Update in Hospital Medicine

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Financial disclosures
None
Objectives

1. Critique recent literature relevant to the care of a hospitalized internal medicine patient.

2. Present new research in hospital medicine that may impact your practice.

Literature selection

Sept 2015 to Sept 2016
Studies relevant to hospital medicine

Case based scenarios
Outline

• Rock N’ Roll
• C. diff testing
• Rate vs. Rhythm post-op
• Aspirin in cardiac surgery
• Over treatment HTN

• Quick hits

Case #1
A patient with recurrent kidney stones asks you for a "natural" way to treat them?

You recommend:

A) Avoid cola
B) Stop taking HCTZ
C) Increase hydration
D) Take a trip to Disneyland
E) All of the above

You are asked to consult on anticoagulation management in the peri-operative setting.
Sitting in the back was better--more jolting

Case #2
A 65yo F with recent treatment with Levofloxacin for pneumonia returns to hospital from skilled nursing facility with non-bloody diarrhea, abdominal pain, and leukocytosis of 17,800.

You suspect *Clostridium difficile* infection.

What is the next best step in making a diagnosis of *C. diff*?

A) Avoid testing, start treatment?
B) Stool *C. diff* toxin?
C) Stool *C. diff* PCR?
D) Bring in the dog?

Cliff--83% sensitivity

*BMJ* 2012; 345
Background

- *C. difficile* infection recognized as important HAI.
- Diarrheal illness following antibiotic exposure allowing overgrowth of *C. diff*.
- Severity mediated by *C. diff* toxin load.

Diagnosis is clinical supported by testing.

EIA toxin testing 2000-2009

PCR testing ~2009

Asymptomatic *C. diff* colonization is common.

- 3-7% healthy folks
- 5-15% hospitalized patients
- ~50% healthcare facility residents

Growing evidence that PCR testing leads to over diagnosis and treatment

- Detects asymptomatic *C. diff*
- Low positive predictive value for true disease.
- Paradoxical increased direct and indirect costs.
- Public health and policy implications.
- ~50% hospitals use PCR exclusively
Overdiagnosis of *Clostridium difficile* Infection in the Molecular Test Era

Christopher R. Polage, MD, MAS; Clare E. Gyorke, BS; Michael A. Kennedy, BS; Jhansi L. Leslie, BS; David L. Chin, PhD; Susan Wang, BS; Hien H. Nguyen, MD, MAS; Bin Huang, MD, PhD; Yi-Wei Tang, MD, PhD; Lenora W. Lee, MD; Kyoungmi Kim, PhD; Sandra Taylor, PhD; Patrick S. Romano, MD, MPH; Edward A. Panacek, MD, MPH; Parker B. Goodell, BS, MPH; Jay V. Solnick, MD, PhD; Stuart H. Cohen, MD

**Design**

• Single center prospective observational trial.

- 1416 patients
Results

- Longer and more severe diarrhea
- More *C. diff* related complications
- Health care facility
- WBC>15,000

Tox-/PCR+ have same clinical outcomes as Tox-/PCR- patients
Commentary

• Tox-/PCR+ same clinical course at Tox-/PCR-
• Consider C. diff treatment only in Tox+/PCR+ patients
• Hospitals using PCR need to develop two-step confirmatory testing with Toxin assay as well.

What is the next best step in making a diagnosis of C. diff?

A) Avoid testing, start treatment?
B) Stool C. diff toxin?
C) Stool C. diff PCR?
D) Bring in the dog?

Cliff--83% sensitivity
BMJ 2012; 345
Quick Hit

Result

- DB-RCT
- ~500 patients each arm
- Addition of TMP/SMX to standard abscess drainage had better cure rate than placebo (92% vs. 85%, P<0.001)
A 74yo M with diabetes, HTN and CAD is post-op day #1 from open heart surgery when he develops Atrial Fibrillation at a rate of 110.

He has been in A-fib for about 2 hours.

He is otherwise asymptomatic and hemodynamically stable.
What is the best first step for post-cardiac op A-fib?

A) Ignore it, it will go away.
B) Use beta-blockers or calcium channel blockers?
C) Direct current cardioversion?
D) Start Amiodarone?
Background

- Atrial fibrillation 20-50% after cardiac surgery.

- Post-op Afib associated more death, cost, complications, and LOS.

- No preventative strategy exists.

- Must manage it--rate control vs. rhythm control.

AFFIRM trial: Rate control vs. Rhythm control in non-surgical patients.
(NEJM 2002; 347:1825-33)

Rhythm control:
- No survival benefit.
- Increased hospitalizations.
- Adverse drug side effects.

