

Update in Hospital Medicine: Practical Lessons from Current Literature

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BACKGROUND: Hospital medicine continues to grow in workforce, clinical scope, and academic inquiry. This article provides a summary of recent high-impact publications for busy clinicians who provide care to hospitalized adults.

METHODS: Authors reviewed articles that were published between March 2017 and March 2018 for the Update in Hospital Medicine presentations at the 2018 Society of Hospital Medicine and Society of General Internal Medicine annual meetings. Nine of the 29 articles presented were selected for this review based on quality and potential to influence practice.

RESULTS: The following key insights were gained: (1) the perioperative continuation of aspirin in patients with previous percutaneous intervention is beneficial; (2) delaying hip fracture surgery beyond a 24-hour window increases complications; (3) oral antibiotics may be effective treatment for select bloodstream infections; (4) pulmonary embolism may not be as common a

cause of syncope as previously suggested; (5) balanced intravenous fluids and normal saline are similar with respect to hospital-free days but a difference exists in renal events at 30 days favoring balanced crystalloids; (6) speaker introductions may reveal gender bias in academic medicine; (7) edoxaban is a reasonable choice for the treatment of venous thromboembolism in cancer; (8) high-flow nasal cannula reduces the need for intubation in respiratory failure when compared with usual oxygen therapy and noninvasive positive pressure ventilation; and (9) diagnostic errors in spinal epidural abscess lead to delays and morbidity.

CONCLUSIONS: This research provides insight into how we can approach common medical problems in the care of hospitalized adults. The selected works have the potential to change or confirm current practices. *Journal of Hospital Medicine* 2019;14:XXX-XXX. © 2019 Society of Hospital Medicine

Hospital medicine continues to expand with respect to the number of practitioners as well as the scope of the practice of those practitioners. In addition, the commitment to, and rigor of, scientific inquiry in the field continues to grow. The authors of this article conducted a review of the medical literature, including articles published between March 2017 and March 2018. The key articles reported studies with high methodological quality, clear findings, and a high potential for impact on clinical practice. The literature was independently reviewed by each author, and candidate works were chosen on the basis of relevance to hospital medicine and expected clinical impact. The articles were organized by subject matter, ranked by applicability to the audience, and selected to meet the time constraints of each talk. Twenty-nine articles were presented at the Update in Hospital Medicine at the 2018 Society of Hospital Medicine and Society of General Internal Medicine annual meetings (B Sharpe, A Burger at SGIM and B Slawski, C Cooper at SHM). Nine articles were included in this review through an iterative voting process. Each

author ranked their top five articles from one to five. Points were tallied for each article, and the five articles with the highest points were included. A second round of voting identified the remaining four articles for inclusion. Ties were adjudicated by group discussion. Each article is summarized below, and their key points are highlighted in the table.

KEY PUBLICATIONS

Aspirin in Patients with Previous Percutaneous Coronary Intervention Undergoing Noncardiac Surgery. Graham MM et al. *Ann Intern Med.* 2018;168(4):237-244.¹

Background

The Perioperative Ischemic Evaluation 2 (POISE-2) trial found that perioperative aspirin use had no significant effect on the risk of perioperative death and nonfatal myocardial infarction (MI) in patients who are at risk for vascular complications; however, the risk of major bleeding increased with aspirin use in these patients.² Nevertheless, the POISE-2 trial did not specifically address the role of aspirin in patients who had undergone previous percutaneous coronary intervention (PCI).

Methods

A post hoc subgroup analysis of POISE-2 evaluated 470 PCI

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TABLE. **Nine Articles, Nine Practical Implications.****Practical Implications**

1. Continuing aspirin may benefit patients with noncardiac surgery and a history of percutaneous coronary intervention.
2. Patients with hip fractures should be medically optimized and expedited to the OR without delay ideally within 24 hours.
3. The judicious use of oral antibiotics is warranted for select but not all blood stream infections.
4. Pulmonary embolism may be uncommon in hospitalized patients with syncope.
5. The jury remains out for balanced crystalloids vs normal saline in general medicine ward inpatients.
6. Give credit where credit is due. The use of titles may be the first step in combating gender bias.
7. Consider oral edoxaban in patients with cancer and acute venous thromboembolism after five initial days of low-molecular-weight heparin. Caution should be taken in patients with an upper gastrointestinal malignancy.
8. High-flow nasal cannula is better than usual oxygen for avoiding intubation.
9. Missed red flags in the history and exam = costly diagnostic errors in spinal epidural abscess.

patients (234 aspirin-treated and 236 placebo-treated patients) aged ≥ 45 years, 90% of whom had stents. The administration of the study drug was initiated within four hours preoperatively and continued postoperatively. Patients who had bare metal stents placed within the six weeks prior to the study or drug-eluting stents placed within the preceding 12 months were excluded.

