AHC Media

Hospital Medicine

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

Vol. 9, Issue 6, August 2014
www.ahcmedia.com

ABSTRACT & COMMENTARY

Protocol-directed Care Does Not Lead to Improved Outcomes in Early Septic Shock

By Richard R. Watkins, MD, MS, FACP

Division of Infectious Diseases, Akron General Medical Center, Akron, OH; Associate Professor of Internal Medicine, Northeast Ohio Medical University, Rootstown, OH.

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

This article originally appeared in the July 2014 issue of Infectious Disease Alert. *It was edited by Stan Deresinski, MD, FACP, FIDSA, and peer reviewed by Timothy Jenkins, MD. Dr. Deresinski is Clinical Professor of Medicine, Stanford University, Associate Chief of Infectious Diseases, Santa Clara Valley Medical Center, and Dr. Jenkins is Assistant Professor of Medicine, University of Colorado, Denver Health Medical Center. Dr. Deresinski does research for the National Institutes of Health, and is an advisory board member and consultant for Merck, and Dr. Jenkins reports no financial relationships relevant to this field of study.*

SYNOPSIS: A large, multicenter clinical trial that compared protocol-based care to usual care for patients presenting to emergency departments with early sepsis and septic shock found no differences in clinical outcomes. However, early recognition and therapy was beneficial and should be the standard of care.

SOURCE: The ProCESS Investigators. A randomized trial of protocol-based care for early septic shock. *N Engl J Med* 2014;370(18):1683-93.

Despite recent improvement, the short-term mortality in patients presenting to emergency departments with early sepsis and septic shock remains unacceptably high, i.e. approximately 20% in the USA. Researchers have tried a variety of interventions to improve outcomes in sepsis and septic shock, one of which is early goal-directed therapy (EGDT). First described in 2001, this paradigm involves a set protocol by which central venous catheterization is used to guide volume resuscitation and vasopressor titration.[1] Because of changes that have occurred in management of septic

Financial Disclosure: *Hospital Medicine Alert*'s physician editor, Kenneth P. Steinberg, MD, peer reviewer John H. Choe, MD, MPH, executive editor Russ Underwood, and associate managing editor Jill Drachenberg have no relevant financial relationship related to the material presented in this issue.

Hospital Medicine [ALERT]

Hospital Medicine Alert,
ISSN 1931-9037, is published monthly by
AHC Media, LLC
One Atlanta Plaza
950 East Paces Ferry NE, Suite 2850
Atlanta, GA 30326.
www.ahcmedia.com

GST Registration Number: R128870672.
Periodicals Postage Paid at Atlanta, GA 30304 and at additional mailing offices.

POSTMASTER: Send address changes to
Hospital Medicine Alert,
P.O. Box 550669,
Atlanta, GA 30355.

SUBSCRIBER INFORMATION
1-800-688-2421
customerservice@ahcmedia.com
www.ahcmedia.com

Editorial E-Mail:
russ.underwood@ahcmedia.com
Questions & Comments:
Please call Russ Underwood, Executive Editor at (404) 262-5521 or email at
russ.underwood@ahcmedia.com

Subscription Prices
United States:
Print: 1 year with free *AMA PRA Category 1 Credits™*: $249
Add $19.99 for shipping & handling.
Online only: 1 year (Single user) with ***free*** *AMA PRA Category 1 Credits™*: $199

Multiple Copies: Discounts are available for group subscriptions, multiple copies, site-licenses or electronic distribution. For pricing information, call Tria Kreutzer at 404-262-5482.

Back issues: Missing issues will be fulfilled by customer service free of charge when contacted within one month of the missing issue's date.

Canada: Add 7% GST and $30 shipping.
Elsewhere: Add $30 shipping.

ACCREDITATION
AHC Media is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

AHC Media designates this enduring material for a maximum of ***20*** *AMA PRA Category 1 Credits™*. Physicians should only claim credit commensurate with the extent of their participation in the activity.

This CME activity is intended for hospitalists, intensivists, and acute care clinicians. It is in effect for 24 months from the date of the publication.