Current joint guidelines from ACC/AHA recommend rate control first for post-op A-fib
(January CT et al. “AHA/ACC/HRS guideline for the management of patients with atrial fibrillation...” Circulation 2014; 130(23): 199-267.)
Background

• Rate vs. Rhythm control unclear in cardiac surgery population.

• Wide practice variation.
**Design**

- Multi-site randomized cohort prospective trial.
- 523 patients
- Rate control with drugs vs. Rhythm control with Amiodarone +/- DC cardioversion.

**Outcome**

- LOS
- Percent with Afib at 7d, 30d, 60d
- Death
- Serious adverse events-bleeding and clotting

**Inclusion**

- Post-op Afib >60 min

**Exclusion**

- Prior history of Afib
**Study protocol**

Rate control
- Beta-blocker (~60%) or CCB (~20%) for goal HR <100.
- Could be switched to rhythm arm at provider discretion.
- If A-fib >48hrs --> Warfarin

Rhythm control
- Amiodarone +/- AV nodal blocker
- If A-fib >24-48hr --> DC cardioversion.
- If A-fib >48hrs --> Warfarin

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**Results**

<table>
<thead>
<tr>
<th>Patient</th>
<th>% A-fib</th>
</tr>
</thead>
<tbody>
<tr>
<td>All (695/2109)</td>
<td>33%</td>
</tr>
<tr>
<td>CABG</td>
<td>28.1%</td>
</tr>
<tr>
<td>Valve</td>
<td>33.7%</td>
</tr>
<tr>
<td>Combo</td>
<td>47.3%</td>
</tr>
</tbody>
</table>

~25% of patients crossed over in each arm.
Results

No differences between groups in any adverse outcome including:
- Bleeding
- Stroke/TIA
- Heart failure
- Warfarin misadventures
- Others...

### Table 3. Hospitalization and Readmission.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Rate Control (N = 262)</th>
<th>Rhythm Control (N = 261)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hospitalization</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No. of days in hospital from randomization to 60 days</td>
<td>5.1 (3.0–7.4)</td>
<td>5.0 (3.2–7.3)</td>
<td>0.76</td>
</tr>
<tr>
<td>After isolated CABG</td>
<td>4.8 (3.0–7.7)</td>
<td>5.1 (3.1–6.8)</td>
<td>0.96</td>
</tr>
<tr>
<td>After isolated valve repair or replacement</td>
<td>5.0 (2.6–7.1)</td>
<td>4.4 (3.1–7.0)</td>
<td>0.76</td>
</tr>
<tr>
<td>After CABG plus valve repair or replacement</td>
<td>5.3 (4.2–8.4)</td>
<td>7.1 (4.4–9.7)</td>
<td>0.11</td>
</tr>
<tr>
<td>No. of days of index hospitalization after randomization</td>
<td>4.3 (2.9–6.6)</td>
<td>4.3 (3.0–7.0)</td>
<td>0.88</td>
</tr>
<tr>
<td>No. of days from randomization to eligibility for cardiac discharge*</td>
<td>4.0 (2.0–6.0)</td>
<td>4.0 (3.0–6.0)</td>
<td>0.99</td>
</tr>
<tr>
<td>No. of days in hospital after discharge from index hospitalization</td>
<td>2.2 (0.6–5.0)</td>
<td>2.1 (1.0–4.7)</td>
<td>0.82</td>
</tr>
<tr>
<td><strong>Readmission</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any cause</td>
<td>79 (18.5)</td>
<td>80 (18.5)</td>
<td>0.99</td>
</tr>
<tr>
<td>Emergency department visit</td>
<td>28 (6.5)</td>
<td>24 (5.6)</td>
<td>0.55</td>
</tr>
<tr>
<td>Hospital stay of &lt;24 hr</td>
<td>5 (1.2)</td>
<td>4 (0.9)</td>
<td>0.73</td>
</tr>
<tr>
<td>Rehospitalization</td>
<td>46 (10.8)</td>
<td>52 (12.0)</td>
<td>0.58</td>
</tr>
<tr>
<td>Cardiovascular cause</td>
<td>29 (6.8)</td>
<td>35 (8.1)</td>
<td>0.48</td>
</tr>
<tr>
<td>Treatment of atrial fibrillation</td>
<td>11 (2.6)</td>
<td>17 (3.9)</td>
<td>0.27</td>
</tr>
<tr>
<td>Other cardiovascular reason</td>
<td>18 (4.2)</td>
<td>18 (4.2)</td>
<td>0.97</td>
</tr>
<tr>
<td>Noncardiovascular cause</td>
<td>50 (11.7)</td>
<td>43 (10.4)</td>
<td>0.57</td>
</tr>
</tbody>
</table>
Commentary

• Largest and best designed trial to date on this topic
• No difference between any meaningful markers
• Did not assess quality of life measures

• Recommend conservative approach
• Start with RATE control before moving to rhythm.
• Avoid costs and potential procedural complications from cardioversion.


