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Hospital Medicine

Evidence-Based Information for Hospitalists Intensivists, and Acute Care Physicians [ALERT]

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ABSTRACT & COMMENTARY

Does Antibiotic Prophylaxis Prevent Postoperative UTIs in Patients Requiring Short-term Catheterization?

By Chiara Ghetti, MD

Associate Professor, Obstetrics and Gynecology, Division of Female Pelvic Medicine and Reconstructive Surgery, Washington University School of Medicine, St. Louis, MO

Dr. Ghetti reports no financial relationships relevant to this field of study.

This article originally appeared in the May 2014 issue of OB/GYN Alert. *It was edited by Jeffrey T. Jensen, MD, MPH, and peer reviewed by Catherine Leclair, MD. Dr. Jensen is Leon Speroff Professor and Vice Chair for Research, Department of Obstetrics and Gynecology, Oregon Health & Science University, Portland, and Dr. LeClair is Associate Professor, Department of OB/GYN, Oregon Health & Science University, Portland. Dr. Jensen is a consultant for and on the Advisory Boards of AbbVie, Agile Pharmaceuticals, Bayer, ContraMed, Evofem, HRA Pharma, Merck, and Teva; and receives grant/research support from AbbVie, Bayer, Evofem, and HRA Pharma. Dr. Leclair reports no financial relationships relevant to this field of study.*

SYNOPSIS: After pelvic floor reconstructive surgery, antibiotic prophylaxis with daily nitrofurantoin during postoperative catheterization does not decrease risk of urinary tract infection.

SOURCE: Dieter AA, et al. Oral antibiotics to prevent postoperative urinary tract infection: A randomized controlled trial. *Obstet Gynecol* 2014;123:96-103.

Catheter-associated urinary tract infections (UTI) are the most frequent hospital-acquired infections. The estimated risk of UTI following pelvic reconstructive surgery is 5-35%.[1] This study attempted to answer the question of whether antibiotics effectively decrease the risk of UTI in patients requiring catheter drainage following reconstructive surgery.

This was a randomized, double-blind, placebo-controlled trial of patients undergoing

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[ALERT]

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surgery for pelvic organ prolapse and/or incontinence requiring postoperative catheterization. The primary outcome was defined as treatment for UTI within 3 weeks of surgery. English-speaking, nonpregnant patients age ≥ 21 years having surgery for pelvic floor disorders were enrolled. Patients undergoing surgery for urethral diverticulum, fistula repair, or sacral modulation or who had an intraoperative urinary tract injury were excluded. Women with an allergy to nitrofuratoin, creatinine clearance < 60 mL/min, or preoperative urinary retention requiring catheterization also were excluded. Subjects requiring postoperative catheterization were randomized to receive daily nitrofurantoin prophlyaxis vs placebo for 7 days starting on postoperative day 1. These included all subjects hospitalized postoperatively with Foley catheter drainage as well as all subjects discharged on day of surgery with Foley catheter or performing clean intermittent self-catheterization. All subjects received guideline-recommended perioperative antibiotic prophylaxis prior to the start of surgery. Treatment for UTI was defined as treatment for either clinically suspected or culture-proven infection. Multiple methods (including query of medical record, postoperative visits, and completion of forms by outside facilities) were used to determine whether UTI treatment had occurred in the 3 weeks following surgery. Sample size calculation estimated that 156 participants were necessary to demonstrate a two-thirds reduction in risk of UTI.

The study enrolled 375 subjects, of which 163 were randomized. Four randomized subjects were excluded from final analysis for protocol deviations. Final analysis included 159 subjects, 81 in the nitrofurantoin treatment group and 78 in the placebo group. Baseline and perioperative characteristics were not different between groups. Groups were also not different in duration or type of catheter use after surgery.