AHC Media

shock such as the less frequent use of central catheters (due to data showing no improvement in outcomes), the ProCESS investigators sought to determine whether protocol-based resuscitation was better than usual care and whether protocol-based resuscitation with central catheter monitoring was superior to a simpler protocol that did not include central catheter monitoring.

The study was a multicenter, randomized clinical trial conducted at 31 hospitals in the United States between March 2008 and May 2013. Subjects were those who presented to an emergency department at a participating site with a suspected diagnosis of sepsis, were at least 18 years of age, had two or more criteria for systemic inflammatory response syndrome (SIRS), and had refractory hypotension or a serum lactate ≥ 4 mmol per liter. Overall, 1,341 patients were enrolled and assigned in a 1:1:1 ratio to the following groups: protocol-based EGDT wherein a central venous catheter was used to monitor pressure and fluids (439 patients); protocol-based standard therapy that used a team approach with a set of 6-hour resuscitation instructions (446 patients); and usual care in which bedside physicians directed all medical therapy (456 patients). The primary outcome of the study was the rate of in-hospital death from any cause at 60 days. Secondary outcomes included mortality at 90 days and 1 year, duration of the need for vasopressors, duration of acute respiratory failure (defined as time spent on a ventilator), duration of acute renal failure (defined as the duration of dialysis), duration of stay in the intensive care unit and hospital, and disposition at hospital discharge.

The use of IV fluids, vasopressors, dobutamine and blood transfusions between 6 and 72 hours did not differ significantly between the groups. By 6 hours the target mean arterial pressure of 65 mm Hg or greater had been achieved in more patients in the two protocol-based groups compared to the usual care group (P = 0.02). The 60-day in-hospital death rate did not differ significantly between any of the three groups (P values between 0.31 and 0.89) and there were no significant differences in 90-day mortality or time to death up to 90 days and 1 year. The incidence of acute renal failure was higher in the protocol-based standard therapy group compared to the other two (6.0% in the protocol-based standard therapy group vs. 3.1% in the EGDT group vs. 2.8% in the usual-care group, P = 0.04). There were no significant differences between the groups in the length of stay in the ICU, incidence and duration of cardiovascular or respiratory failure, length of hospital stay or discharge disposition. Even when the investigators restricted the analysis to the sickest third of the patients (those with the highest APACHE II scores and serum lactate), no benefit was seen in the two protocol-based groups.

Finally, serious adverse events were rare during the study and did not differ between the treatment groups.

■ COMMENTARY

No improvement in outcomes, including mortality and length of stay in the ICU and hospital, was seen in patients who received protocol-based care. However, there are some aspects of the study that limit the generalizability of its findings to other settings. The patients were enrolled as soon as they were recognized to be in septic shock, so the observed benefits might not be as significant when septic shock is recognized later. Also, the care patients received before randomization may have had an impact on their subsequent clinical course. Finally, decisions to withdraw care in patients on life support are variable and their impact on in-hospital mortality during the study is unclear.

There are several interesting findings from the trial that can impact clinical practice. The rate of antibiotic administration in the first 6 hours after randomization was 97%, an exceptionally high and impressive figure. Data from multiple studies strongly supports the dictum that early recognition and antibiotic treatment are the keys to surviving sepsis. Patients in the two protocol-based treatment groups overall received more intravenous fluids, vasoactive agents and blood transfusions yet these interventions did not lead to improved outcomes. When analyzing these results, it is important to remember that all 3 of the study groups were treated according to the Surviving Sepsis Campaign guidelines[2] including early recognition of sepsis and septic shock, early

antimicrobial treatment and conservative transfusion thresholds as well as moderate glycemic control, low tidal-volume ventilation and serial monitoring of serum lactate levels. Indeed, this latter intervention has been shown to be equivalent to the use of invasive central catheters for monitoring physiological parameters. Thus, this study provides clinicians with strong evidence that central hemodynamic monitoring should not be a priority in the management of septic shock. Instead, the focus should be on early recognition via serum lactate, prompt antibiotic administration and volume resuscitation with care taken to ascertain the adequacy of circulation. The ProCESS trial is likely to become an important milestone for the evidence-based management of septic shock.