What is the best first step for post-cardiac op A-fib?

A) Ignore it, it will go away.
B) Use beta-blockers or calcium channel blockers?
C) Direct current cardioversion?
D) Start Amiodarone?
Quick Hit

Result
No benefit in pain at 1 week from addition of Cyclobenzaprine OR Oxy/Aceta over Naproxen alone
Case #4

70yo M with diabetes, CKD stage III (Cr 2), HTN, had knee surgery 2 years ago, now needs CABG.

You are asked to do the pre-op evaluation.

He takes a daily Aspirin, statin, insulin, and metoprolol.

What are your recommendations regarding the Aspirin?

A) Continue Aspirin?

B) Hold Aspirin for 5 days pre-op and restart day after surgery?

C) Hold Aspirin day of surgery and for 1 week post-op?

D) Stop Aspirin now and forever?
Background

• Most patients with CAD are on Aspirin (ASA) to prevent thrombotic complications.

• ASA also presents theoretical bleeding risk.

• Variability in how aspirin is prescribed peri-operatively.
  - ASA often held 5d pre-op and restarted 24hr after CABG.

• Role of cardiac surgery peri-operative aspirin has not been rigorously tested to date.

Background

• Role of peri-operative aspirin in non-cardiac surgery HAS been studied. POISE-2 trial.

• Peri-operative ASA in non-cardiac surgery had no cardiac protective benefit but did increase bleeding risk.

Devereaux, PJ et al. “Aspirin in Patients Undergoing Noncardiac Surgery” NEJM 370; 16 April 17, 2014
Background

2015 meta-analysis

Aspirin and coronary artery surgery: a systematic review and meta-analysis
S. Hastings¹, P. Myles¹,² and D. McIlroy¹,²

• 13 randomized trials (1985-2013)
• 2399 patients

Pre-op ASA
• Reduced risk of MI (OR 0.56)
• Increased bleeding
  • Chest tube drainage (+168 ml)
  • RBC transfusion (+141 ml)
  • Surgical re-exploration (OR 1.85)

Authors state included studies of poor methodological merit.
Design
- Multi-center RDBCT
- 2127 patients 2x2 design
Outcome

• Primary composite
• Death, MI, CVA, renal failure, PE, bowel infarction

• Major bleeding leading to reoperation
• Cardiac tamponade

Results

30 day outcomes

<table>
<thead>
<tr>
<th>Event</th>
<th>Aspirin (N = 1047)</th>
<th>Placebo (N = 1053)</th>
<th>Risk Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary outcome: death, myocardial infarction, stroke, renal failure, pulmonary embolism, or bowel infarction — no./total no. (%)</td>
<td>202/1046 (19.3)</td>
<td>215/1052 (20.4)</td>
<td>0.94 (0.80–1.12)</td>
<td>0.55</td>
</tr>
<tr>
<td>Death</td>
<td>14 (1.3)</td>
<td>9 (0.9)</td>
<td>1.56 (0.68–3.60)</td>
<td>0.30</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>144 (13.8)</td>
<td>166 (15.8)</td>
<td>0.87 (0.71–1.07)</td>
<td>0.20</td>
</tr>
<tr>
<td>Stroke</td>
<td>14 (1.3)</td>
<td>12 (1.1)</td>
<td>1.17 (0.55–2.52)</td>
<td>0.70</td>
</tr>
<tr>
<td>Renal failure</td>
<td>49 (4.7)</td>
<td>41 (3.9)</td>
<td>1.20 (0.80–1.80)</td>
<td>0.39</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>8 (0.8)</td>
<td>10 (1.0)</td>
<td>0.81 (0.12–2.03)</td>
<td>0.81</td>
</tr>
<tr>
<td>Bowel infarction</td>
<td>0</td>
<td>2 (0.2)</td>
<td>—</td>
<td>0.50</td>
</tr>
<tr>
<td>Reoperation for hemorrhage — no. (%)</td>
<td>19 (1.8)</td>
<td>22 (2.1)</td>
<td>0.87 (0.47–1.60)</td>
<td>0.75</td>
</tr>
<tr>
<td>Cardiac tamponade — no. (%)</td>
<td>11 (1.1)</td>
<td>4 (0.4)</td>
<td>2.77 (0.88–8.66)</td>
<td>0.08</td>
</tr>
</tbody>
</table>

Myles, PS et al. “Stopping vs. Continuing Aspirin before Coronary Artery Surgery” NEJM 374; 8 Feb 25, 2016
Commentary

• No difference between ASA or placebo for complication prevention.
• Results conflict with prior meta-analysis.
• Largest single RCT.

• Leaning towards continuing ASA pre-op.

