EVIDENCE-BASED INFORMATION FOR HOSPITALISTS, INTENSIVISTS, AND ACUTE CARE CLINICIANS

HOSPITAL MEDICINE ALERT

AHC Media Home Page—www.ahcmedia.com

CME for Physicians—www.cmeweb.com

AHC Media

INSIDE

Incidence of Constrictive Pericarditis

ABSTRACT & COMMENTARY

By Michael H. Crawford, MD

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

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

This article originally appeared in the November 2011 issue of Clinical Cardiology Alert. *It was peer reviewed by Ethan Weiss, MD. Dr. Weiss is Assistant Professor of Medicine, Division of Cardiology and CVRI, University of California, San Francisco. Dr. Weiss is a scientific advisory board member for Bionovo.*

Source: Imazio M, et al. Risk of constrictive pericarditis after acute pericarditis. *Circulation* 2011;124:1270-1275.

Since there is a lack of prospective data on the frequency of which constrictive pericarditis (CP) develops after acute pericarditis (AP), this group of investigators from Torino, Italy, conducted such a study. From 2000 until 2008 all cases of first AP were followed and evaluated for the development of CP at 1 month, 3 months, and every 6 months thereafter for a median follow-up of 72 months (range, 24-120). Follow-up evaluation included ECG, blood tests, and echocardiograms. The study included 500 consecutive patients with AP; 416 (83%) had viral or idiopathic AP; 36 (7%) had pericardial injury (e.g., surgery) or connective tissue disease; 25 (5%) had neoplastic; 20 (4%) had tuberculosis; and three (0.6%) had purulent. Recurrent AP was the most frequent subsequent adverse event (30%), followed by tamponade (4%). Transient CP was detected by echocardiography in 15% with resolution in 3 months. Effusive CP was seen in 1%. CP developed in nine (1.8%): two had viral or idiopathic AP and seven had other etiologies of AP. Purulent and tuberculosis patients had the highest incidence of CP. All the patients with permanent CP were confirmed by surgery. Pathology showed normal pericardial thickness in 11% of the permanent CP patients. Those who developed CP were more likely than those who did not to have fever (67% vs 15%),

Financial Disclosure:

Hospital Medicine Alert's physician editor, Kenneth P. Steinberg, MD, executive editor Russ Underwood, and associate managing editor Jill Von Wedel have no relevant financial relationship related to the material presented in this issue.

incessant course (56% vs 7%), non-idiopathic/viral etiology (78% vs 16%), large pericardial effusion (67% vs 9%), tamponade (44% vs 4%), and nonsteroidal anti-inflammatory drug failure (67% vs 19%), all $P < 0.002$. There was a trend toward more steroid use and a lower use of colchicine in those who developed CP, but these differences were not statistically significant. The authors concluded that CP is a rare complication of viral or idiopathic AP, but is more common with other etiologies such as bacterial pericarditis.

■ **COMMENTARY**

The important message of this prospective study is that we can reassure patients with viral or idiopathic pericarditis that the likelihood of them developing CP is very low. Thus, intense follow-up after the first 6 months is unwarranted in these patients. Also, recurrent AP in viral/idiopathic patients has a good prognosis.

Other etiologies are another matter. Tuberculosis has a higher rate of CP ranging from 5%-60% depending on the study and the stage of the disease. The relatively low rate of CP in tuberculosis in this study may be because it was infrequent or the follow-up was not long enough. Other etiologies, such as uremic and neoplastic, may have low rates because the patients do not survive long enough to develop CP. The described risk factors for CP may be a guide for whom to follow more closely. Most useful would be an incessant course, a large effusion, tamponade, or failure of anti-inflammatory therapy. Also of interest clinically was the observation that about 10% of those who developed CP had normal pericardial thickness on pathology and imaging. Thus, normal pericardial thickness does not exclude CP. Another interesting finding was that effusive CP was unusual, occurring in about 1% of the AP patients. Finally, transient CP was observed in 15% and it resolved in 3 months. Thus, surgery should not be considered until 3 months have passed with CP.