References

1. Rivers E, et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. *N Engl J Med* 2001; 345:1368-77.
2. Dellinger RP, et al. Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock: 2008. *Crit Care Med* 2008; 36:296-327. ■

ABSTRACT & COMMENTARY

Value of Electronic Surveillance for Hospital CAUTIs

By Joseph F. John, Jr., MD, FACP, FIDSA, FSHEA

Associate Chief of Staff for Education, Ralph H. Johnson Veterans Administration Medical Center; Professor of Medicine, Medical University of South Carolina, Charleston

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

This article originally appeared in the July 2014 issue of Infectious Disease Alert. *It was edited by Stan Deresinski, MD, FACP, FIDSA, and peer reviewed by Timothy Jenkins, MD. Dr. Deresinski is Clinical Professor of Medicine, Stanford University, Associate Chief of Infectious Diseases, Santa Clara Valley Medical Center, and Dr. Jenkins is Assistant Professor of Medicine, University of Colorado, Denver Health Medical Center. Dr. Deresinski does research for the National Institutes of Health, and is an advisory board member and consultant for Merck, and Dr. Jenkins reports no financial relationships relevant to this field of study.*

SYNOPSIS: Compared to manual surveillance methods, an electronic surveillance tool for catheter-associated urinary tract infections had a high negative predictive value but a low positive predictive value.

SOURCE: Wald HL, et al. Accuracy of electronic surveillance of catheter-associated urinary tract infection at an Academic Medical Center. *Infect Control Hosp Epidemiol* 2014;35:685-91.

A group from the University Of Colorado School of Medicine constructed this study to determine if electronic surveillance for catheter-associated urinary tract infections (CAUTIs) was as good or better than standard surveillance. They identified 1695 patients from 2009 and 2010 that met inclusion criteria and that were used for this analysis. They developed an algorithm designed to try to detect UTI from the electronic health record and other sources of administrative data for these 1695 patients. The patients were included if they had a "high clinical suspicion" of having a CAUTI. The 425-bed hospital was in a urban setting. Patients were adults 18 years of age or older. Manual surveillance was the comparator arm. The average age was 57 years, and there was a male to female split of 49% to 42% with the remainder unknown. Of the 1695 patients included in this analysis, the electronic algorithm identified 64 cases thought to likely be CAUTI (15 were actually true positive urinary tract infections); in contrast, only 19 were identified through manual surveillance to have CAUTI. Electronic surveillance had a high negative predictive value (NPV) but a low positive predictive value (PPV = 23%). There was a 97% agreement between the electronic algorithm and the manual method. On the basis of these predictive values, the authors felt that electronic surveillance would be a good screening tool. The authors suggest that the test characteristics of the electronic algorithm could be improved in order to improve data pulls.

■ COMMENTARY

The best thing to say about this study is that, while creative, electronic surveillance could be used in its present form primarily for screening to eliminate negative cases, i.e., its high NPV. This conclusion is somewhat disappointing, but electronic surveillance is in its infancy so that the test characteristics when improved may raise the PPV and the tool could be a stand along.

In the meantime, manual surveillance has a wisdom that electronic surveillance cannot approach in documenting true infections. That does not mean that we should not try to continue to use innovative software to help us in this era of mega-data. This

article used a Structured Query Language code in Microsoft Access to apply an algorithm that ends in either a CAUTI or an asymptomatic catheter-associated infection. To result in a CAUTI, the patient needs to have symptoms, and that is the challenging rub for the software to figure out. If there are no symptoms, but a positive blood culture, the diagnosis is considered at least a level of CAUTI. If there are no symptoms and the blood culture is negative, the urine culture positive for less than 2 organisms at a count of 100,000/cc, then there is not a CAUTI, but a CAASB, a catheter-associated asymptomatic bacteriuriaa. While all this process through the algorithm sounds complex — and it is — the use to Infection Control will be a final software that should be easy to apply.

Keep eyes peeled for use of algorithms in software that detects common hospital-acquired infections. For the time being, let us hope this electronic detection of CAUTI can be refined and demonstrate more sensitivity. ■

ABSTRACT & COMMENTARY

Conservative Fluid Management Reduces the Incidence of VAP

By Richard H. Kallet, MS, RRT, FAARC, FCCM

Director of Quality Assurance, Respiratory Care Services, San Francisco General Hospital

Mr. Kallet reports no financial relationships relevant to this field of study.