Findings

The composite endpoint of risk of death and nonfatal MI was 11.5% in the placebo group and 6% in aspirin-treated patients (HR 0.50; CI, 0.26-0.95). Most of the difference in primary outcome was attributed to an increase in nonfatal MI in the placebo group. Major and life-threatening bleeding were not substantially increased in PCI patients but increased in the overall POISE-2 trial (absolute risk increase 0.8% for major bleeding [95% CI, 0.1%-1.6%]; HR 1.22 [95% CI, 1.01-1.48]). Stent type had no effect on death and nonfatal MI.

Cautions

This was a non-prespecified subgroup analysis with a small sample size.

Implications

Perioperative aspirin use in patients with previous PCI appears to provide more benefit than harm, unless a substantial bleeding risk exists.

Association Between Wait Time and 30-Day Mortality in Adults Undergoing Hip Fracture Surgery.
Pincus D et al. *JAMA*. 2017;318(20):1994-2003.³

Background

Wait times to hip fracture surgery have been associated with mortality in previous studies; however, the wait time associated with complications remains controversial.^{4,5}

Methods

This retrospective cohort study of 42,230 adults modeled the probability of complications in accordance with wait time from hospital arrival to hip fracture surgery. It aimed to identify the optimal time window in which to conduct surgery before complications increased. This window to increased complications was used to define early and delayed surgery. The matched cohorts of early and delayed patients were then used to compare outcomes.

Findings

Overall 30-day mortality was 7%. Complication rates increased when wait times reached 24 hours. Comparing the propensity-matched early (<24 hours) and late (≥ 24 hours) surgery patients revealed that late surgery patients had significantly higher 30-day mortality (6.5% vs 5.8%; % absolute RD 0.79; 95% CI, 0.23-1.35) than early surgery patients and the composite outcome of mortality or other medical complications (MI, DVT, PE, and pneumonia; 12.2% vs 10.1%; % absolute RD 2.16; 95% CI, 1.43-2.89).

Cautions

Only 34% of patients in this study had surgery within 24 hours. The observational cohort study design may result in unmeasured confounders, eg, less sick patients go to surgery more quickly than sicker patients.

Implications

A preoperative wait time of 24 hours appears to represent a threshold of increased risk for 30-day perioperative complications and mortality in hip fracture surgery.

When are Oral Antibiotics a Safe and Effective Choice for Bacterial Bloodstream Infections? An Evidence-Based Narrative Review. Hale AJ et al. *J Hosp Med*. 2018;13(5):328-335.⁶

Background

Bloodstream infections (BSIs) are significant causes of morbidity and mortality in the United States. Traditionally, clinicians have relied on intravenous antibiotics for treatment. A recent “Choosing Wisely[®]” initiative recommends that clinicians should use “oral formulations of highly bioavailable antimicrobials wherever possible.”⁷ Thus, the authors searched for evidence for scenarios wherein BSIs could be safely treated with oral antibiotics.

Methods

A narrative review was conducted given that robust clinical data for an extensive systematic review were insufficient.

Findings

Key decision points on the use of an oral antibiotic for a diagnosed BSI are as follows: (1) Source control must be attained prior to the consideration of oral antibiotics. (2) A highly bioavailable oral option to which the pathogen is sensitive must be available. (3) Patients must be able to comply with the therapy for the full course and not be on interfering medications. Good evidence for use of oral antibiotics against sensitive gram-negative bacilli other than *Pseudomonas* exists. Evidence for treating *Streptococcus pneumoniae* with early transition (within three days) to oral antibiotics is robust when treating bacteremia and pneumonia but not for other primary sites of infection. Evidence for the use of oral antibiotics for B-hemolytic streptococcus, including necrotizing fasciitis and *Enterococcus*, is insufficient. The evidence supports at least two weeks of IV antibiotics for the treatment of *Staphylococcus aureus*.