The risk of UTI in the 3 weeks following surgery was 18% in all subjects (28/159). The risk was not statistically different (and may have been higher) in the nitrofurantoin group (22%) compared to the placebo group (13%) (relative risk 1.73; 95% confidence interval [CI], 0.85-3.52; $P = 0.12$). Of those treated, 68% were treated for a culture-proven UTI and 32% were treated empirically for a clinically suspected UTI. Using regression analysis, there was no difference in risk of UTI when controlling for menopausal status, diabetes, preoperative post-void residual, creatinine clearance, hysterectomy, and duration of catheterization. The authors conclude that nitrofurantoin prophylaxis for each day of catheterization does not reduce UTI risk in patients undergoing reconstructive pelvic surgery requiring short-term transurethral catheterization.

■ COMMENTARY

UTIs account for 40% of hospital-acquired infections and the majority (80%) of these are associated with the use of indwelling catheters.[2] Catheter-associated urinary tract infections (CAUTI) can be associated with increased morbidity and mortality, increased hospitalization, as well as increased health care costs. CAUTI have received increased attention in recent years with the publication of numerous guideline documents and adoption of quality measures. In 2009, as part of National Hospital Inpatient Quality Measures, removal of catheter on postoperative day 1 or 2 was

added as a Surgical Care Improvement Project (SCIP) measure to improve surgical care by reducing surgical complications. In 2012, the Joint Commission published a new National Patient Safety Goal specific to CAUTI based on the Compendium of Strategies to Prevent Healthcare-Associated Infections in Acute Care Hospitals and the CDC Guideline for Prevention of Catheter-associated Urinary Tract Infections.[3,4] In January 2013, there was full implementation of CAUTI surveillance of evidence-based practices to prevent indwelling CAUTI.

The main tenets employed to reduce CAUTI are to avoid unnecessary catheterization and to limit duration of catheterization.[5] Due to antibiotic side effects and risk of antimicrobial resistance, the role of prophylactic antibiotics has been debated. The 2013 Cochrane review concluded that there is limited evidence suggesting that receiving prophylactic antibiotics reduces the rate of bacteriuria and other signs of infection in surgical patients who undergo bladder drainage for at least 24 hours postoperatively. This randomized, double-blind, placebo-controlled study found that nitrofurantoin prophylaxis during time of catheterization following reconstructive surgery did not reduce the risk of UTI. While this well-designed study adds important information regarding this clinical dilemma, what remains unanswered is whether antibiotic prophylaxis with another agent or whether prophylaxis that extends beyond the period of catheterization would reduce UTI risk in this population. ■

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ABSTRACT & COMMENTARY

Acute on Chronic Liver Failure: New Definition and Implications

By Deborah J. DeWaay, MD, FACP

Assistant Professor, Medical University of South Carolina, Charleston, SC

Dr. DeWaay reports no financial relationships in this field of study

SYNOPSIS: Acute on chronic liver failure is a distinct clinical entity marked by systemic inflammation, organ failure and high mortality.

Source: Moreau R, Arroyo V. Acute on Chronic Liver Failure: A New Clinical Entity. *Clinical Gastroenterology and Hepatology*. 2014. ePub ahead of print.

■ SUMMARY

Ascites, gastrointestinal hemorrhage, hepatic encephalopathy and bacterial infections are common complications experienced by patients with cirrhosis. Traditionally, when a cirrhotic patient experiences one of these complications and develops worsening liver function, he or she is diagnosed with acute on chronic liver failure. The mortality of these patients is very high. However, up until 2013, there was no evidence-based definition of acute on chronic liver failure, only expert opinion. The European Association for the Study of the Liver/Chronic Liver Failure Consortium (EASL-CLIF Consortium) performed the CLIF Acute on Chronic Liver Failure in Cirrhosis (CANONIC) study with the purpose of defining acute on chronic liver failure (ACLF). This study is a prospective, observational, and multicenter study.

The study enrolled 1343 cirrhotic patients who were hospitalized for at least one day for one or more of the following: hepatic en-

cephalopathy, large-volume ascites, bacterial infection, or gastrointestinal hemorrhage. The patients were assessed for organ failure; the number and degree of organ failure was used to grade the degree of acute on chronic liver failure, and determine the associated transplant-free mortality rates. Liver failure was considered a bilirubin of 12.0 mg/dL or more. Kidney failure was the requirement of renal replacement therapy or a creatinine of greater than 2.0 mg/dL. Coagulation failure was defined as an INR of more than 2.5 or platelets of 20,000/microL or less. Circulatory failure was defined as the use of vasopressor support to maintain blood pressure. Cerebral failure was defined as grade 3 or 4 hepatic encephalopathy. Lastly, respiratory failure was present when the partial pressure of arterial oxygen to the FiO2 was 200 or less.