The study did not address drug therapy, although there was a trend for more CP in those treated with steroids. Also, the study confirms the use of colchicine as first-line therapy since lower colchicine use correlated with development of CP. ■

Hospital Medicine Alert, ISSN 1931-9037, is published monthly by AHC Media, a division of Thompson Media Group LLC, 3525 Piedmont Rd., NE, Bldg. 6, Suite 400, Atlanta, GA 30305.

EXECUTIVE EDITOR: Russ Underwood.
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 105109, Atlanta, GA 30348.

Back Issues: $42. Missing issues will be fulfilled by customer service free of charge when contacted within one month of the missing issue's date.

AHC Media

Subscriber Information

Customer Service: 1-800-688-2421.
Customer Service E-Mail: customerservice@ahcmedia.com
Editorial E-Mail: russ.underwood@ahcmedia.com

Subscription Prices

United States
1 year with free AMA Category 1 credits: $249
Add $17.95 for shipping & handling.
(Student/Resident rate: $125)

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.

Canada
Add 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 claim only the 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 36 months from the date of the publication..

Questions & Comments
Please call Russ Underwood, Executive Editor, at (404) 262-5521 or e-mail at russ.underwood@ahcmedia.com.

Risk of Perioperative MI in Patients with Stents Undergoing Surgery

ABSTRACT & COMMENTARY

By Andrew J. Boyle, MBBS, PhD

Assistant Professor of Medicine, Interventional Cardiology, University of California, San Francisco

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

This article originally appeared in the November 2011 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: Albaladejo P, et al. Non-cardiac surgery in patients with coronary stents: The RECO study. *Heart* 2011;97:1566-1572.

Patients who have had percutaneous coronary intervention (PCI) with either bare metal stents (BMS) or drug-eluting stents (DES) require dual antiplatelet therapy until the stent struts are endothelialized. However, patients who have had prior PCI often need to undergo surgery. There is thought to be less risk of perioperative myocardial infarction (MI) when surgery is performed late after PCI; however, the precise risk and the optimal management of dual antiplatelet therapy remains unknown. Albaladejo and colleagues performed a multicenter, prospective, observational study in 47 centers in France to address this question.

They enrolled 1134 patients undergoing non-cardiac surgery (including diagnostic endoscopy). DES were used in 55%, BMS in 32%, and unknown stent type in 13%. DES use was associated with younger age (67 ± 11 vs 70 ± 10 years, $P < 0.001$), higher prevalence of diabetes (33% vs 22%, $P < 0.001$), and higher number of stents per patient (2.3 ± 1.4 vs 1.6 ± 0.9, $P < 0.001$). There were no differences between DES and BMS patients in terms of preoperative antiplatelet therapy and the level of risk of the surgery.

Continuation or discontinuation of antiplatelet therapy was not prespecified, but was at the discretion of the physician at the preoperative visit.

The primary endpoints were any major adverse cardiac and cerebrovascular events (MACCE) or hemorrhagic complication. MACCE was defined as MI, stent thrombosis, stroke, heart failure, significant arrhythmia, or cardiogenic shock. Bleeding was considered major if it resulted in death, fall in hemoglobin ≥ 2g/dL, transfusion, extra surgical or medical treatment, or if it was in a critical location (intracerebral, intraspinal, intraocular, pericardial retroperitoneal). All other bleeding was considered minor. All-cause mortality was a secondary endpoint.

MACCE occurred in 10.9%, typically around 3.3 ± 3.8 days after surgery, and was predominantly MI. Patients who experienced MACCE were older (71 ± 10 vs 68 ± 11 years, P < 0.01) and more likely to have heart failure (19.4% vs 8.4%, P < 0.001) and a high American Society of Anesthesiologists classification. There was no difference in gender or type of stent. Independent predictors of MACCE were: complete interruption of antiplatelet therapy for > 5 days preoperatively (odds ratio [OR] 2.11, P < 0.01), preoperative hemoglobin < 10 g/dL (OR 3.0, P = 0.016), creatinine clearance < 30 mL/min (OR 3.5, P < 0.01), urgent surgery (OR 3.1, P < 0.001), and high-risk surgery (OR 3.6, P < 0.001). Importantly, the time interval between stenting and surgery was not predictive of MACCE. Patients who experienced MACCE had a 14.5% mortality. Stent thrombosis (definite, probable, or possible) occurred in 2.5% when the delay from PCI to surgery was < 12 months, and 1.3% when the interval was > 12 months. The rate of stent thrombosis did not differ between DES and BMS. The mortality associated with stent thrombosis was 29%.