Myles, PS et al. “Stopping vs. Continuing Aspirin before Coronary Artery Surgery” NEJM 374; 8 Feb 25, 2016
SUMMARY AND COMMENT

Point-of-Care Ultrasound in Cardiac Arrest

Absence of cardiac activity by POCUS is a grim sign.

Result

- 6,420 vaccinated vs. 36,357 unvaccinated post-op Kaiser surgical patients.
- No difference in:
  - Fever
  - Infection
  - Inpatient visits
Case #5

54yo M admitted for gallstone pancreatitis has a blood pressure of 185/76 on routine vitals check.

He has NO chest pain, SOB, visual changes or neurologic findings.

The bedside RN asks you to address his in-hospital hypertension based on a “call MD if SBP>170” order.

What do you order to treat his blood pressure?

A) No orders, provide reassurance
B) Clonidine 0.2mg po prn SBP>180
C) Hydralazine IV
D) Transfer to ICU for intensive management
Background

- Asymptomatic blood pressure elevations are common in hospitalized patients.
- Often treated with IV anti-hypertensives.
- No evidence that short term treatment has benefits.
- Too rapid lowering of BP can be detrimental.
- Oral regimens may be more appropriate and cost effective.

Design

• Single center retrospective review
• 800 bed, urban training hospital

Inclusion

• Nov 2010-Jan 2011
• All patients with an order for IV hydralazine, enalaprilat, labetalol, or metoprolol.

Exclusion

• <18, >89 y.o.
• ICU/CCU
• Target organ injury

Outcomes

• How many patients received IV BP meds
• Use of IV vs PO adjustments

• Adverse events
• >25% drop in BP center retrospective review
• Need for IV fluids
• Holding other BP meds
• Change in level of care
• End organ damage.
• Tachy or bradycardia
Results

Variability in MD ordering and RN administration practice

**TABLE 2. Blood Pressure Criteria in Orders**

<table>
<thead>
<tr>
<th>BP Criteria for Administration of IV Antihypertensive, mm Hg</th>
<th>Did Not Receive IV Antihypertensive, n (%)</th>
<th>Did Receive IV Antihypertensive, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP &gt;120</td>
<td>2 (28)</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>SBP &gt;130</td>
<td>2 (28)</td>
<td>9 (6.8)</td>
</tr>
<tr>
<td>SBP &gt;140</td>
<td>2 (28)</td>
<td>5 (3.8)</td>
</tr>
<tr>
<td>SBP &gt;150</td>
<td>4 (5.6)</td>
<td>8 (6)</td>
</tr>
<tr>
<td>SBP &gt;160</td>
<td>27 (38)</td>
<td>58 (43.7)</td>
</tr>
<tr>
<td>SBP &gt;170</td>
<td>26 (35.6)</td>
<td>29 (21.8)</td>
</tr>
<tr>
<td>SBP &gt;180</td>
<td>8 (11.4)</td>
<td>18 (13.5)</td>
</tr>
<tr>
<td>SBP &gt;200</td>
<td>-</td>
<td>4 (3)</td>
</tr>
<tr>
<td>DBP &gt;100</td>
<td>-</td>
<td>1 (0.7)</td>
</tr>
</tbody>
</table>
**Results**

Change in BP control when oral regimen was adjusted
**Results**

Adverse outcomes

56/172 (32.6%) had BP drop >25%
-2 needed IVF
-6 had oral BP med held
-13 with HR >100 bpm
-1 bradycardia
-no transfer to higher level or new end organ damage

**Commentary**

Treatment of asymptomatic BP in hospitalized patients is common but practice is non-standardized and arbitrary.

Use of IV meds have downstream adverse events.

IV meds increase direct and indirect costs ($10-100x).

Oral med regimen adjustments should be first line in hospital.
54yo M admitted for gallstone pancreatitis has a blood pressure of 185/76 on routine vitals check.

He has NO chest pain, SOB, visual changes or neurologic findings.

The bedside RN asks you to address his in-hospital hypertension based on a “call MD if SBP>170” order.

What do you order to treat his blood pressure?

A) No orders, provide reassurance

B) Clonidine 0.2mg po prn SBP>180

C) Hydralazine IV

D) Transfer to ICU for intensive management

Summary

START
• Using C. diff toxin first, as part of a two step testing process.
• Begin with AV nodal blockade in post-op Afib.
• Continue ASA pre-op for cardiac surgery.
• TMP/SMX to drained abscesses suspicious for MRSA.
• Influenza vaccines in post-op patients.

STOP
• Routine IV anti-hypertensives for asymptomatic in-hospital hypertension.
• Using Cyclobezaprine and/or Oxy/Acetaminophen as adjuncts to anti-inflammatories in acute low back pain.
Thank you!

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