The patients were divided into four groups: no ACLF and ACLF grades 1-3. No ACLF was defined as no organ failure, or single organ failure without kidney dysfunction or hepatic encephalopathy. Grade 1 ACLF was single organ failure with a creatinine of 1.5-1.9mg/dL and/or hepatic encephalopathy grade 1 or 2. Grade 2 and 3 ACLF were defined as two-organ and three-organ failures respectively.

The 28-day transplant free mortality rate of each group rose with increasing in organ dysfunction: no ACLF 4.7%, ACLF grade 1 22.1%, grade 2 32.0%, grade 3 78.6%. Patients with ACLF were slightly younger, 56 years old compared to 58 years old (P = 0.02). They were significantly more likely to have alcoholic cirrhosis and be active alcoholics, but were less likely to have cirrhosis from hepatitis C. In almost half of the ACLF patients, no precipitating event was identified. In those that did have an event, infection in general and from spontaneous bacterial peritonitis and pneumonia specifically were significantly more common in the ACLF group than the no-ACLF group. In addition, the ACLF group had higher plasma C-reactive proteins (CRP) compared to those with no ACLF, 39.9mg/L vs. 25.4mg/L respectively (P = <0.001). Interestingly, ACLF is not the same as end-stage cirrhosis, as 23.2% of patients developed ACLF without any previous history of acute decompensated cirrhosis; 17.6% of ACLF patients developed it within <3 months of their first episode of decompensation, which was significantly higher than the 10.8% of those with no ACLF (P = 0.02).

Lastly, the authors divided the patients into three groups irrespective of ACLF: nonalcoholic cirrhosis, alcoholic cirrhosis without active alcohol consumption and alcoholic cirrhosis with active alcohol consumption. The group with active alcohol consumption was significantly younger, more likely to have ACLF, a higher white cell count, bilirubin, INR and AST when compared to the other two groups. There was no significant difference between the nonalcoholic cirrhosis and alcoholic cirrhosis without active alcohol consumption groups in these areas. In conclusion, the authors argue that ACLF is a new clinical entity from traditional decompensated cirrhosis that is marked by younger age, organ failure, high mortality and systemic inflammation, which includes subcategories such as severe alcoholic hepatitis and severe sepsis.

■ COMMENTARY

The defining of acute on chronic liver failure as a new clinical entity is important for hospitalists for several reasons. First, although a subspecialist will certainly be involved in the care of these patients at most institutions, the hospitalist will be integral to the discussion with the patient and family regarding discussions of prognosis. It is crucial that hospitalists understand the high mortality among patients with acute on chronic liver failure. Second, the study highlights that acute on chronic liver failure is not necessarily equivalent to the end stages of cirrhosis and can happen at any time during the disease. In this study, almost half of the ACLF patients experienced this complication without ever having an episode of decompensation or within 3 months of their first episode of decompensation. Lastly, I think the differences in patients with alcoholic cirrhosis with and without active alcohol intake is significant. The patients without active alcohol intake had a lower 28-day mortality and less acute on chronic liver failure. Although these findings are intuitive, they should motivate hospitalists to get patients with alcoholic cirrhosis into alcohol rehabilitation treatment since it is literally life or death for the patient. ■

ABSTRACT & COMMENTARY

Beta-Blockers in CAD Patients Undergoing Non-Cardiac Surgery

By Michael H. Crawford, MD

Professor of Medicine, Chief of Clinical Cardiology, University of California, San Francisco

This article originally appeared in the May 2014 issue of Clinical Cardiology Alert. *It was peer reviewed by Ethan Weiss, MD, Assistant Professor of Medicine, Division of Cardiology and CVRI, University of California, San Francisco. Dr. Crawford reports no financial relationships relevant to this field of study, and Dr. Weiss is a scientific advisory board member for Bionovo.*

SOURCES: Andersson C, et al. Association of beta-blocker therapy with risks of adverse cardiovascular events and deaths in patients with ischemic heart disease undergoing noncardiac surgery: A Danish nationwide cohort study. *JAMA Intern Med* 2014;174:336-344.