Bleeding complications occurred in 9.5%, typically occurred 5.3 ± 5.3 days after surgery, and were at the surgical site in 85%. Patients who experienced bleeding complications had lower body weight (75.7 ± 14.1 kg vs 78.4 ± 14.6 kg, P = 0.04) and a higher rate of congestive heart failure (16.7 vs 8.4%, P = 0.001). Independent predictors of bleeding complications were: preoperative hemoglobin < 10 g/dL (OR 2.6, P < 0.05), creatinine clearance 30-60 mL/min (OR 1.96, P < 0.01), high-risk surgery (OR 3.3, P < 0.001), and time from PCI to surgery < 3 months (OR 2.9, P = 0.001). Patients who experienced bleeding complications had a 12% mortality.

The authors conclude that patients with coronary stents undergoing an invasive procedure are at high risk of perioperative cardiovascular and bleeding complications, and that these are associated with a high mortality. Interruption of antiplatelet therapy > 5 days prior to an invasive procedure increased the rate of MACCE but did not change risk of bleeding.

■ COMMENTARY

Current guidelines recommend postponing elective surgery for at least 6 weeks after BMS and 12 months after DES. This study is one of the largest series published to date and one of the few that reports both ischemic (MACCE) and bleeding complications together. Several factors are noteworthy in this dataset. Firstly, preoperative anemia and renal impairment predict both bleeding and ischemic complications. This may be because anemia and renal impairment are dangerous per se, or because they are indicators of severe underlying disease that predisposes to post-operative complications. In this series, high-risk surgery was a predictor of postoperative events as well, whereas in other series this has not been the case. One reason for this may be that this cohort included diagnostic endoscopy, which is not really a surgery and should have little bleeding and ischemic risk. This may introduce bias by lowering the rate of complications in the "low risk" category here because some of the low-risk surgeries were not actually surgeries. Many other series do not include endoscopy.

The type of stent (DES vs BMS) had no effect on MACCE. This contradicts the hype and dogma that stent thrombosis is a great danger with DES. In fact, this has been borne out in other series as well. Importantly, this cohort was recruited starting in 2007, when media attention on DES stent thrombosis was at fever pitch. Consequently, many DES patients in this cohort underwent surgery on dual antiplatelet therapy, which may have reduced their perioperative MACCE rate. It is also possible that the high bleeding rate in this study also may have been due to continuation of dual antiplatelet therapy throughout the operative period in many patients. This study does not inform us how to manage dual antiplatelet therapy in every patient with coronary stents prior to every surgery. We must continue to individualize treatment based on the surgical bleeding risk vs the risk of peri-operative MI. But it would seem prudent in light of these data, and other series showing similar findings, that antiplatelet therapy not be ceased for more than 5 days preoperatively. ■

Saddle Pulmonary Embolism: Is It the Same as 'Massive' PE?

ABSTRACT & COMMENTARY

By David J. Pierson, MD

Professor Emeritus, Pulmonary and Critical Care Medicine, University of Washington, Seattle

This article originally appeared in the November 2011 issue of Critical Care Alert. *It was peer reviewed by William Thompson, MD. 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: *Saddle pulmonary embolism was found in 37 of 680 patients with documented pulmonary embolism (PE) in this community hospital study. The great majority of these patients did well on standard therapy without thrombolytics, emphasizing that the radiographic finding of saddle PE should not by itself be equated with the much more serious clinical entity of massive PE.*

