td>
<td>41 (7.9)</td>
<td>59 (11.3)</td>
<td>0.71 (0.48–1.06)</td>
<td>0.09</td>
</tr>
<tr>
<td>Recurrent deep-vein thrombosis — no. (%)</td>
<td>19 (3.6)</td>
<td>35 (6.7)</td>
<td>0.56 (0.32–0.97)</td>
<td></td>
</tr>
<tr>
<td>Recurrent pulmonary embolism — no. (%)†</td>
<td>27 (5.2)</td>
<td>28 (5.3)</td>
<td>1.00 (0.59–1.69)</td>
<td></td>
</tr>
<tr>
<td>Major bleeding — no. (%)</td>
<td>36 (6.9)</td>
<td>21 (4.0)</td>
<td>1.77 (1.03–3.04)</td>
<td>0.04</td>
</tr>
<tr>
<td>Severity of major bleeding among those with major bleeding — no./total no. (%)‡</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Category 1</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Category 2</td>
<td>24/36 (66.7)</td>
<td>8/21 (38.1)</td>
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<tr>
<td>Category 3</td>
<td>12/36 (33.3)</td>
<td>12/21 (57.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Category 4</td>
<td>0</td>
<td>1/21 (4.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinically relevant nonmajor bleeding — no. (%)§</td>
<td>76 (14.6)</td>
<td>58 (11.1)</td>
<td>1.38 (0.98–1.94)</td>
<td></td>
</tr>
<tr>
<td>Major or clinically relevant nonmajor bleeding — no. (%)§§</td>
<td>97 (18.6)</td>
<td>73 (13.9)</td>
<td>1.40 (1.03–1.89)</td>
<td></td>
</tr>
<tr>
<td>Death from any cause — no. (%)</td>
<td>206 (39.5)</td>
<td>192 (36.6)</td>
<td>1.12 (0.92–1.37)</td>
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<tr>
<td>Event-free survival — no. (%)</td>
<td>287 (55.0)</td>
<td>296 (56.5)</td>
<td>0.93 (0.77–1.11)</td>
<td></td>
</tr>
</tbody>
</table>
Conclusion

01
Edoxaban was noninferior to dalteparin with respect to composite outcome or recurrent venous thromboembolism

02
Higher rate of GI bleed in Edoxaban
- Similar to previous NOACs

03
If considering using Edoxaban- have to use LMWH for 5 days prior to initiating
58 year old female with history of ovarian cancer presents with shortness of breath and pleuritic chest pain. Her oxygen saturation is 85% on room air, blood pressure is stable, HR is 115. CTA Chest shows pulmonary embolism. You start her on enoxaparin and admit her as an inpatient. She’s afraid of needles and wants to avoid giving herself shots if possible. What are the options for her anticoagulation at discharge?

A. Daily warfarin
B. Tell her to get over the fear of needles and you start Enoxaparin Daily
C. Fondaparinux
D. Edoxaban daily.
https://gomerblog.com/2014/09/cell-phone/
Clinical Decision-Making: Observing the Smartphone User An Observational Study in Predicting Acute Surgical Patients' Suitability for Discharge

Prospective Observational Study

Over 2 year period at South Australia

• All patients admitted by junior surgical doctors were eligible

221 patients observed
Results and Conclusion

11.3% were observed to use smartphone and 23.5% were discharged home on day 1.

Those who were observed to be using a smartphone were 5.29 times more likely to be discharged home on day 1 and were less likely to be subsequently readmitted.
55 yr old male with history of T2DM, HTN, CAD with a bare metal stent that was placed 16 months ago presents to your clinic with a ventral hernia. He wants to get his ventral hernia repaired. His medications include aspirin, metformin, carvedilol, clopidogrel, lisinopril and atorvastatin. Besides continuing atorvastatin, which of these will be beneficial in the perioperative period?

