Update in Hospital Medicine 2012

• Updated literature since March 2011

Process:
• CME collaborative review of journals
  • Including ACP J. Club, J. Watch, etc.
• Five hospitalists ranked articles
  • Definitely include, can include, don’t include
• Limited articles covered by others

Chose articles if they will:
1) Change, modify, or confirm your practice.

• Hope to limit the use of the words
  • Markov model, Kaplan-Meier, Student’s t-test
• Focus on breadth, not depth
Update in Hospital Medicine 2012

- Major reviews/short takes
- Three cases
- Multiple choice questions

Case Presentation

On a busy on-call day your resident approaches you to present a case.

He describes a 63 year-old man with a history of HTN who presented with a few hours of shortness of breath and a new cough. At triage, he was afebrile, had a heart rate of 105, respiratory rate of 28, and a normal oxygen saturation.

The evaluation in the ED was negative – unremarkable exam, negative troponin x 2, normal EKG, normal CXR.
Case Presentation

The resident states “So, we thought about PE but he feels fine now – his shortness of breath has resolved and his heart rate is 60-70 and he is breathing at 14. If we use the normal vitals, his Wells and Geneva are basically negative. I was just going to have the ED discharge him.”

How do you respond to the resident?

Vital Signs in PE

Question: Does normalization of vital signs in the ED help rule out PE?
Design: Prospective, obs study, 1 med center; Pts who got a CT scan for PE; vital signs at triage & per standard of care; Follow-up at 45 & 90 days

Results

- Prevalence of PE was 18% (35/192)
- Most pts got 2, 3, or 4 sets of vitals

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**Vital Signs in PE**

**Question:** Does normalization of vital signs in the ED help rule out PE?

**Design:** Prospective, obs study, pts eval for PE in ED, vitals at triage & per protocol

**Conclusion:** Overall PE prevalence = 18%; no single vital predicted PE; normalization of vitals did not rule out PE in the ED

**Comment:** Small study, may be missing pts who didn’t get CT because of normalization of vitals. Many clinicians use vital sign normalization. Prediction rules use **most abnormal** vital sign during evaluation

How do you respond to the resident regarding this patient?

A. Why don’t we get a d-dimer, that could help us to rule out PE.
B. If the vitals have normalized, it is unlikely to be a PE – sounds like a plan.
C. You know, you can’t trust that the vitals have normalized – it still could be PE.
D. Great job using clinical prediction rules and evidence-based medicine, I like your plan.
E. You fist bump the resident, state “Block it baby! Yeah!” And then blow it up.

Case Presentation

After reviewing this article, you decide to perform a CT scan and the patient has an acute subsegmental pulmonary embolism.

You find him ambulating around his room with normal vital signs including a heart rate of 65, respiratory rate of 16, and an oxygen saturation of 98% on room air.

His physical exam is normal and he asks you if he can take the blood thinners at home rather than staying in the hospital.

How do you know if he is safe to be treated as an outpatient?

A. If he has a negative troponin and BNP <100.
B. He has a normal respiratory rate and oxygen saturation on room air.
C. No evidence of right heart strain on echocardiogram.
D. If he is low risk using a severity scoring system.
E. If he has said goodbye to his wife and kids and is ready to meet his maker.

Outpatient vs. Inpatient PE

Question: Can patients with acute pulmonary embolism be managed as outpatients?

Design: Randomized trial, 19 EDs; pts with acute PE, low risk; inpt vs. outpt

- Low risk defined by PESI Score

Pulmonary Embolism Severity Index

- Age > 80
- Male Gender
- History of Cancer, HF, COPD
- Pulse > 110 bpm
- Systolic BP < 100
- Respiratory Rate > 30 bpm
- Temperature < 36
- Altered Mental Status
- Arterial oxygen sat < 90%

Low risk = 0-2 risk factors

Outpatient vs. Inpatient PE

Question: Can patients with acute pulmonary embolism be managed as outpatients?

