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Hospital Medicine

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ABSTRACT & COMMENTARY

Warfarin may decrease morbidity and mortality in patients with kidney disease and atrial fibrillation after MI

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

SYNOPSIS: Patients with chronic kidney disease, acute myocardial infarction and atrial fibrillation and treated with warfarin had a lower risk for death, MI and ischemic stroke without a higher risk of bleeding.

SOURCE: Carrero J, Evans M, etal. Warfarin, Kidney Dysfunction, and Outcomes Following Acute Myocardial Infarction in Patients with Atrial Fibrillation. *JAMA*. 2014; 311(9):919-928.

Patients with chronic kidney disease (CKD) are at increased risk of bleeding, atherosclerotic and thromboembolic events. These risks increase with progression of the CKD. Atrial fibrillation is common in patients with CKD. Warfarin is traditionally used in patients with atrial fibrillation to prevent thromboembolic disease. Observational studies analyzing the efficacy of warfarin in patients with CKD and atrial fibrillation have mixed results. This study sought to analyze outcomes of warfarin treatment in patients with CKD, cardiovascular disease and atrial fibrillation.

This study is an observational, multicenter, prospective cohort study that used the Swedish Web-System for Enhancement and Development of Evidence-Based Care in Heart Disease Evaluated According to Recommended Therapies (SWEDEHEART) registry (2003-2010) data. This registry uses data from all Swedish hospitals that give care to patients with acute cardiac disease. Patient past medical history was obtained from the registry and supplemented from the National Inpatient Registry, which includes data from all hospitalizations. Patient outcomes were stratified by renal function, which were cat-

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egorized by eGFR (estimated glomerular filtration rate): those with eGFR higher than 60mL/min/1.73m^2 were grouped together (normal renal function, CKD stage 1, or CKD stage 2); those with eGFR of 30-60mL/min/1.73m^2 were defined as having moderate dysfunction (CKD stage 3); those with eGFR of 15-30mL/min/1.73m^2 were defined as having severe dysfunction (CKD stage 4); and those with eGFR of <15mL/min/1.73m^2 were defined as having end-stage renal disease (CKD stage 5). The study compared patients with a recent cardiovascular event and atrial fibrillation treated with warfarin vs. those that did not. Exposure to warfarin was defined as a prescription being given to the patient at discharge per the data in SWEDEHEART. The Swedish population registry was used to obtain mortality data. The following outcomes were analyzed: death, readmission for myocardial infarction (MI), stroke or bleeding within 1 year. The authors defined bleeding as anemia caused by bleeding, gastrointestinal bleeding or hemorrhagic stroke. Two sensitivity analyses were performed to minimize confounding variables and to calculate propensity scores in order to appropriately match patients.

More than 158,000 patients were admitted for MI during the period 2003 – 2010. Of these patients, over 34,000 had also had atrial fibrillation. Patients were excluded if they did not have information in the data set regarding their age, kidney function or warfarin treatment status. There were 24,317 patients who were included in the final analysis, and 21.8% of them had taken warfarin. There were no significant differences between the two groups in terms of basic demographics; however, the warfarin group was more likely to have heart failure, diabetes and stroke. The group that did not receive warfarin was more likely to have a clinical history of bleeding or hemorrhagic stroke, and 51.7% of patients had CKD III or higher.