This article originally appeared in the July 2014 issue of Critical Care Alert. *It was edited by David J. Pierson, MD, and peer reviewed by William Thompson, MD. Dr. Pierson is Professor Emeritus, Pulmonary and Critical Care Medicine, University of Washington, Seattle, and Dr. Thompson is Associate Professor of Medicine, University of Washington, Seattle. Drs. Pierson and Thompson report no financial relationships relevant to this field of study.*

SYNOPSIS: Patients on mechanical ventilation who were managed with both conservative fluid administration and aggressive diuresis weaned faster, had significantly more ventilator-free days, and experienced reduced incidences of both ventilator-associated complications and ventilator-associated pneumonia.

SOURCE: Mekontso Dessap A, et al. Ventilator-associated pneumonia during weaning from mechanical ventilation: Role of fluid management. *Chest* 2014; Mar 20. doi: 10.1378/chest.13-2564. [Epub ahead of print.]

This article reports a secondary analysis of patients enrolled into a multicenter, randomized, controlled trial that examined the impact of B-type natriuretic peptide (BNP)-directed fluid management ("fluid-depletion strategy") vs. "usual care."[1] The relationship between fluid balance and the incidence of ventilator-associated pneumonia (VAP) over the first 14 study days was analyzed in patients who met weaning-readiness criteria. Weaning was standardized using an automated pressure-support titration algorithm. When daily BNP values were ≥ 200 pg/mL, patients in the fluid-depletion arm had fluid restriction (baseline infusion ≤ 0.5 L/day; parental nutrition ≤ 1 L/day) along with aggressive diuresis (furoseminde: 10-30 mg boluses, Q-3h), targeting a urine output of 4.5-9 mL/kg over 3 hours. In the usual care group, clinicians were blinded to the BNP results, and both fluids and diuretics were administered per clinician practice. VAP diagnosis was standardized and required positive quantitative cultures from distal pulmonary sampling.

The 304 medical-surgical patients studied (152 in each group) were not different in terms of baseline characteristics and risk factors for VAP, and they had been receiving mechanical ventilation (MV) for approximately 4-5 days at randomization. There was a significantly lower incidence of VAP in the BNP-managed group (8.6%) vs. the usual care group (17.8%, $P = 0.03$). This also coincided with a more negative daily fluid balance, faster weaning time, and more ventilator-free days.

■ COMMENTARY

Both the parent trial[1] and the seminal NIH FACTT study[2] have validated the emerging concept that "keeping the lungs dry" during critical illness improves outcomes, in part by reducing the need for MV. The current study augments these findings by showing that reducing the need for MV provides an additional benefit of decreasing the incidence of VAP. Patients in the BNP group were successfully weaned approximately 1 day earlier (27 hours) than those in the usual care group, and on average were successfully extubated < 48 hours of enrollment

into the trial. The most obvious explanation is that the lower incidence of VAP stems from reduced risk exposure related to the presence of the endotracheal tube.

Because the duration of MV is a risk for VAP (and VAP increases the duration of MV), the investigators used a competing risk model to analyze the effects of the fluid-depletion strategy while controlling for weaning outcome. They found that the fluid-depletion strategy itself significantly reduced the risk of both ventilator-associated complications and VAP (sub-hazard ratios of 0.44 (P = 0.02) and 0.50 (P = 0.03), respectively). These findings lead the authors to speculate that pulmonary edema may increase the risk for developing VAP by two mechanisms: 1) the long-recognized impairment of pulmonary host-defense mechanisms, and 2) an interesting hypothesis of enhanced growth and virulence of *Pseudomonadaceae* because these bacteria characteristically thrive in wet conditions. In this study, *Pseudomonadaceae* accounted for 44% of all positive bronchoalveolar lavage fluid cultures. The independent effect of pulmonary edema on VAP is an enticing explanation as some of the highest at-risk patients are those suffering from acute respiratory distress syndrome, traumatic injuries, and massive burns, conditions commonly associated with large fluid requirements and pulmonary edema formation.