Design: Randomized trial, 19 EDs; pts with acute PE, low risk; inpt vs. outpt

- Low risk defined by PESI Score
- All received ≥ 5 days of LMWH & 90 days of oral anticoagulation
- Excluded if hypoxic, hypotensive, etc. or patients unable to participate

Results

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### Results

- A total of 344 patients randomized

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<td>3.9 days</td>
<td>p &lt;0.001</td>
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### Outpatient vs. Inpatient PE

**Question:** Can patients with acute pulmonary embolism be managed as outpatients?

**Design:** Randomized trial, 19 EDs; pts with acute PE, low risk; inpt vs. outpt

**Conclusion:** Outpt not inferior to inpt; similar rates of recurrent VTE & bleeding; LOS much shorter with outpt treatment

**Comment:** Small study, not real-life management; long LOS for hospitalized pts?

- Raises question of outpt management of PE
- Likely not ready for prime time
- But, use PESI to consider earlier discharge


### How do you know if he is safe to be treated as an outpatient?

- A. If he has a negative troponin and BNP <100.
- B. He has a normal respiratory rate and oxygen saturation on room air.
- C. No evidence of right heart strain on echocardiogram.
- D. If he is low risk using a severity scoring system.
- E. If he has said goodbye to his wife and kids and is ready to meet his maker.
Case Continued

The patient is low risk but you are (appropriately) anxious about discharging that day. He is started on LMWH and warfarin.

The following morning the medical student presents the case and at the end states, “So for GI prophylaxis, the patient was started on a proton pump inhibitor.”

What do you think about this choice for GI prophylaxis?

Acid-Suppression & Nosocomial GI Bleeding

Question: For non-ICU inpatients, do PPIs or H2 blockers lower the incidence of nosocomial GI bleeding?

Design: Observational cohort study; 78,394 adult inpatients; compared PPI or H2 blocker usage to no therapy; Standard definition for nosocomial GI bleeding

Results

- Incidence of nosocomial UGIB: 0.29%
- Incidence of clinically significant UGIB: 0.22%

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Controlled for anticoagulation Independent of DVT prophylaxis

### Results

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<td>Clin Sig UGIB</td>
<td>0.58 (0.37-0.91)</td>
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*With propensity scoring*

- Incidence of nosocomial UGIB: 0.29%
- Incidence of clinically significant UGIB: 0.22%

Herzig, SJ et al. *Arch Int Med*. 2011;171:991

### Acid-Suppression & Nosocomial GI Bleeding

**Question:** For non-ICU inpatients, do PPIs or H2 blockers lower the incidence of nosocomial GI bleeding?

**Design:** Observational cohort study, 79,287 adult inpatients; compared PPI or H2 vs. nothing

**Conclusion:** Incidence of nosocomial UGIB out of the ICU very low; PPI or H2 blockers reduced bleeding; independent of DVT proph

**Comments:** Retrospective, administrative data

Beneficial, but rare event and meds have costs/side effects; OK to continue if on it

Not routinely use GI proph. in non-ICU pts

Herzig, SJ et al. *Arch Int Med*. 2011;171:991

### What do you think about this choice for GI prophylaxis in this patient?

A. A PPI is a good choice.
B. Should go with an H2 blocker
C. Tums tums tums tums tums.
D. This patient should not get GI prophylaxis.
E. You’re staring at your Nexium pen, your Wyeth badge holder, and your Pfizer breath mints (why breath mints?) with fond memories of that fancy Aciphex® dinner and wonder what to do...

### Short Take: Proton Pump Inhibitors

In a systematic review, proton pump inhibitors are associated with an increased susceptibility to:

- *Clostridium difficile*-associated diarrhea
- *Salmonella*
- *Campylobacter*

Summary

**Definitely**
1) Don’t use normalization of vital signs in the ED to rule out pulmonary embolism.
2) Don’t routinely give GI prophylaxis to non-ICU medical inpatients.

**Consider**
1) Using the PESI score to determine low-risk in patients with PE.
2) Why patients are on PPIs as they can increase the risk for *C diff*.