Cautions

This is a narrative review due to limited evidence.

Implications

The early use of oral antibiotics in the setting of bacteremia may be appropriate in select clinical situations.

Prevalence of Pulmonary Embolism in Patients with Syncope. Costantino et al. *JAMA Intern Med.* 2018;178(3):356-362.⁸

Background

Data on the prevalence of pulmonary embolism in patients presenting with syncope are conflicting.

Methods

This was a retrospective observational study involving five databases in four countries of >1.6 million adults identified through syncope ICD codes. The rates of pulmonary embolism at first evaluation and pulmonary embolism or venous thromboembolism within 90 days were calculated for emergency room patients and a hospitalized subgroup.

Findings

Pulmonary embolism was rare in patients with syncope, eg, less than 3% for hospitalized patients in this database study.

Cautions

The results of this study are based on the use of administrative databases to confirm the diagnosis of syncope. Additionally, the results include hospitalized and nonhospitalized patients. The design of this study differs significantly from those of the PESIT study, which showed a prevalence of 17% in hospitalized patients.⁹ The PESIT study specifically sought the diagnosis of pulmonary embolism even when other etiologies for syncope existed.

Implications

Ultimately, the clinical impetus to search for pulmonary embolism in hospitalized patients admitted with syncope will depend on individual presentations. The authors argued that pulmonary embolism is rare in syncope and much lower than 17% but should be considered in appropriate patients.

Balanced Crystalloids versus Saline in Noncritically Ill Patients. Self WH et al. *N Engl J Med.* 2018;378(9):819-828.¹⁰

Background

Data on the optimal composition of intravenous fluids (IVF) are limited. Limited experimental evidence suggests that IVF-induced hyperchloremia results in renal vasoconstriction and acute kidney injury.

Methods

This was a single-center, open-label, multiple crossover trial of >13,000 non-ICU hospitalized patients admitted from the Emergency Department. Patients were randomized to receive either only normal saline or a “balanced crystalloid,” eg, either Lactated Ringer’s or Plasmalyte. The primary outcome was hospital-free days. Secondary outcomes were major adverse kidney events (MAKE) at 30 days.

Findings

The study found no difference in the primary outcome of hospital-free days. However, balanced IVF resulted in a lower incidence of hyperchloremia and a slightly reduced incidence of MAKE 30 (4.7% vs 5.6%; adjusted OR 0.82).

Cautions

The incidence of acute kidney injury was low in this single-center ED population. This study, however, did not include hospitalized patients. The long-term effects on renal function could not be ascertained.

Implications

Hospital-free days after inpatient randomization to either normal saline or “balanced IVF” were not significantly different. “Balanced IVF” may be beneficial in select high renal-risk populations.

Speaker Introductions at Internal Medicine Grand Rounds: Forms of Address Reveal Speaker Bias.

Files et al. *J Womens Health*. 2017;26(5):413-419.¹¹**Background**

Gender bias is known to contribute to leadership disparities between men and women in several academic medical centers.

Methods

This was a retrospective observational study reviewing video-archived introductions at Internal Medicine Grand Rounds at two connected institutions. All speakers had doctoral degrees. The outcome measured was the use of a speaker's professional title during his/her introduction as a function of the introducer's gender.

Findings

Women were more likely than men to introduce speakers of any gender by their professional title in the 321 forms of address analyzed (96% vs 66%, $P < .001$). When the introducer and speaker were of different genders, women were more likely to introduce male speakers with formal titles than men introducing female speakers (95% vs 49%, $P < .001$).

Cautions

This study was done at two associated academic institutions and may not reflect the practice or customs of physicians in other departments or institutions.

Implications

Despite the study's limitations, it supports a theme of prevalent gender bias within academic medical institutions that may affect the outcomes of leadership, promotion, and scholarship.

Edoxaban for the Treatment of Cancer-Associated Venous Thromboembolism. Raskob GE et al. *N Engl J Med*. 2018;378(7):615-624.¹²**Background**

Low-molecular-weight heparin (LMWH) is the standard of care for the treatment of venous thromboembolism (VTE) in patients with cancer. Direct oral anticoagulants have not been studied for this indication.

Methods

This open-label, noninferiority trial randomized patients with cancer and acute VTE to either LMWH for a minimum of five days followed by oral edoxaban vs subcutaneous dalteparin.