The authors compared patients taking warfarin with those who did not with respect to a composite outcome of death, myocardial infarction, and ischemic stroke. A Cox regression analysis showed the following results, in terms of number of events per 100 person-years. For patients with an eGFR>60 (normal, CKD stage 1 or CKD stage 2), the event rate was 28.0 for warfarin vs. 36.1 for no warfarin, and adjusted hazard ratio (HR) was 0.73 (95% CI, 0.65 to 0.81); for CKD stage 3, the event rate was 48.5 for warfarin vs. 63.5 for no warfarin (HR 0.73, 95% CI 0.66 to 0.80); for CKD stage 4, the event rate was 84.3 for warfarin vs. 110.1 for no warfarin (HR 0.84, 95% CI 0.70-1.02); and for end-stage renal disease, the event rate was 83.2 for warfarin vs. 128.3 for no warfarin (HR 0.57, 95% CI 0.37-0.86). The bleeding risk for patients on warfarin compared with those not on warfarin, stratified by renal function, were as follows: For normal, CKD stage 1 or CKD stage 2, HR 1.10 [95% CI, 0.86-1.41]; for CKD stage 3, HR 1.04 [95% CI 0.81-1.33]; for CKD stage 4, HR 0.82 [95% CI 0.48-1.39]; and for end-stage renal disease, HR 0.52 [95% CI 0.16-1.65].

■ COMMENTARY

Patients with atrial fibrillation and CKD are very common. Hospitalists often start warfarin for patients with CKD and newly diagnosed atrial fibrillation. Although this practice is common, there has been little data as to the safety and efficacy of this practice in these patients. In addition, these patients tend to have multiple comorbidities, and they are not able to take the newer drugs for atrial fibrillation. One limitation of the study was that it is administrative data, which can be flawed. The definition of warfarin use was that the patient received a prescription at discharge. There were no data presented that the patients on warfarin were successfully anticoagulated based on an INR between 2 and 3. In addition, there were differences in comorbidities between the groups that were analyzed. However, the number of patients analyzed is impressive, and a randomized controlled trial would be incredibly challenging to do to answer this question. Based on this study, hospitalists should be comfortable prescribing warfarin for atrial fibrillation to their CKD patients in the absence of specific contraindications to warfarin or anticoagulation in general. ■

ABSTRACT & COMMENTARY

Prognosis of Ventricular Fibrillation in Acute Myocardial Infarction

By Michael H. Crawford, MD

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This article originally appeared in the March 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.*

SOURCE: Bougouin W, et al. Incidence of sudden cardiac death after ventricular fibrillation complicating acute myocardial infarction: A 5-year cause-of-death analysis of the FAST-MI 2005 registry. *Eur Heart J* 2014;35:116-122.

At this time, ventricular fibrillation (VF) early after acute myocardial infarction (MI) is not an indication alone for an implantable cardioverter-defibrillator (ICD) therapy. However, there is concern that despite the efficacy of mechanical and pharmacological therapy for acute MI, the risk of subsequent sudden cardiac death (SCD) in patients with VF complicating acute MI may be higher and the guidelines should be revisited. Thus, these investigators from the French registry on Acute ST-elevation and non-ST elevation Myocardial Infarction (FAST-MI) registry enrolled 3670 patients with acute MI in October 2005 and reported the 5-year follow-up data from this study population. Enrolled patients had to present within 48 hours of symptom onset and meet the international definition of acute MI. Excluded were iatrogenic MIs (e.g., postsurgical). The primary endpoints were deaths, classified as sudden cardiac death (SCD), non-SCD, and non-cardiac deaths, and related to early (< 48 hours after admission) or late (prior to hospital discharge) VF. A variety of clinical and demographic features were used in a multivariate model.

The incidence of in-hospital VF was 3.2% with 79% being early. VF patients were younger and more often smokers compared to the rest of the MI population. Beta-blocker therapy did not differ according to VF occurrence. Only anterior MI location was associated with VF occurrence. Interestingly, the presence of atrial fibrillation on the first ECG was associated with VF by multivariate analysis (hazard ratio [HR], 2.5; 95% confidence interval [CI], 1.4-4.4; $P = 0.003$). In-hospital mortality was higher in the VF group (25% vs 5%; $P < 0.001$) with an adjusted HR of 7.38 (95% CI, 4.27-12.75; $P < 0.001$). Also, mortality was higher with early vs late VF (33% vs 23%; $P < 0.001$). In-hospital death in the VF group was mainly from arrhythmias (82%) whereas cardiogenic shock was the most common cause in non-VF patients (62%). The overall survival at 5 years was 74% and was not associated with the occurrence of in-hospital VF on multivariate analysis. Also, the incidence of SCD was not more frequent in the VF group (13% in both groups at 5 years) despite a very low rate of ICD placement (1.2% overall). The authors concluded that the development of VF in the acute phase of MI was associated with a higher in-hospital mortality, but not long-term mortality or SCD.