This study underscores the beneficial effects of fluid restriction and aggressive diuresis in critically ill patients *once they have achieved hemodynamic stability*. Despite the growing body of evidence supporting this approach, it has not been enthusiastically embraced, particularly in the management of trauma patients. Unarguably, persistent hypotension caused by sustained capillary leak is a daunting problem. But overzealous crystalloid therapy also has been a well-recognized problem for more than 70 years, and one that "every generation of surgeons must discover for themselves."[3] However, with mandatory public reporting of ventilator-associated complications looming in the near future, complacency toward managing "correctable" risk factors leading to avoidable patient complications will not be tolerated by society. The cumulative evidence clearly suggests that much more can be done to improve this aspect of patient care. ■

REFERENCES

1. Mekontso Dessap A, et al. Natriuretic peptide-driven fluid management during ventilator weaning. *Am J Respir Crit Care Med* 2012;186:1256-1263.
2. National Heart, Lung, and Blood Institute ARDS Clinical Trials Network. Comparison of two fluid management strategies in acute lung injury. *N Engl J Med* 2006;354:2564-2575.
3. Gomez AC. Pulmonary insufficiency in nonthoracic trauma. *J Trauma* 1968;8:656-686.

ABSTRACT & COMMENTARY

Predictors of Seizures After Trauma

By Nitin K Sethi, MD

Assistant Professor of Neurology, Weill Cornell Medical College

Dr. Sethi reports no financial disclosures relevant to this field of study.

This article originally appeared in the July 2014 issue of Neurology Alert. It was edited by Matthew E. Fink, MD, and peer reviewed by M. Flint Beal, MD. Dr. Fink is Professor and Chairman, Department of Neurology, Weill Cornell Medical College and Neurologist-in-Chief, New York Presbyterian Hospital, and 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.

SYNOPSIS: In this large prospective study of trauma patients, the most important factor associated with post-traumatic seizures was the presence of alcohol intoxication.

SOURCE: Vaaramo K, et al. Predictors of new-onset seizures: A 10-year follow-up of head trauma subjects with and without traumatic brain injury. *J Neurol Neurosurg Psychiatry* 2014;85:598-602.

Recent reports indicate that both civilian and military cases of traumatic brain injury (TBI) are on the rise. An estimated 1.5-2.5 million civilian TBI cases occur per year in the United States. Mild TBI has also been recognized as the "signature injury" of America's global war on terrorism in Iraq and Afghanistan. Seizures are a long-recognized sequela of head injury, especially when complicated by moderate-to-severe TBI. While seizures occur soon after head trauma in immediate and early post-traumatic epilepsy (PTE), epilepsy can be a delayed consequence with seizures occurring as far

out as 5-20 years. Penetrating head trauma, brain contusion, subdural hematoma, epidural hematoma, intracranial hemorrhage, and depressed skull fracture all increase the risk of PTE. Other predictors include age 65 years or older, Glasgow Coma Scale (GCS) of 3-8, loss of consciousness (LOC) > 30 minutes, and post-traumatic amnesia (PTA) lasting more than 24 hours.

The authors investigated risk factors for new-onset seizures in a cohort of 739 trauma patients. There were 362 trauma patients without TBI (GCS score of 15, no LOC, no PTA); 297 with mild TBI (GCS scores from 13-15, LOC < 30 minutes or PTA < 1 hour, no traumatic intracranial findings on CT/MRI); and 80 with moderate-to-severe TBI (GCS < 13, evidence of traumatic injury on CT/MRI). Those with a prior history of seizures, dementia, stroke, and other neurological disease were excluded. Out of 42 patients who developed new-onset seizure(s), alcohol-related seizures occurred in 19 (45.2%), most commonly among those with no TBI. Seventeen of these 19 patients (89.5%) with alcohol-related new-onset seizures were intoxicated at the time of the index trauma. Moderate-to-severe TBI patients had higher mortality and were more likely to develop PTE. Alcohol-related head injury, moderate-to-severe TBI, and preceding psychiatric disease were all found to be independent predictors of new-onset seizure.