A. Aspirin
B. Lisinopril
C. Metformin
D. Clopidogrel
In the POISE-2 trial, 10,010 patients were randomly assigned that were having non-cardiac surgery to receive aspirin or placebo.

2-by-2 factorial design
- Received Aspirin or placebo vs. Clonidine or placebo

Patients started taking Aspirin 200mg before surgery and continued at a daily dose of 100 mg for 30 days

Primary outcome was composite of death or nonfatal myocardial infarction at 30 days
Hazard ratio, 0.99 (95% CI, 0.86–1.15); P=0.92

No. at Risk

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>4724</th>
<th>4696</th>
<th>4680</th>
<th>4669</th>
<th>4662</th>
<th>4652</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Aspirin</td>
<td>4713</td>
<td>4678</td>
<td>4665</td>
<td>4660</td>
<td>4653</td>
<td>4643</td>
</tr>
<tr>
<td>Day at Start of Risk Analysis</td>
<td>Aspirin†</td>
<td>Placebo†</td>
<td>Absolute Increase in Risk with Aspirin</td>
<td>P Value</td>
<td></td>
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<tr>
<td></td>
<td>no./total no. (%)</td>
<td>percentage points</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day of surgery</td>
<td>311/4953 (6.3)</td>
<td>254/4978 (5.1)</td>
<td>1.2</td>
<td>0.01</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Day 1 after surgery</td>
<td>191/4832 (4.0)</td>
<td>129/4852 (2.7)</td>
<td>1.3</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Day 2 after surgery</td>
<td>138/4779 (2.9)</td>
<td>92/4813 (1.9)</td>
<td>1.0</td>
<td>0.002</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Day 3 after surgery</td>
<td>102/4741 (2.2)</td>
<td>59/4777 (1.2)</td>
<td>1.0</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
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<tr>
<td>Day 4 after surgery</td>
<td>73/4710 (1.6)</td>
<td>33/4748 (0.7)</td>
<td>0.9</td>
<td>&lt;0.001</td>
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<tr>
<td>Day 5 after surgery</td>
<td>59/4693 (1.3)</td>
<td>27/4739 (0.6)</td>
<td>0.7</td>
<td>&lt;0.001</td>
<td></td>
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<tr>
<td>Day 6 after surgery</td>
<td>43/4674 (0.9)</td>
<td>25/4736 (0.5)</td>
<td>0.4</td>
<td>0.03</td>
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<tr>
<td>Day 7 after surgery</td>
<td>39/4667 (0.8)</td>
<td>22/4731 (0.5)</td>
<td>0.3</td>
<td>0.03</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Day 8 after surgery</td>
<td>20/2623 (0.8)</td>
<td>14/2662 (0.5)</td>
<td>0.3</td>
<td>0.29</td>
<td></td>
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<tr>
<td>Day 9 after surgery</td>
<td>15/2617 (0.6)</td>
<td>14/2660 (0.5)</td>
<td>0.1</td>
<td>0.82</td>
<td></td>
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<tr>
<td>Day 10 after surgery</td>
<td>14/2614 (0.5)</td>
<td>12/2657 (0.5)</td>
<td>0.0</td>
<td>0.67</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

* Among patients who were alive and had not already had life-threatening or major bleeding, we determined the risk of the composite of life-threatening or major bleeding until day 30, starting on the day of surgery and then on each subsequent day. We also determined the absolute increase in risk among patients in the aspirin group and the P value for the comparison between aspirin and placebo. This allows the inference that, for example, if aspirin is started on the day of surgery, the cumulative incremental risk of bleeding attributable to aspirin over the next 30 days is 1.2%. If aspirin had been started on day 4 after surgery, the cumulative incremental risk over the next 26 days would be 0.9%, and so forth. Starting on day 8 after surgery, the sample was restricted to patients in the initiation stratum because all patients in the continuation stratum stopped taking the study drug in the aspirin trial on day 8 after surgery and resumed their regular aspirin regimen.