■ COMMENTARY

It seems that the indications for ICD placement just keep expanding, so it is interesting to see results that go against this trend. The VF group in this study was different from the rest of the MI patients in that they had lower LVEFs and were more likely to be on ACE/ARB and amiodarone. Also, they were more likely to have an ICD (3.4% vs 0.2%, $P < 0.001$), but the overall ICD rate in this study was low (about 1%). Despite these differences, neither the raw or adjusted HRs reached significance for a worse prognosis in the VF patients who survived the initial MI and could be followed long-term. Prior studies employing ICDs early (< 40 days) after MI, so-called primary prevention, showed no benefit. Now this study, which could be viewed as an observational study of secondary prevention of SCD, has shown that even in patients with VF early post MI, no benefit is likely to be obtained from ICD placement. This result is in agreement with the current guidelines and prior smaller studies.

The results also support our practice of ECG monitoring of all patients after an acute MI, since those who developed VF had a higher in-hospital mortality. However, it leaves the duration of such monitoring unclear. This is an issue since the deployment of primary PCI has decreased hospital stays for acute MI patients who are treated promptly and successfully. Bucking this trend may be difficult in the current hospital cost-containment era, and perhaps we should be giving more thought to placing a defibrillator vest on higher-risk patients being discharged early. My current practice is to keep all acute MIs in the hospital on ECG telemetry monitoring for a minimum of 48 hours. Those deemed at higher risk,

such as patients with LVEF < 35% who may meet ICD criteria later (> 40 days), I am sending out with a defibrillator vest. However, this is a fast-moving field and further guidelines are sure to be emerging.

This study has limitations. It is an observational registry study, but the numbers of subjects are large, permitting robust statistical adjustments. It is a multicenter study and no control was exercised on the protocols used at each hospital. Also, categorizing cause of death can be challenging, but standard definitions were used and carefully adjudicated. Thus, for this type of study, it was well conducted. ■

ABSTRACT & COMMENTARY

Mechanical Chest Compressions in CPR

By Michael H. Crawford, MD

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This article originally appeared in the March 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.*

SOURCE: Rubertsson S, et al. Mechanical chest compressions and simultaneous defibrillation vs conventional cardiopulmonary resuscitation in out-of-hospital cardiac arrest: The LINC randomized trial. *JAMA* 2014;311:53-61.

Effective cardiopulmonary resuscitation (CPR) is partly dependent on the adequacy of manual chest compressions, but they are limited by interruptions and less than ideal conditions such as during transport. Mechanical chest compression devices have been developed that improve organ perfusion vs manual compressions in experimental studies, but there is little evidence of their clinical effectiveness and safety compared to manual compressions. Thus, these investigators from Sweden, the Netherlands, and the United Kingdom conducted a randomized trial to compare whether CPR using a mechanical chest compression device (LUCAS) resulted in superior 4-hour survival in patients with out-of-hospital cardiac arrest as compared to standard CPR with manual chest compressions. All patients in whom CPR was performed by six emergency medical systems in three countries between January 2008 to August 2012 were entered. Exclusion criteria were traumatic cardiac arrest, known pregnancy, age < 18 years, or body size inappropriate for the device (too large or small). Several secondary outcomes were evaluated, including survival with good neurologic outcome at 6 months.