Whelton SP, Bansal S. Perioperative beta-blockers revisited: Good for what ails you? *JAMA Intern Med* 2014;174:345-346.

Recent controversy has erupted concerning the use of prophylactic beta-blockers in patients with known or suspected coronary artery disease (CAD) undergoing non-cardiac surgery. Thus, these investigators from Stanford University and Denmark analyzed the Danish National Patient Registry for patients with a history of ischemic heart disease who underwent non-cardiac surgery from 2004-09. Two cohorts were identified, those with and without heart failure. Among those without heart failure, patients were further grouped as to whether they had had a myocardial infarction (MI) or not. Of the 28,263 surgeries included in this analysis, 7990 (28%) were in patients with heart failure, 12,601 (45%) who had a prior MI, 3964 (14%) who had prior coronary bypass surgery, and 6760 (24%) who had a percutaneous intervention. Orthopedic surgery was most common (40%), followed by abdominal surgery (20%); 33% were urgent or emergent. Beta-blockers were prescribed for 41% of the patients.

Sophisticated statistical techniques were used: multivariate analysis, propensity matching, and sensitivity analyses. Five percent of the patients experienced a major adverse cardiac or cerebral event (MACCE). These major events included death (75%), stroke (3.5%), and MI (22%). MACCE were more common in the heart failure patients (10% vs 3%). Beta-blocker use overall did not significantly affect outcomes (adjusted MACCE hazard ratio [HR], 0.90; 95% CI, 0.79-1.02). In heart failure patients, beta-blocker use reduced MACCE (HR, 0.78; 95% CI, 0.66-0.91). Among the patients without heart failure, a recent MI (< 2 years) favored beta-blocker therapy (MACCE HR, 0.54; 95% CI, 0.37-0.78). Patients with a history of revascularization did not benefit from beta-blocker therapy. The type of surgery did not influence the results of beta-blocker therapy. The authors concluded that among those with ischemic heart disease, 30-day MACCE was only improved by beta-blockers in those with heart failure or recent MI.

■ COMMENTARY

The concept that excess adrenergic tone during and after surgery could lead to cardiac events in susceptible individuals such as those with ischemic heart disease and that beta-blocker therapy in the perioperative period may abrogate this risk is attractive. Early randomized trials, although small, supported this hypothesis and beta-blockers quickly became the go-to intervention for preventing perioperative MI and death, especially in known CAD patients undergoing moderate-to-high risk surgery. The 2009 European Society of Cardiology (ESC) Guidelines recommend beta-blockers for all CAD patients and the American College of Cardiology/American Heart Association (ACC/AHA) guidelines from the same year recommend beta-blockers in CAD patients undergoing high-risk surgery (class IIa), and if a patient is already on beta-blockers to continue them (class I). However, newer studies have shown an increased risk of bradycardia and hypotension with beta-blockers and no consistent reduction in adverse cardiovascular events. This raises the question of whether we have pushed this concept too far (into lower-risk individuals) or whether it is no longer of value with modern anesthesia and surgical care.

This study addresses these issues by analyzing a large registry database from Denmark of patients with ischemic heart disease undergoing non-cardiac surgery. They found that

beta-blockers were only beneficial in those with heart failure or recent MI. Neither prior revascularization nor the type of surgery influenced the results. The results make sense in that heart failure and recent MI are strong indications for beta-blockers in all patients. This would support the ACC/AHA class I indications for beta-blockers in those who already have an indication for them, but not the class IIa and ESC recommendation for all CAD patients undergoing major surgery. Also, prior revascularization seems to be protective as beta-blockers were ineffective in these patients.