Source: Sardi A, et al. Saddle pulmonary embolism: Is it as

bad as it looks? A community hospital experience. *Crit Care Med* 2011;Jun 23. [Epub ahead of print]

Saddle pulmonary embolism (SPE) is defined as the presence of a thromboembolus located at the bifurcation of the main pulmonary artery. Once identified at post-mortem examination or by pulmonary arteriography, SPE is now most commonly encountered by clinicians as a radiographic finding on computed tomography angiography (CTA). The authors of this retrospective study of all CTAs that were read as positive for PE over a 4.75-year period at Albert Einstein Medical Center in Philadelphia sought to determine the clinical features, associated findings, management, and outcomes of all patients with SPE. Patients older than 18 years were identified by IDC-9 codes indicating a positive CTA for PE, and the images were then reviewed independently by two radiologists who were unaware of the patients' clinical status or other data. The findings on transthoracic echocardiography (TTE) on patients determined to have SPE by CTA were assessed by standardized criteria, and other clinical information was extracted from the patients' charts.

During the study period, which ended in early 2009, 680 patients had the diagnosis of PE established by CTA, and 37 (5.4%) of them met the authors' criteria for SPE. With a median age of 60 years, these patients were predominately women (60%) and African American (84%), and 81% of them were admitted through the emergency department. The most frequent comorbidities were history of stroke (24%), surgery within 3 months (24%), and malignancy (22%). Fifteen of the 37 patients (41%) were admitted to the ICU and one required mechanical ventilation.

The amount of thrombus present by CTA in the patients with SPE, estimated using a 40-point clot burden score, was a median of 31 points, believed to correspond to 79% occlusion. The median radiographic right-to-left ventricle diameter ratio was 1.39 (normal < 0.7), with a median pulmonary artery-to-aorta diameter ratio of 1.0 and a median superior vena cava diameter 23 mm. TTE was performed in 27 of the 37 patients with SPE (73%); 21 (78%) had right ventricular enlargement, which was severe in seven patients, moderate in eight, and mild in six. Right ventricular dysfunction by TTE was noted in 21 patients (78% — severe in five, moderate in eight, and mild in seven), and 18 (67%) had elevated pulmonary arterial systolic pressure (not defined). Interventricular septum flattening and/or leftward deviation was found in seven patients (26%).

Transient hypotension occurred in six patients (16%) and persistent shock (systolic blood pressure 90 mmHg or less after intravenous administration of at least 500 mL of crystalloid) was present in three (8%). Most of the patients (87%) were treated with unfractionated heparin, and only four (11%) received thrombolytics. One heparin-treated patient had a gastrointestinal bleed; two who were given thrombolytics had major and a third had a minor hemorrhagic complication. Seventeen patients (46%) received inferior vena cava filters. Two patients died, one in the emergency department, presumably of PE, and one 2 weeks after admission with multiple-organ failure.

■ COMMENTARY

This study's authors asked the following research question: "What are the demographics, laboratory findings, TTE results, CTA findings, treatment, and outcomes of patients with SPE in our institution?" This is the type of question that can be addressed pretty well in a retrospective study, as long as relevant data are available on a high proportion of all patients with the variable of interest (SPE in this case). A more important (though unstated) research question would be, "What are the clinical implications of the radiographic finding of SPE among patients with CTA-confirmed PE?" Unfortunately, the present study cannot help us with this second question, which would require comparing the information in the paper with the same data from an appropriately-selected control group — in this instance, a sample of the 94.6% of all patients with PE who did not have SPE. As it is, while the description of this consecutive case series adds to the literature on SPE, the applicability of the findings beyond the authors' institution is uncertain, and the most important questions about what the clinician should do when the radiologist reports the finding of SPE remain unanswered.