Case Presentation

A 62 year-old woman with a history of HTN, CAD, and COPD presented with three days of shortness of breath and productive cough. She has had four COPD exacerbations this year.

After discussing her past medical history (PMH), you learn that she has been taking metoprolol 50mg twice a day. You wonder, what is the impact of her long-term β-blocker use on her COPD?

Short Take: COPD & β-blockers

In a Scottish cohort of ~ 6000 patients with known COPD, after controlling for other variables, β-blocker use (vs. no β-blocker) was associated with fewer COPD exacerbations and lower mortality.

β-blockers are safe in patients with COPD and may be beneficial. Long-term b-blockers should be continued.

“Half of what you’ll learn in medical school will be shown to be either dead wrong or out of date within five years of your graduation.....

.....the trouble is that nobody can tell you which half”

David Sackett

Case Presentation

The 62-year-old woman is continued on her β-blocker and admitted with a COPD exacerbation.

She is started on nebulized β-agonists and α-cholinergics as well as antibiotics and steroids.

Given the systemic steroids, she is at risk for hyperglycemia. In hospitalized patients, what is your goal blood sugar?

In hospitalized patients, what is your goal blood sugar?

A. 60-80 mg/dL
B. 80-110 mg/dL
C. 110-150 mg/dL
D. 140-200 mg/dL
E. Anything less than 300 mg/dL
F. I just let it ride. She probably has CHF and glucose is a “natural” diuretic.

Goal Blood Sugar in the Hospital

Question: What are the benefits and harms of intensive insulin therapy in the hospital?
Design: Syst. review & meta-analysis; 21 trials, 14,768 pts (ICU, periop, MI, stroke)

- All RCT of “strict” vs. “less strict”
- “Strict” = goal 80-110 mg/dL

Results

- No Impact on Short Term Mortality
- No Impact on Infection Rates
- No Impact on Length of Stay
- No Impact on Need for Dialysis
- Six fold increased risk of hypoglycemia
- True for all hospital settings/diseases


Goal Blood Sugar in the Hospital

**Question:** What are the benefits and harms of intensive insulin therapy in the hospital?

**Design:** Syst. Review & meta-analysis; 21 trials, 14,768 pts (ICU, periop, MI, stroke)

**Conclusion:** Intensive insulin (80-110mg/dL) with no benefit over less strict; increased risk of hypoglycemia; true in all cases

**Comment:** Well-done but some evidence only moderate

No good RCT in non-ICU general medical patients

Intensive insulin is out (pendulum)

Goal of 140-200 mg/dL is reasonable.


In hospitalized patients, what is your goal blood sugar?

A. 60-80 mg/dL
B. 80-110 mg/dL
C. 110-150 mg/dL
D. 140-200 mg/dL
E. Anything less than 300 mg/dL
F. I just let it ride. She probably has CHF and glucose is a “natural” diuretic.

Case Presentation

You use meal-time and long-acting insulin to keep her blood sugar around 150 mg/dL.

She is slowly improving but on hospital day 3 she develops mild abdominal pain and diffuse watery diarrhea.

She has no fever and very mild tenderness on exam. Her WBC is 10,000 and her creatinine remains normal.

Her *C difficile* toxin returns positive. What is the optimal initial treatment?
What is the optimal initial treatment?

A. Fidoximicin PO
B. Vancomycin PO
C. Metronidazole PO
D. Clindamycin PO
E. Stool transplant

Comparing treatments for *C. difficile*

Question: What is the comparative effectiveness and harms of different antibiotic treatments for *C. difficile*?