Findings

A total of 1,046 patients were included in the modified intention-to-treat analysis. Patients received treatment for six to twelve months total. A composite outcome of recurrent VTE or major bleed within 12 months occurred in 67 of 522 (12.8%) of patients in the edoxaban group vs 71 of 524 (13.5%) of patients in the dalteparin group (HR 0.91, 95% CI 0.70-1.36, $P = .006$ for noninferiority). Recurrent VTE occurred more commonly with

dalteparin than with edoxaban (11.3% vs 7.9%), whereas major bleeding was less common with dalteparin than with edoxaban (4% vs 6.9%). The increased bleeding rate with edoxaban was predominantly in patients with an upper gastrointestinal (GI) malignancy.

Cautions

This was an open-label study. Patients in the edoxaban group still received five days of LMWH prior to oral edoxaban. More patients in the edoxaban group continued treatment for the entire 12-month period, which contributes to the observed decreased bleeding and increased VTE rates in the dalteparin group.

Implications

Oral edoxaban is noninferior to subcutaneous dalteparin for the primary composite endpoint of VTE and bleeding. Notably, the patients in the edoxaban group experienced a lower rate of recurrent VTE and a higher rate of major bleeding than the patients in the dalteparin group. Additional caution about bleeding risk in those with a GI malignancy is recommended.

Can High-flow Nasal Cannula Reduce the Rate of Endotracheal Intubation in Adult Patients with Acute Respiratory Failure Compared with Conventional Oxygen Therapy and Noninvasive Positive Pressure Ventilation? Ni Y-N et al. *Chest*. 2017;151(4):764-775.¹³**Background**

High-flow nasal cannula (HFNC) can deliver heated and humidified oxygen at rates of up to 60 L/min. Evidence on the benefits of HFNC over usual oxygen therapy or noninvasive positive pressure ventilation (NIPPV) is conflicting.

Methods

This systematic review and meta-analysis included 18 studies (12 RCTs, four retrospective, and two prospective cohort studies) with 3,881 patients with respiratory failure (medical and surgical causes). The included studies compared HFNC with usual oxygen therapy or NIPPV.

Findings

HFNC was associated with lower rates of endotracheal intubation (OR 0.47, 95% CI 0.27-0.84, $P = .01$) relative to oxygen therapy. Intubation rates did not differ between HFNC and NIPPV (OR 0.73, 95% CI 0.47-1.13, $P = .16$). No differences in ICU mortality or ICU length of stay (LOS) were found when HFNC was compared with either usual oxygen therapy or NIPPV.

Cautions

The significant heterogeneity in study design across studies is mainly attributable to varying causes of respiratory failure and differences in flow rate, oxygen concentration, and treatment duration across studies.

Implications

In patients with respiratory failure, HFNC may reduce intubation when compared with usual oxygen therapy and has similar ICU mortality when compared with usual oxygen and NIPPV.

Errors in the Diagnosis of Spinal Epidural Abscesses in the Era of Electronic Health Records. Bhise V et al. *Am J Med.* 2017;130(8):975-981.¹⁴

Background

Diagnostic errors are common in patients with spinal epidural abscess, but the main contributing factors are unclear.¹⁵

Methods

All patients who were newly diagnosed with spinal epidural abscess in 2013 were identified from the Veterans Affairs (VA) national database. Charts were reviewed for diagnostic delay and contributing factors, including the presence of "red flag" symptoms (eg, fever and neurological deficits).

Findings

Of the 119 patients with a new diagnosis of spinal epidural

abscess, 66 (56%) had a diagnostic error. The median time to diagnosis in those with a diagnostic error was 12 days vs four days in those without error ($P < .01$). Common missed red flags in error cases included fever ($n = 57$, 86.4%), focal neurologic deficit ($n = 54$, 81.8%), and active infection ($n = 54$, 81.8%). Most errors occurred during the provider-patient encounter (eg, information not gathered during the history or physical). The magnitude of harm was serious for most patients ($n = 40$, 60.6%) and contributed to death in eight patients (12.1%).

Cautions

The study may not be generalizable because it was limited to the VA health system.

Implications

Diagnostic errors are common in patients with spinal epidural abscesses and can lead to serious harm. Health systems should build mechanisms to support providers in the evaluation of patients with back pain.

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