One thing this study brings out, though, is the distinction between SPE and massive pulmonary embolism (MPE). MPE is a clinical syndrome with high mortality defined by the degree of hemodynamic compromise present in a patient with acute PE — essentially, cardiogenic shock or persistent hypotension, further specified as a systolic blood pressure persistently < 90 mmHg, or a drop in baseline blood pressure of at least 40 mmHg for > 15 minutes.[1] SPE is very common among patients with MPE, but the reverse is not necessarily the case, as the data of Sardi et al illustrate. CTA has become the gold standard for diagnosing PE, and is performed far more often today than in past decades. Today, clinicians are increasingly likely to hear the words "massive pulmonary embolism" from a radiologist, meaning that the clot burden visualized on the exam is extensive, and it is important to realize that this term can be used in more than one way. Additional studies are needed to determine whether the finding of SPE by itself constitutes an important prognostic factor, or whether it should be taken into consideration separately from other clinical information in deciding how the patient with acute PE should be managed. ■

Reference

1. Kucher N, Goldhaber SZ. Management of massive pulmonary embolism. *Circulation* 2005;112:e28-32.

Risks of ICU Admission Include Unintentional Discontinuation of Medications

ABSTRACT & COMMENTARY

By Leslie A. Hoffman, RN, PhD

Department of Acute/Tertiary Care, School of Nursing, University of Pittsburgh

Dr. Hoffman reports no financial relationship to this field of study.

This article originally appeared in the November 2011 issue of Critical Care Alert. *It was edited by David J. Pierson, MD, and was 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: *Admission to an ICU increased risk for unintentional medication discontinuation in four of five medication groups commonly used to manage a chronic illness.*

Source: Bell CM, et al. Association of ICU or hospital admission with unintentional discontinuation of medications for chronic diseases. *JAMA* 2011;306:840-847.

To determine the risk of potentially unintended discontinuation of common, evidence-based medications for chronic disease, Bell and colleagues examined administrative records for 12 years (1997–2009) for all hospitalized patients and all outpatient prescriptions in Ontario, Canada. Patients were included if they were ≥ 66 years of age and continuously prescribed one of five medications for at least 12 months: 1) statins, 2) antiplatelet/anticoagulants, 3) levothyroxine, 4) an inhaled respiratory drug (anticholinergic, beta-agonist, steroid), or 5) a gastric acid-suppressing drug. Three cohorts were formed: 1) patients discharged after an admission that included an ICU stay (n = 16,474), 2) patients discharged after an admission that did not include an ICU admission (n = 171,438), and 3) patients not hospitalized (controls; n = 208,468). The study controlled for a number of potential confounding variables, including age, sex, income, length of stay, and disease burden (number of medications prescribed). Separate analyses were performed for each of the five medication groups.

Patients admitted to a hospital were more likely to experience a potentially unintentional discontinuation of a medication compared to controls across all medication groups examined. The adjusted odds ratio (AOR) ranged from 1.18 (95% confidence interval [CI], 1.14-1.23) for discontinuing levothyroxine in 12.3% of hospitalized patients vs 11.0% of controls to an AOR of 1.86 (95% CI, 1.77-1.97) for discontinuing antiplatelet/anticoagulant agents in 19.4% of hospitalized patients vs 11.8% of controls. With ICU exposure, the AOR ranged from 1.48 (95% CI, 1.39-1.57) for discontinuing statins in 14.6% of ICU patients to an AOR of 2.31 (95% CI, 2.07-2.57) for discontinuing antiplatelet/anticoagulant agents in 22.8% of ICU patients vs the control group. Admission to an ICU was associated with an additional risk of medication discontinuation in four of five medication groups compared to hospitalizations without an ICU admission. A 1-year follow-up of patients with discontinued medications showed an elevated AOR for the secondary composite outcome of death, emergency department visit, or emergent hospitalization of 1.07 (95% CI, 1.03-1.11) for statins and of 1.10 (95% CI, 1.03-1.16) in the antiplatelet/anticoagulant agents group.

■ COMMENTARY

This study highlights a serious risk factor common to all care transitions. When patients change care providers, critical information may be omitted or not clearly communicated, resulting in an increased risk for adverse events. In this study, hospitalized patients experienced an increased risk for unintentional discontinuation of a medication at discharge. Admission to an ICU was associated with a higher risk for this outcome. At 1 year, there was an increased risk of death, an emergency department visit, or emergent hospitalization when two groups of medications — statins and antiplatelet/anticoagulant agents — were not continued after hospitalization.