Design: Systematic review of 11 RCTs

- Studies involved 1463 participants
- 3 compared metronidazole vs. vancomycin
- 8 compared another abx vs. metronidazole or vancomycin
- Strength of evidence *moderate* for:
  - Initial cure with metronidazole vs. vancomycin
  - Initial cure or recurrence with vancomycin vs. fidaxomicin


**Results**

Vancomycin vs. metronidazole (3 studies, 335 patients)

- Initial cure with vancomycin: 84-94%
- Initial cure with metronidazole 73-94%


Vancomycin vs. metronidazole (3 studies, 335 patients)

- Initial cure with vancomycin: 84-94%
- Initial cure with metronidazole 73-94%
- Recurrence with vancomycin 7-17%
- Recurrence with metronidazole 5-21%

Results

Vancomycin vs.
- Fidaxomicin (1 study, 629 patients)"
- Nitazoxanide (1 study, 50 patients)
- Bacitracin (1 study, 81 patients)

Metronidazole vs.
- Nitazoxanide (1 study, 142 patients)
- Metronidazole plus rifampin (1 study, 39 patients)

No difference in initial cure or recurrence

** Subgroup analysis of comparing fidaxomicin vs. vancomycin found decreased recurrence with fidaxomicin (15% vs. 25%, \( P = 0.005 \))


Comparing treatments for *C. difficile*

Question: What is the comparative effectiveness and harms of different antibiotic treatments for *C. difficile*?

Design: Systematic review of RCTs

Conclusion: No antibiotic is superior for initial cure with *C. diff*. Recurrence less common with fidaxomicin vs. vancomycin.

Comment: Well-done analysis but quality only moderate
Follow guidelines: metronidazole for mild-mod, PO vanco for severe *C diff.*
Role of fidoximicin unclear (cost)


What is the optimal initial treatment?

a. Fidoximicin PO
b. Vancomycin PO
c. Metronidazole PO
d. Clindamycin PO
e. Stool transplant

Short Take: Relapse vs. Reinfection

In a molecular typing experiment of patients with recurrent *C difficile* infection, the majority of cases were relapse and not new infection.

For recurrent episodes within 2 months, 88% were relapses. For those after 2 months, 65% were relapses.

**Short Take: Fecal transplant for C. Diff**

In a systematic review of 27 published articles involving 317 patients (all case series or case reports), intestinal microbiota transplantation (stool transplant) was successful in eradicating recurrent *C difficile* infection in 92% of cases.

Stay tuned for future randomized controlled trials.


**Summary**

**Definitely**

1) Continue β-blockers in patients with COPD.
2) Stop using intensive insulin therapy in hospitalized patients; a blood sugar goal of 140-200mg/dL seems reasonable.

**Consider**

1) Using metronidazole to treat *C difficile* colitis.
2) Most recurrent episodes of *C difficile* infection are relapses and not new infections.
3) Stool transplant in the future for refractory recurrent *C difficile* infection

**Case Presentation**

You are rounding on-call with your team and the intern presents a 48 year-old woman with metastatic breast cancer who was admitted with fever and confusion. Based on the evaluation, the team is concerned about a line infection.

She has borderline blood pressures despite an appropriate fluid resuscitation.

The intern states, “You know, we need to leave now to make our duty hours and we think she might need a pressor. Can you look up which is the best one in septic shock and start it if she continues to tank her pressures?”
How do you respond to the interns question about pressors in septic shock?

A. Dopamine is the best agent.
B. I’d go with phenylephrine (Neosynephrine®).
C. Definitely norepinephrine (Levophed®=“Leave-’em-dead”).
D. I like vasopressin.
E. You’re about to start in with a statement that begins with “Listen squirt” and references “when I was a resident . . .” But, instead you pause, sigh, ever-so-gently shake your head . . . and go to write the order.

Dopamine vs. Norepinephrine

Question: In patients with septic shock, what is the optimal first-line vasopressor agent, dopamine or norepinephrine?

Design: Meta-analysis of observational studies and RCTs; dopamine vs. norepinephrine

- Five observational studies, 1360 patients
- Six RCTs, 1408 patients


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• No difference in ICU LOS or hospital LOS
• Absolute risk reduction: ~ 3.5%

* p<0.05


### Dopamine vs. Norepinephrine

**Question:** In pts with septic shock, what is the optimal first-line pressor agent, dopamine or norepinephrine?

**Design:** Meta-analysis of observational studies and RCTs; dopamine vs. norepinephrine

**Conclusion:** Increased mortality with dopamine in septic shock in observational and RCTs; Arrhythmias more common with dopamine

**Comments:** Well done, good methodology;
- Use norepi as first-line agent in septic shock;
- Likely should be first-line in other shock;
- Work with ED/ICU providers.