The strengths of this study are the large population of unselected patients and the sophisticated analyses that were done to offset the non-randomized study design limitation. These registry studies are becoming more popular and complex as we realize that many clinical questions, such as the ones studied here, will never be subjected to a randomized trial. Other weaknesses of this study are the lack of information on drug doses, compliance, and adverse effects. Also, we don't know how ischemic heart disease and heart failure were diagnosed; these categories were determined using administrative data from ICD codes and not directly from chart review.

This study adds to the body of literature on this topic and supports the ACC/AHA class I medication for perioperative beta-blockers in those who already have an indication for their use. It does not support beta-blockers for all CAD patients undergoing major surgery, but doesn't preclude the judicious use of them in selected high-risk patients. Selective therapy fits the new mantra of personalized medicine. ■

ABSTRACT & COMMENTARY

Should Dialysis Patients with Atrial Fibrillation Be Treated with Warfarin?

By Edward P. Gerstenfeld, MD

Professor of Medicine, Chief, Cardiac Electrophysiology, University of California, San Francisco

Dr. Gerstenfeld does research for Biosense Webster, Medtronic, and Rhythmia Medical.

This article originally appeared in the May 2014 issue of Clinical Cardiology Alert. *It was edited by Michael H. Crawford, MD, and peer reviewed by Ethan Weiss, MD. Dr. Crawford is Professor of Medicine, Chief of Clinical Cardiology, University of California, San Francisco, and Dr. Weiss is Assistant Professor of Medicine, Division of Cardiology and CVRI, University of California, San Francisco. Dr. Crawford reports no financial relationships relevant to this field of study, and Dr. Weiss is a scientific advisory board member for Bionovo.*

SOURCE: Shah M, et al. Warfarin use and the risk for stroke and bleeding in patients with atrial fibrillation undergoing dialysis. *Circulation* 2014;129: 1196-1203.

This was a retrospective cohort study from Quebec and Ontario, Canada, examining patients ≥ 65 years of age admitted to a hospital with a diagnosis of atrial fibrillation (AF) between 1998 and 2007. Patients were divided into dialysis patients and non-dialysis patients, as well as warfarin users and nonusers. The association between warfarin use and risk of stroke or bleeding was examined. There were 1626 dialysis patients and 204,210 nondialysis patients included. Among the dialysis patients, only 46% were prescribed warfarin. Warfarin use was not associated with a lower risk of stroke in dialysis patients (hazard ratio [HR], 1.14; 95% CI, 0.78-1.67); however, it was associated with a lower stroke risk in nondialysis patients (HR, 0.87; 95% CI, 0.85-0.90). Warfarin use was associated with a significantly increased bleeding risk in dialysis (HR, 1.44; 95% CI, 1.13-1.85) and a slightly increased risk in nondialysis (HR, 1.19; 95% CI, 1.16-1.22) patients. The authors concluded that warfarin therapy in dialysis patients does not reduce stroke risk, but does increase the risk of bleeding.

■ COMMENTARY

Multiple prospective, randomized trials have proven that systemic anticoagulants significantly reduce the stroke risk in patients with AF and stroke risk factors. The oral Factor Xa and direct thrombin inhibitors, which have a fixed daily dose and no requirement for blood testing or dietary restriction, have been a welcome addition to our treatment armamentarium. However, since all these agents are predominantly metabolized in the kidneys,

they cannot be used in patients with end-stage renal disease on hemodialysis (HD). Warfarin remains the main therapeutic option for HD patients, although it is well known that they have higher bleeding risk because of platelet dysfunction. In addition, repeated access to AV fistulae is needed, and anticoagulation can lead to persistent bleeding after HD catheter removal. However, HD patients also often have diabetes, congestive heart failure, peripheral vascular disease, and older age, which all increase stroke risk. Therefore, most believe that the benefit of systemic anticoagulation in dialysis patients with AF outweighs the risk. In this study, the authors question this wisdom. Interestingly, warfarin use was not associated with a lower stroke risk in HD patients and was associated with a 44% increased risk of bleeding. Were the included patients truly at high stroke risk? Since 73% of their HD patients had a CHADS2 score ≥ 2, this was in fact a high-risk group. Of note, 85% also had a HAS-BLED score ≥ 3, identifying that these patients also had a high risk of bleeding on anticoagulation.