Given the retrospective design, it is possible that decisions to discontinue medications may have been intentional. However, the authors took multiple steps to minimize this potential. All of the selected medications had well-established long-term efficacy for the management of a chronic disease. Only patients who had taken the medication continuously for 1 year were included. Unintentional discontinuation was defined as no renewal within 90 days plus a grace period to allow for medications remaining from past prescriptions. New prescriptions within the same drug classification were not categorized as a discontinuation. Given these constraints, the percentage of patients who experienced unintentional medication discontinuation is very alarming. For hospitalized patients, antiplatelets/anticoagulants (19.1%) led, followed by statins (13.5%), gastric acid suppressors (12.7%), levothyroxine (12.1%), and respiratory inhalers (4.4%). For ICU patients, the sequence was the same but the percentage was higher, e.g., antiplatelets/anticoagulants (22.8%), followed by statins (14.6), gastric acid suppressors (15.4%), levothyroxine (15%), and respiratory inhalers (5.4%). The authors posed several explanations for a higher risk in ICU patients. ICU patients likely experience more transitions. Care is focused on the critical episode, not an underlying chronic illness.

Some medications get discontinued and this increases the risk that they will be forgotten at ICU discharge.

Given these findings, what can be done to improve patient safety? Enhanced awareness of the potential for unintentional discontinuation on the part of all providers is one option. However, the hectic nature of critical care makes it doubtful that omissions will not occur, despite good intentions. The best solution is likely electronic medical records that list prior medications and, therefore, make it easier to recall what needs to be continued or reordered during each care transition. ■

Daily Prompting on ICU Checklist Use Improves Patient Outcomes as Well as Processes of Care

ABSTRACT & COMMENTARY

By David J. Pierson, MD

Professor Emeritus, Pulmonary and Critical Care Medicine, University of Washington, Seattle

This article originally appeared in the November 2011 issue of Critical Care Alert. *It was peer reviewed by William Thompson, MD. 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: *In this study from a single medical ICU, prompting physicians to discuss all six items on a daily rounding checklist, as compared with the use of the same checklist without prompting, significantly improved several processes of care and appeared to decrease length of stay and mortality as well.*

Source: Weiss CH, et al. Prompting physicians to address a daily checklist and process of care and clinical outcomes: A single-site study. *Am J Respir Crit Care Med* 2011;184:680-686

Previous studies have shown that the use of a multi-part daily rounding checklist reduces errors of omission in the ICU — such as failure to discontinue empirically started antibiotics, to perform spontaneous breathing trials to see whether ventilated patients can be weaned and extubated, or to provide prophylaxis against deep venous thrombosis (DVT). This study sought to determine whether daily prompting of physicians to deal with the items in such a checklist during ICU rounds would improve processes of care and patient outcomes in comparison to simply introducing the same checklist into the ICU.

The study was carried out in the medical ICU of a major academic medical center. After introduction of the ICU rounding checklist to the unit, patients cared for by the two unit teams (each with an attending physician, ICU fellow, several residents, and a clinical pharmacist) comprised a control group and an intervention group. In the intervention group, a resident working on the study came on rounds (but had no involvement with managing the patients) and prompted the attending or fellow to discuss any of the six target items omitted from the checklist while the team was still rounding on each patient. The control team had the checklist available but no explicit efforts were directed at its implementation on rounds. Data from 1283 patients admitted to the unit before the checklist was introduced were compared to prospective data collected from intervention and control patients during the 82-day study period.

The checklist contained color-coded items to be filled out by nurses (e.g., lines and tubes), pharmacists (e.g., antibiotics and DVT prophylaxis), and physicians (e.g., sedative use and appropriateness of daily weaning trial), and entries were to be made each day the patient remained in the ICU. There were 140 patients in the intervention (prompted) group and 125 in the control group. Patient demographics, admitting diagnoses, time and day of admission, illness severity (APACHE IV), and proportion requiring mechanical ventilation (29%) were the same in the two groups.