### How do you respond to the interns question about pressors in septic shock?

A. Dopamine is the best agent.
B. I’d go with phenylephrine (Neosynephrine®).
C. Definitely norepinephrine (Levophed®="Leave-‘em-dead").
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### Short Take: Early v Late TPN

In a randomized, multi-center trial comparing early (day 2) to late (day 8) initiation of TPN in critically ill patients, late TPN was associated with:

- Better ICU and hospital survival
- Fewer infections
- Less time on the ventilator
- Lower healthcare costs

**Case Presentation**

You do not start TPN but continue the enteral feeding.

Unfortunately the patient does not do well. She is intubated, stays on norepinephrine and develops multi-organ system failure.

You meet with her husband (DPOA) describe her condition and state clearly “It is unlikely she will survive. That means she is likely to die.”

What do you think his estimated percent chance of survival is for her based on this statement?

- A. 0%
- B. 5%
- C. 50%
- D. 30%
- E. It is not effective to be quantitative with patients or surrogates as they may not understand.
- F. It was hard to come up with an appropriate “joke” answer for this one. But, if you’re the one person that has to answer F, go right ahead.

**Interpretation of Prognostic Information**

**Question:** How do surrogates interpret prognostic statements and why?

**Design:** Mixed qualitative/quantitative; 3 ICUs; Approached surrogates of critically ill patients; Asked to interpret 16 prognostic statements, estimate % survival

- Using a numeric probability scale (0-100%)
- Ranging from “he will definitely survive” to “definitely not”
- If discordant, asked why estimate was different

- Total of 80 surrogates included

Results

- Surrogates over-estimated prognosis when given survival estimates of < 50%.
- Some unaware of over-estimation.
- Four main explanations:

1) Need to express optimism.
2) Belief in patient’s fortitude.
3) Disbelief in physician ability to prognosticate.
4) Interpretation of prognosis as a “gist” and not a precise estimate.

Interpretation of Prognostic Information

Question: How do surrogates interpret prognostic statements and why?
Design: Mixed qualitative/quantitative; surrogates of critically ill pts; interpreted prognostic statements;
Conclusion: Surrogates inaccurately interpret poor prognostic statements; accurate with better prognoses; many complex reasons for this
Comments: Small study, hypotheticals on paper;
- Surrogates may be overly optimistic, be aware
- Not just about the misunderstanding;
- May need to address reasons for optimism
Case Presentation

You have a good discussion with the husband and after a few more days everyone agrees to withdraw care. She dies peacefully with her husband and two kids at her bedside.

The husband says very clearly that he wants an autopsy, “So you all can learn from taking care of her – she would have wanted that.”

What is the chance that an autopsy will find a major diagnosis which could have impacted treatment?

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Short Take: Autopsy ICU Patients

In a prospective single-center study of 834 autopsies in ICU patients revealed 7.5% had a major error which could have impacted treatment and 11.4% had major unexpected findings which would not have changed treatment.

The most common major diagnoses discovered were pulmonary embolism, pneumonia, secondary peritonitis, invasive aspergillus, endocarditis, and MI.


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Short Take: Voluntary Urinary Retention

In a prospective study, healthy volunteers drank 250ml of water every 15 minutes while doing cognitive tests (had to hold it).

Voluntary urinary retention reduced decision-making speed and delayed retrieval from working memory (like a BAL of 0.05%).

Performance on cognitive tests returned to normal after micturition.


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Summary

Definitely

1) Use norepinephrine as your first-line agent in patients with septic shock.
2) Understand how surrogates may be overly optimistic if presented with poor prognostic information.

Consider

1) Delaying TPN until after at least a week in the ICU.
2) Other major diagnoses that might be found at autopsy in critically ill patients.
Update in Hospital Medicine
2012

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