A total of 4998 cases were screened and 2593 were enrolled. Informed consent was done after successful resuscitation and four patients withdrew consent, leaving 2589 study subjects. The first defibrillation was delivered 1.5 minutes later and there were more defibrillations in the mechanical compression group, but otherwise the groups were well matched. The primary outcome of survival to 4 hours was not different between the two groups (both 24%). Nor was there a significant difference in any of the secondary outcomes. There were 23 device-related adverse events among 1282 deployments of the device and eight of these required discontinuing use of the device. There were seven serious adverse events with the device vs three with manual compressions; these included pneumothorax and flail chest. The authors concluded that there was no significant difference in 4-hour post out-of-hospital cardiac arrest survival between those in whom a mechanical chest compression device was used vs. manual compressions during CPR.

■ COMMENTARY

This seems to be the glass half full or empty parable. One could look at this study and conclude that these mechanical chest compression devices are not worth buying or could say that they are just as good as the manual way, so what could an emergency medical technician (EMT) do to benefit the arrest victim if he/she is not pushing on the chest. Also, they produce consistent excellent chest compressions with a compression fraction of 0.84 vs 0.78 for manual. So, this might allow highly skilled but smaller people with less arm strength to be EMTs. One of my colleagues was urging us to buy these devices because he didn't want a small relatively weak resident doing chest compressions on him when he collapses during rounds (he is a large man). In addition, these devices seem safe; serious complications from the device were unusual and not statistically different from manual compressions. Also, device malfunction was rare (< 1%). There were issues with very large and small people with device fit, but overall it fit 95% of people. This could easily be corrected by having different sized devices or other technical improvements.

Given all these pluses, why didn't use of this device improve outcomes? There are several plausible

reasons. First, the device group's CPR protocol was different to try to take advantage of the device's strengths. Chest compressions were done in 3-minute intervals rather than 2 minutes with manual compressions to take advantage of the lack of fatigue with the device. Second, the first defibrillation shock was given without stopping compressions in the device group, again to take advantage of the automatic chest compressions without human contact with the victim during the shocks. Third, since compressions were not stopped for the first shock, it was given as quickly as possible without efforts to determine the patient's rhythm. Fourth, the first shock was delivered 1.5 minutes later in the device group due to the time needed to employ the device. Finally, since this study was done in the field by EMS personnel, it is likely that all the EMTs were excellent at chest compressions, which may not be the case in less selective environments. Which of these potential explanations for the failure to show better outcomes with the device is the most important is difficult to determine. However, I believe the device has promise and is at least as good as manual compressions. Further work to capitalize on the advantages of mechanical chest compressions seems warranted. If your CPR results aren't what you want them to be, perhaps looking into deploying a mechanical chest compression device makes sense. ■

ABSTRACT & COMMENTARY

The Concept of Healthcare-Associated Pneumonia Is Not Accurate for Predicting Antibiotic Resistant Pathogens

By Richard R. Watkins, MD, MS, FACP

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

This article originally appeared in the March 2014 issue of Infectious Disease Alert. *It was edited by Stan Deresinski, MD, FACP, FIDSA, and peer reviewed by Timothy Jenkins, MD. Dr. Deresinki 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 systematic review and meta-analysis found that the healthcare-associated pneumonia concept was based on low-quality evidence confounded by publication bias and does not accurately identify antibiotic-resistant pathogens.

SOURCE: Chalmers JD, et al. Healthcare-Associated Pneumonia Does Not Accurately Identify Potentially Resistant Pathogens: A Systematic Review and Meta-Analysis. *Clin Infect Dis* 2014; 58:330-339.