†† Percentages were calculated with the use of the Kaplan–Meier method.
Conclusion

Aspirin did not prevent the primary composite outcome of death and non fatal MI but did increase risk of bleeding
Annals of Internal Medicine

Original Research

Aspirin in Patients With Previous Percutaneous Coronary Intervention Undergoing Noncardiac Surgery

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Figure 1. Study flow diagram.
Figure 2. Effect of aspirin on risk for composite of death and nonfatal myocardial infarction among patients with a history of percutaneous coronary intervention.

Figure 3. Effect of aspirin on risk for major bleeding among patients with a history of percutaneous coronary intervention.

$P$ for interaction $= 0.036$.

$P$ for interaction $= 0.73$. 
<table>
<thead>
<tr>
<th>Outcome</th>
<th>Aspirin</th>
<th>Placebo</th>
<th>Absolute risk diff</th>
<th>HR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality or MI</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall trial</td>
<td>7.0%</td>
<td>7.1%</td>
<td>0.1%</td>
<td>0.99 (.96-1.15)</td>
<td>0.036</td>
</tr>
<tr>
<td>No prior PCI</td>
<td>7.1%</td>
<td>6.9%</td>
<td>-0.2%</td>
<td>1.03 (.89-1.20)</td>
<td></td>
</tr>
<tr>
<td>Prior PCI</td>
<td>6.0%</td>
<td>11.5%</td>
<td>5.5%</td>
<td><strong>0.50 (.26-95)</strong></td>
<td></td>
</tr>
<tr>
<td>MI</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall trial</td>
<td>6.2%</td>
<td>6.3%</td>
<td>0.1%</td>
<td>0.98 (.84-1.15)</td>
<td>0.021</td>
</tr>
<tr>
<td>No prior PCI</td>
<td>6.2%</td>
<td>6.1%</td>
<td>-0.2%</td>
<td>1.03 (.88-1.21)</td>
<td></td>
</tr>
<tr>
<td>Prior PCI</td>
<td><strong>5.1%</strong></td>
<td><strong>11.0%</strong></td>
<td><strong>5.9%</strong></td>
<td><strong>0.44 (.22-87)</strong></td>
<td></td>
</tr>
<tr>
<td>Major or life threatening bleeding</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.86</td>
</tr>
<tr>
<td>Overall trial</td>
<td>6.3%</td>
<td>5.1%</td>
<td>-1.1</td>
<td>1.22 (1.03-1.44)</td>
<td></td>
</tr>
<tr>
<td>No prior PCI</td>
<td>6.3%</td>
<td>5.2%</td>
<td>-1.1</td>
<td>1.21 (1.03-1.44)</td>
<td></td>
</tr>
<tr>
<td>Prior PCI</td>
<td><strong>5.6%</strong></td>
<td><strong>4.2%</strong></td>
<td><strong>-1.3</strong></td>
<td><strong>1.26 (.55-2.88)</strong></td>
<td></td>
</tr>
</tbody>
</table>

Limitations: Nonspecified subgroup analysis, small sample – only addresses prior PCI (not other cardiac pts)

NNT: 18
Conclusion

Peri-operatively, for patients with prior PCI continue aspirin is beneficial.

The bleeding risk was not statistically significant.
55 yr old male with history of T2DM, HTN, CAD with a bare metal stent that was placed 1 year ago presents to your clinic with a ventral hernia. He wants to get his ventral hernia repaired. His medications include aspirin, metformin, carvedilol, clopidogrel, lisinopril and atorvastatin. Besides continuing atorvastatin, which of these will be beneficial in the perioperative period.

A. Aspirin
B. Lisinopril
C. Metformin
D. Clopidogrel
80 yr old female with HTN, COPD presents to the ER at 10 pm on a Friday with a fall that caused a hip fracture on the right side. Orthopedic surgeon wants to delay the procedure till Monday. Which of these are not one of the complications due to the delay?