■ COMMENTARY

One of the sequelae of trauma with TBI, in both the civilian and military setting, is the emergence of seizures and development of PTE, which may occur as far out as 5 years following head injury. While the severity of head trauma is the main predictor for the emergence of PTE, active alcohol and drug abuse at the time of the index injury predisposes to new onset seizures via a complex and multifaceted interaction. Alcohol impairs reaction time, hand-eye coordination, judgment, and driving skills, predisposing one to trauma and TBI. It further lowers the seizure threshold via its effects on glutamate NMDA and GABA receptors.[1] Chronic alcoholics are prone to electrolyte and glucose imbalance and seizures may occur both in the setting of binge drinking (rum fits) as well as abrupt cessation (alcohol withdrawal seizures and delirium tremens). Patients may at times present with new onset status epilepticus. All patients with head trauma should be screened for alcohol and drug abuse and effective intervention strategies should be implemented if abuse is identified. These patients remain at risk for post-traumatic seizures and should be kept under observation. While benzodiazepines such as lorazepam are efficacious for primary and secondary prevention of recurrent seizures in the alcoholic patient, long-term anticonvulsant therapy may not be needed in abstinent patients or those with mild TBI.[2,3] ■

References

1. Hillbom M, et al. Seizures in alcohol-dependent patients: Epidemiology, pathophysiology and management. *CNS Drugs* 2003;17:1013-1030.
2. McMicken DB, Freedland ES. Alcohol-related seizures. Pathophysiology, differential diagnosis, evaluation, and treatment. *Emerg Med Clin North Am* 1994;12:1057-1079.
3. Bråthen G, et al. EFNS Task Force on Diagnosis and Treatment of Alcohol-Related Seizures. EFNS guideline on the diagnosis and management of alcohol-related seizures: Report of an EFNS task force. *Eur J Neurol* 2005;12:575-581.

ABSTRACT & COMMENTARY

Get Thee to the Pharmacy! Delays in Clopidogrel After Coronary Stenting Can be Deadly

By Jeffrey Zimmet, MD, PhD

Associate Professor of Medicine, University of California, San Francisco, Director, Cardiac Catheterization Laboratory, San Francisco VA Medical Center

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

This article originally appeared in the July 2014 issue of Clinical Cardiology Alert. *It was edited by Michael H. Crawford, MD, and peer reviewed by Susan Zhao, MD. Dr. Crawford is Professor of Medicine, Lucie Stern Chair in Cardiology, Director, Cardiology Fellowship Program, Chief of Clinical Cardiology, University of California, San Francisco, and Dr. Zhao is Director, Adult Echocardiography Laboratory, Associate Chief, Division of Cardiology, Department of Medicine, Santa Clara Valley Medical Center. Dr. Crawford and Dr. Zhao report no financial relationships relevant to this field of study.*

Source: Cruden NL, et al. Delay in filling first clopidogrel prescription after coronary stenting is associated with an increased risk of death and myocardial infarction. *J Am Heart Assoc* 2014;3:e000669.

During my final year of interventional cardiology training, a woman in her 60s was brought emergently to the cath lab in cardiogenic shock, with diffuse ST-segment elevations. She had undergone PCI of the RCA and LAD coronary arteries just over a week earlier at an outside hospital. During her catheterization procedure, both stents were found to be occluded with clot. After successfully treating both vessels and inserting an intra-aortic balloon pump, we met with the family to go over her condition and review her history. There in the neatly organized discharge folder the family had brought in from her recent hospitalization was her prescription for clopidogrel, unfilled.

We all know that dual antiplatelet therapy after coronary stenting is an essential component of avoiding stent thrombosis and related downstream events. Issues with medication adherence are an underappreciated source of poor outcomes. In this study, Cruden and colleagues reviewed records from all patients receiving coronary stents in British Columbia from 2004-2006. Data from cardiac revascularization reports, community pharmacy, and hospital administrative records were reviewed, yielding information on 15,629 patients post-stent, with data out to 2 years. Among this group, 3599 patients had at least one drug-eluting stent (DES) placed, while the remaining 12,030 patients received only bare-metal stents (BMS). While the median elapsed time from hospital discharge to filling of the first clopidogrel prescription was 1 day, a substantial proportion took considerably longer. In fact, approximately 30% of patients in both the DES and BMS groups failed to fill their clopidogrel within 3 days of discharge.