Should we no longer recommend warfarin for HD patients with AF? I think it is premature to change practice based on this retrospective, nonrandomized study. However, in an HD patient with relatively lower risk (CHADS2 = 1) where warfarin might be recommended, it is reasonable to reconsider its use. In addition, in patients with high HAS-BLED scores or those who have already experienced bleeding complications, ongoing use of warfarin should be carefully considered after weighing the risks and benefits. A prospective, multicenter study of HD patients with AF is certainly warranted based on these interesting data. ■

Stroke Alert

Hemicraniectomy in Older Patients with Large Middle Cerebral Artery Infarcts Reduces Mortality

By Matthew E. Fink, MD

Professor and Chairman, Department of Neurology, Weill Cornell Medical College, and Neurologist-in-Chief, New York-Presbyterian Hospital

This article originally appeared in the May 2014 issue of Neurology Alert. *It was peer reviewed by M. Flint Beal, MD. Dr. Beal is Anne Parrish Titzel Professor, Department of Neurology and Neuroscience, Weill Cornell Medical Center. Dr. Fink is a retained consultant for Procter & Gamble, and Dr. Beal reports no financial relationships relevant to this field of study.*

SOURCE: Juttler E, et al, for the DESTINY II Investigators. Hemicraniectomy in older patients with extensive middle-cerebral-artery stroke. *N Engl J Med* 2014;370:1091-1100.

In an earlier study of early decompressive hemicraniectomy for large middle cerebral artery strokes, the same investigators demonstrated reduced mortality without increasing the risk of very severe disability among patients ≤ 60 years of age. These investigators now report the results of a similar trial in 112 patients, ≥ 61 years of age (mean age 70 years; range 61-82) who were randomized to either hemicraniectomy within 48 hours or conservative treatment in the intensive care unit. The primary endpoint was survival without severe disability, defined as a modified Rankin score of 0 to 4.

Hemicraniectomy improved the primary outcome, with the proportion of patients who survived without severe disability being 38% in hemicraniectomy group, compared to 18% in the control group. This result was a direct result of a lower mortality in the surgical group, and no difference between the groups in the degree of severe disability. The results of this trial in an older age group is quite similar to what was found in younger patients, and this procedure therefore remains an option for patients of all ages. However, patients and families should be made aware that a successful hemicraniectomy may improve survival, but it will not improve neurological recovery. ■

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5. Once the completed evaluation is received, a credit letter will be e-mailed to you instantly.

CME QUESTIONS

1. Which of the following statements is true regarding the randomized, double-blind, placebo-controlled trial by Dieter and colleagues of nitrofurantoin versus placebo to reduce the risk of postoperative UTI in women?

a. Post-menopausal women had significantly fewer UTIs with nitrofurantoin
b. Women with diabetes mellitus had significantly fewer UTIs with nitrofurantoin
c. Women with chronic kidney disease had significantly fewer UTIs with nitrofurantoin
d. Nitrofurantoin did not reduce the risk of UTI regardless of risk factor
e. A, B, and C

2. As defined by the CANONIC study reported by Moreau and Arroyo, all of the following conditions were used to classify the presence of acute on chronic liver failure EXCEPT:

a. Kidney failure
b. Ascites
c. Hepatic encephalopathy
d. Respiratory failure
e. Coagulopathy

3. In the cohort study by Andersson, et al., which of the following patients with CAD benefitted from preoperative beta-blockers for non-cardiac surgery?

a. Patients with congestive heart failure
b. Patients with a distant MI (> 3 years)
c. Patients with atrial fibrillation
d. Patients with prior coronary artery bypass surgery
e. Patients with a recent stroke (< 2 years)

CME OBJECTIVES

Upon completion of this educational activity, participants should be able to:

- discuss pertinent safety, infection control and quality improvement practices;
- explain diagnosis and treatment of acute illness in the hospital setting; and;
- discuss current data on diagnostic and therapeutic modalities for common inpatient problems.