The prompter was present on 68% of study days in the intervention group, although all days and patients in that group were included. Overall, prompting on at least one omitted checklist item occurred on 65% of patient days — i.e., the great majority of days on which the prompter attended rounds. Of the six items targeted for prompting, discussion of continued need for a Foley catheter was most frequently omitted (41% of patient days), followed by empirical antibiotics (36%), a central venous catheter (26%), mechanical ventilation (14%), DVT prophylaxis (1.5%), and stress ulcer prophylaxis (1%).

Compared with the control group, the prompted group had more median ventilator-free days (22 vs 16, P = 0.028), fewer days of empirical antibiotics (2 vs 3, P = 0.012), shorter duration of central venous catheter (3 vs 5 days, P = 0.007), and significantly more administration of DVT and stress-ulcer prophylaxis. Although hospital mortality was not different between the retrospectively examined preintervention patients and the control group, both ICU and hospital mortalities were lower in the prompted group (9% vs 17%, P = 0.05). APACHE IV-predicted ICU lengths of stay were the same in the control and prompted groups, but prompted patients had shorter ICU stays when calculated according to observed/predicted length of stay ratio (0.59 vs 0.87, P = 0.02). The authors conclude that daily prompting on checklist use improved multiple processes of care and may also have reduced mortality and length of stay, compared with the presence of the checklist without such prompting.

■ **COMMENTARY**

In this study, preintervention process-of-care data from the same unit (no checklist) were not different from results in the control group after the checklist was added. Little information is provided about just how the checklist was introduced in the unit. However, studies showing improved outcomes with checklists have also implemented substantial cultural change in the institution at the same time. In this study the cultural change was the prompting, and the control group results suggest that simply having a checklist available in the unit is not sufficient to change practice.

Patients managed by the team in which daily physician prompting occurred had improved processes of care and better outcomes. But several questions are raised as to how this finding might persist with different prompting scenarios. The prompter here was a physician (a resident), obviously an unrealistic situation for broader implementation. Would attending physicians and fellows (or community practitioners) be as receptive to real-time, face-to-face prompting by a nurse, or a clinical pharmacist — or a non-clinical hospital employee — during ICU rounds? Would some sort of automated, computerized prompting, perhaps tied to electronic order entry, work as well?

As pointed out by the authors, small pilot studies from single sites may have more impressive results than larger-scale multicenter studies of the same intervention. However, if the findings of this study hold up in broader contexts and with larger investigations, just how prompting is to be done may become an important issue. The decreased antibiotic use, shorter duration of mechanical ventilation, and reduced ICU length of stay found in this study have substantial potential economic implications that might be of interest to system administrators, third-party payers, and regulators. Some form of checklist-based, real-time prompting might well become part of daily practice in the ICU, making this matter one of considerable interest to the clinicians who work there. ■.

ACE Inhibitors/ARBs for Aortic Stenosis?

ABSTRACT & COMMENTARY

By Andrew J. Boyle, MBBS, PhD

Assistant Professor of Medicine, Interventional Cardiology, University of California, San Francisco

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

This article originally appeared in the October 2011 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: Nadir MA, et al. Impact of renin-angiotensin system blockade therapy on outcome in aortic stenosis. *J Am Coll Cardiol* 2011;58:570-576.

In severe symptomatic aortic stenosis (AS), surgical AVR improves mortality, but there is no medical therapy proven to slow progression of the valvular stenosis. Because AS is accompanied by left ventricular (LV) hypertrophy and fibrosis, and because the risk factors for AS are similar to those for coronary artery disease (CAD), it makes sense that blockade of the renin-angiotensin system may benefit patients with AS. Nadir and colleagues performed a retrospective observational study to address this issue. They linked several databases in the Tayside region of Scotland and were able to ascertain patient level data, including echocardiographic data, mortality, hospital admissions, medications, and laboratory tests. The use of angiotensin converting enzyme inhibitors (ACEIs) or angiotensin receptor blockers (ARBs) in patients with AS identified by echocardiography was then studied in terms of clinical outcomes.