Patients who delayed filling their prescriptions by at least 3 days were older, had a higher burden of comorbidities, and were more likely to have been treated for ST-elevation myocardial infarction (MI) compared to those who filled their prescriptions without that delay. Using a regression analysis, delayed filling of clopidogrel prescriptions by > 3 days was associated with an increased probability for death, repeat admission for MI, and the combined endpoint of death and recurrent MI (hazard ratio [HR], 2.4; 95% confidence interval [CI], 1.7-3.4; HR, 2.0; 95% CI, 1.5-2.7; and HR, 2.0; 95% CI, 1.6-2.6, respectively, for DES; HR, 2.2; 95% CI, 1.9-2.6; HR, 1.8; 95% CI, 1.5-2.1; and HR, 2.0; 95% CI, 1.8-2.3, respectively, for BMS). As seen from these data, the increased risks associated with delay in filling clopidogrel prescriptions were similarly increased for both BMS and for DES. The effect was greatest in the first 30 days after hospital discharge, but a delay in filling the clopidogrel prescription remained a predictor of death and MI out to 2 years of follow-up. The authors concluded that delays in filling the first prescription for clopidogrel after coronary stenting are common and associated with adverse clinical outcomes, regardless of stent type.

■ COMMENTARY

Nothing about this study should be particularly surprising. It is well-known that stopping dual antiplatelet therapy early is an important predictor of poor outcomes including stent thrombosis, MI, and death. As the risk of stent thrombosis is greatest early after stent implantation, when endothelialization is least complete, it stands to reason that a failure to initiate outpatient treatment in a timely fashion can have disastrous results.

Previous work has looked at similar data but with smaller sample sets, or with only a single stent type. Nevertheless, the overall findings are similar. A prior study in the United States found that one in six patients had a significant delay in filling post-discharge clopidogrel prescriptions, but questions were raised about the completeness of their pharmacy data. In the current study performed in a province-wide fashion in Canada, nearly one in three patients delayed filling their prescriptions. This should put us all on alert, and refocus our efforts to do those things that have been proven to improve post-hospitalization medication adherence: namely, good discharge planning and patient education, ensuring close telephone and clinic follow-up, and addressing barriers to obtaining and affording medications. Some hospital systems have taken to supplying patients with medications at the time of discharge, thus bypassing the need to go to the pharmacy themselves soon after a hospital admission. More and better systems' approaches to this problem are needed or more cardiologists will not place a stent if they are concerned that the patient will not be compliant. ■

CME INSTRUCTIONS

To earn credit for this activity, please follow these instructions:
1. Read and study the activity, using the provided references for further research.
2. Scan the QR code to the right or log on to **www.cmecity.com** to take a post-test; tests can be taken after each issue or collectively at the end of the semester. First-time users will have to register on the site using the 8-digit subscriber number printed on their mailing label, invoice or renewal notice.
3. Pass the online tests with a score of 100%; you will be allowed to answer the questions as many times as needed to achieve a score of 100%.
4. After successfully completing the last test of the semester, your browser will be automatically directed to the activity evaluation form, which you will submit online.
5. Once the completed evaluation is received, a credit letter will be e-mailed to you instantly.

CME QUESTIONS

1. In the randomized controlled trial of protocolized versus standard care for the early management of sepsis, published by the ProCESS investigators, mortality was not different across the study groups. However, which of the secondary outcomes were statistically improved in the early goal-directed therapy protocol groups?

a. ICU length of stay
b. Duration of shock
c. Incidence of acute kidney injury
d. None of the above

2. In the study by Wald and colleagues, an electronic surveillance tool for catheter-associated urinary tract infections had what degree of accuracy compared to a manual surveillance method?

a. The electronic surveillance tool was never correct.
b. The electronic surveillance tool had a high negative predictive value but a low positive predictive value.
c. The electronic surveillance tool had a low negative predictive value but a high positive predictive value.
d. The electronic surveillance tool had both a high negative predictive value and a high positive predictive value.

3. In the study by Mekontso Dessap, et al., a conservative fluid strategy had what effect on respiratory failure?

a. Higher incidence of acute renal failure
b. Longer weaning times
c. Lower incidence of ventilator-associate pneumonia
d. Prolongation of hospital length of stay

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.

[IN FUTURE ISSUES]

More original, peer-reviewed content by and for hospitalists