A. 30 day mortality
B. Deep Venous Thrombosis
C. Pulmonary Embolism
D. Myocardial Infarction
E. 90 day mortality.
Objective: to identify the optimal time window in which to conduct hip fracture surgery before the risk of complications increases

Methods:
• Retrospective cohort study of adult hip fracture patients
• 42,230 patients at 72 hospitals in Ontario Canada (2009-2014)
• Analyzed time elapsed from hospital arrival to surgery; identified time thresholds associated with complications
Association Between Wait Time and 30-Day Mortality in Adults Undergoing Hip Fracture Surgery

Results:

- Mean age: 80.1
- Women: 70.5%
- Mean time to surgery: 38.8 hours
- Overall mortality at:
  - 30-days: 7%
  - 90-days: 11%
  - 365-days: 20%

Probability of 30-day mortality according to wait times for surgery

34% of patients had surgery within 24 hrs

Association Between Wait Time and 30-Day Mortality in Adults Undergoing Hip Fracture Surgery

Results:
• In addition to 30-day mortality, other significant outcomes associated with delays over 24-hours:
  – Myocardial infarction
  – Pulmonary embolism (but not DVT)
  – Pneumonia
  – 90-day mortality
  – 365-day mortality
Association Between Wait Time and 30-Day Mortality in Adults Undergoing Hip Fracture Surgery

Limitations: Retrospective study, possible confounding

Conclusions and implications:
• 24-hour wait time seems to be the threshold for increased risk (mortality, complications)
• Prompt preoperative assessment is important
• Delaying surgery for medical optimization remains sensible...but what does that mean?

80 yr old female with HTN, COPD presents to the ER at 10 pm on a Friday with a fall that caused a hip fracture on the right side. Orthopedic surgeon wants to delay the procedure till Monday. Which of these are not one of the complications due to the delay?

A. 30 day mortality
B. Deep Venous Thrombosis
C. Pulmonary Embolism
D. Myocardial Infarction
E. 90 day mortality.
45 yr old female presents to the Emergency department with diarrhea occurring 5-6 times a day. She has no other past medical history. *Clostridioides difficile* testing is positive. What would be the appropriate treatment as an outpatient?

A. Metronidazole 500mg oral for 10 days
B. Metronidazole 500mg IV for 10 days as outpatient
C. Oral Cholestyramine
D. Oral Vancomycin 125mg qid for 10 days
E. IV Vancomycin for 10 days.
Background

- For 30 years, metronidazole and oral vancomycin have been the main antibiotic agents used in the treatment of CDI.
- Two RCTs conducted in the 1980s and 1990s that compared metronidazole therapy and vancomycin therapy found no difference in outcomes but included <50 patients per study arm.
Since 2000, additional randomized, placebo-controlled trials have shown that oral vancomycin was superior to metronidazole

Study 1: 150 patients, metronidazole vs. vancomycin
- Cure was superior for all patients given oral vancomycin (97%) compared to metronidazole (84%; P < .006).
- Clinical cure superiority was also observed in 69 patients with severe disease given vancomycin (97%) compared to metronidazole (76%; P = .02).
Background

- Study 2: an analysis of 2 multinational studies that compared the efficacy of tolevamer (n = 563), with oral vancomycin 125 mg 4 times daily (n = 266) and oral metronidazole 250 mg 4 times daily (n = 289).

- Metronidazole clinical response rates (72.7%) were also inferior to vancomycin (81.1%) response rates (P = .02).