A total of 2117 patients with AS were identified, 46% were male and the mean age was 73 ± 12 years. Aortic stenosis was mild or moderate in 75%, and severe in 25%. One-third of patients were on ACEI or ARB therapy. There were significant baseline differences between those who received ACEIs or ARBs and those who did not receive them. Those receiving ACEIs or ARBs were older, and had a higher prevalence of LV dysfunction, diabetes, and prior cardiovascular (CV) events. However, they had less severe AS and more of them were receiving aspirin, beta-blockers, digoxin, anti-coagulants, and statins.

After a mean follow-up of 4.2 years, patients taking ACEIs or ARBs had lower mortality and fewer cardiovascular (CV) events. Adjusted hazard ratio [HR] for death was 0.76 ($P < 0.0001$) and for CV events was 0.77 ($P < 0.0001$). When stratified by severity of AS, the use of ACEI or ARB therapy was associated with a greater reduction in CV events in patients with severe AS (HR 0.64, $P = 0.04$) than in mild or moderate AS (HR 0.78, $P = 0.01$). To confirm these findings, the authors performed a propensity score matched cohort analysis on 532 patients. In this analysis, they also found that the use of ACEI or ARB therapy was associated with a reduction in all-cause mortality (HR 0.67) and CV events (HR 0.71). They also performed a time-scale analysis (Kaplan Meier) that confirmed these results. Importantly, for those patients in whom on-treatment blood pressure recordings were available (330 patients), there was no difference in systolic or diastolic blood pressure between groups. The authors conclude that this large observational study suggests ACEI or ARB therapy is associated with an improved survival and a lower risk of CV events in patients with AS.

■ **COMMENTARY**

Arterial vasodilators have long been relatively contraindicated in patients with severe LV outflow obstruction. Several

medications, including ACEIs, have failed to prevent progression of AS severity in clinical trials. This dataset from Nadir and colleagues is intriguing because they did not study the severity of the valve disease, but instead chose to study clinical events in AS patients. They demonstrate a striking reduction in CV events and death in patients taking ACEIs or ARBs, and this reduction in CV events was greater in those with more severe AS. The mechanism of the benefit is not immediately clear. It may relate to protection against myocardial fibrosis and hypertrophy, which are arrhythmogenic substrates. Alternatively, it may reduce vascular events, such as myocardial infarction. It is important to recognize that there were significant differences in baseline characteristics between groups. The authors performed several different statistical analyses that all demonstrated similar findings, which increases the confidence in their results. Despite this rigorous statistical methodology, there are likely to be confounding factors for which their analyses could not account. Therefore, it is important to interpret the data cautiously. However, their data do suggest that ACEIs or ARBs are safe in AS.

In light of these data, should all patients with AS be treated with ACEIs or ARBs? I think it is too soon to make such recommendations. However, if another indication for such a therapy exists, such as concomitant hypertension, then ACEIs or ARBs would be a reasonable choice for an antihypertensive. Future studies into the mechanism of any potential benefit, as well as prospective, randomized, controlled clinical trials are needed before we can recommend ACEIs or ARBs in patients with AS. ■

CME Questions

1. In the retrospective study by Sardi et al., the presence of a saddle pulmonary embolus (SPE) on CT angiography (CTA) was associated with persistent shock in what proportion of patients?

a. 8%

b. 23%

c. 50%

d. 81%

2. According to the prospective study by Imazio et al., patients presenting with acute viral or idiopathic acute pericarditis:

a. Require intense follow up for development of complications.

b. Have a high risk of developing constrictive pericarditis.

c. Have a high risk of developing tamponade.

d. Have a low risk of complications.

3. Daily prompting of physicians to discuss the items on an ICU rounding checklist resulted in what outcomes in the study by Weiss et al.?

a. Reduced mortality.

b. Reduced ICU length of stay.

c. Increased number of ventilator-free days.

d. All of the above.

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. ■

CME Instructions

1. Read and study the activity, using the provided references for further research.

2. 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 evaluation is received, a credit letter will be sent to you. ■