- Combined, these RCTs published since 2000 demonstrated that metronidazole was inferior to oral vancomycin for clinical cure in patients with CDI (P = .002).
Table 1. Recommendations for the Treatment of *Clostridium difficile* Infection in Adults

<table>
<thead>
<tr>
<th>Clinical Definition</th>
<th>Supportive Clinical Data</th>
<th>Recommended Treatment*</th>
<th>Strength of Recommendation/ Quality of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial episode, non-severe</td>
<td>Leukocytosis with a white blood cell count &gt;15000 cells/mL and a serum creatinine level &lt;1.5 mg/dL</td>
<td>VAN, 125 mg 4 times per day by mouth for 10 days, OR FDX 200 mg given twice daily for 10 days</td>
<td>Strong/High</td>
</tr>
<tr>
<td>Initial episode, severe*</td>
<td>Leukocytosis with a white blood cell count of ≥15 000 cells/mL or a serum creatinine level &gt;1.5 mg/dL</td>
<td>VAN, 500 mg 4 times per day by mouth or by nasogastric tube. If ileus, consider adding rectal instillation of VAN. Intravenously administered metronidazole (500 mg every 8 hours) should be administered together with oral or rectal VAN, particularly if ileus is present.</td>
<td>Strong/Moderate (oral VAN); Weak/Low (rectal VAN); Strong/Moderate (intravenous metronidazole)</td>
</tr>
<tr>
<td>Initial episode, fulminant</td>
<td>Hypotension or shock, ileus, megacolon</td>
<td>VAN 125 mg given 4 times daily for 10 days if metronidazole was used for the initial episode, OR Use a prolonged tapered and pulsed VAN regimen if a standard regimen was used for the initial episode (eg, 125 mg 4 times per day for 10–14 days, 2 times per day for a week, once per day for a week, and then every 2 or 3 days for 2–8 weeks), OR FDX 200 mg given twice daily for 10 days if VAN was used for the initial episode</td>
<td>Weak/Low</td>
</tr>
<tr>
<td>First recurrence</td>
<td>…</td>
<td>VAN in a tapered and pulsed regimen, OR VAN, 125 mg 4 times per day by mouth for 10 days followed by rifaximin 400 mg 3 times daily for 20 days, OR FDX 200 mg given twice daily for 10 days, OR Fecal microbiota transplantation*</td>
<td>Weak/Low</td>
</tr>
<tr>
<td>Second or subsequent recurrence</td>
<td>…</td>
<td>…</td>
<td>Weak/Low</td>
</tr>
</tbody>
</table>

Abbreviations: FDX, fidaxomicin; VAN, vancomycin.

*All randomized trials have compared 10-day treatment courses, but some patients (particularly those treated with metronidazole) may have delayed response to treatment and clinicians should consider extending treatment duration to 14 days in those circumstances.

*The criteria proposed for defining severe or fulminant *Clostridium difficile* infection (CDI) are based on expert opinion. These may need to be reviewed in the future upon publication of prospectively validated severity scores for patients with CDI.

*The opinion of the panel is that appropriate antibiotic treatments for at least 2 recurrences (ie, 3 CDI episodes) should be tried prior to offering fecal microbiota transplantation.
45 yr old female presents to the Emergency department with diarrhea occurring 5-6 times a day. She has no other past medical history. Clostridium difficile testing is positive. What would be the appropriate treatment as an outpatient?

A. Metronidazole 500mg oral for 10 days
B. Metronidazole 500mg IV for 10 days as outpatient
C. Oral Cholestyramine
D. Oral Vancomycin 125mg qid for 10 days
E. IV Vancomycin for 10 days.
Take Home Points

Hydrocortisone shortens the duration of septic shock

Adding Fludrocortisone with Hydrocortisone may improve survival if continued for a total of 7 days

Lactated Ringer likely has a role in reducing MAKE

Pulmonary Embolism should still be in a differential for syncope but likely not as prevalent the PESIT trial made it out to be

Edoxaban could be used in patients with cancer induced VTE
Take Home Points

Aspirin should be continued in patients for those that have a h/x of PCI undergoing surgery.

Delaying surgery over 24 hours for hip repair seems to be associated with higher mortality and complications.

Oral metronidazole is no longer recommended as the first choice for treating mild C diff.
References


Mcdonald L et al, Clostridium difficile; *Clinical Infectious Diseases*.2018:66 (April 1)
QUESTIONS?

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