The term healthcare-associated pneumonia (HCAP) was first proposed in the 2005 guidelines from the American Thoracic Society and the Infectious Diseases Society of America.[1] It was defined as pneumonia occurring in nursing-home residents, patients hospitalized for 2 or more days in the preceding 3 months, patients receiving home infusion therapy or wound care, and patients attending a hemodialysis center in the preceding 30 days. The concept of HCAP was based on the reasoning that patients with frequent healthcare contacts would initially require broad-spectrum antibiotic therapy because they would be at higher risk for resistant pathogens (and consequently higher mortality) compared to patients without such contacts. However, HCAP has been controversial, with some experts questioning the quality of the studies while others have suggested the HCAP concept varies geographically. Therefore, because of these uncertainties Chalmers and colleagues sought to determine how accurately HCAP identifies patients with resistant pathogens, to evaluate the quality of the HCAP studies and their potential for bias, and to validate or refute the HCAP concept.

The study was a systematic review and meta-analysis of papers published between January 1980 and January 2013. Of the 16,520 publications initially identified, 24 studies that included 22,456 patients were evaluated in the meta-analysis. The entry criteria were: (1) original publications that included a cohort of patients with HCAP compared with a CAP cohort; and (2) reporting of one of the study outcomes (microbiology or clinical). The primary outcome measured was the frequency of potentially resistant organisms in the HCAP group compared to the CAP group. Potentially resistant organisms included methicillin-re-

sistant *Staphylococcus aureus* (MRSA), *Pseudomonas aeroginosa*, and Gram-negative Enterobacteriaceae. The secondary outcomes were the frequency of the organisms individually, and the frequency of typical and atypical CAP pathogens. The denominator for the frequency of the pathogens in each group was the total number of patients with HCAP or CAP. Finally, the clinical outcomes measured were intensive care unit admission and mortality.

Of the 24 studies included in the meta-analysis, 4 were rated to be low risk for bias, while 10 were judged to be at high risk. Only 5 used the ATS/IDSA guidelines definition for HCAP, while the others used modified versions such as including immunocompromised patients. There were statistically significant differences in the frequency of pathogens isolated in the HCAP group compared to the CAP group; *Streptococcus pneumoniae* and the atypical pathogens were less common (P <.05) while *S. aureus*, MRSA, Enterobacteriaceae and *P. aeruginosa* were more common (P <.0001). The authors chose to identify a test as being clinically meaningful if it reached a threshold of having a positive likelihood ratio (PLR) >10 or a negative likelihood ratio (NLR) <0.1, or was associated with an area under the receiver operator characteristic curve (AUC) > 0.75. For this study, they were trying to determine whether using the concept of HCAP reached any of these thresholds for being a clinically meaningful distinction. None of the pathogens identified had a PLR > 10 or a NLR < 0.1 nor did HCAP reach the AUC threshold of 0.75 in any of the analyses. Thus, HCAP was not a clinically useful parameter by these statistical criteria. Moreover, limiting the analysis to only prospective studies found no increased risk for ICU admission (n = 4 studies; odds ratio (OR), 0.99; 95% CI, 0.45-2.17; P = .98). The rate of HCAP did vary by region, which was increased in studies from North America (OR, 1.55; 95% CI, 1.35-1.78; P <.0001) but not in Europe (OR, 1.06; 95% CI, 0.56-2.01; P = .90) or Asia (OR, 1.47; 95% CI, 0.92-2.36; P = .10). In the 4 studies that provided adjusted ORs based on age and comorbid illnesses, no significant increase in mortality was associated with HCAP (OR, 1.20; 95% CI, 0.85-1.70; P = .30). Subanalyses found that HCAP performed poorly in European studies (sensitivity 40.0; specificity 75.0), prospective studies (sensitivity 56.3; specificity 70.3), and high-quality studies (sensitivity 51.5; specificity 74.5), none of which reached the AUC threshold of 0.75.

■ COMMENTARY

The results from this study do not support HCAP being a useful clinical concept. The HCAP definition was poor at discriminating between patients who needed antibiotic coverage for MDR pathogens and those who did not. It is therefore logical to conclude that treating all HCAP cases the same will lead to over treatment in areas of low MDR organism prevalence and under treatment in areas of high prevalence. The authors found a publication bias for small studies which had unusually high frequencies of MDR pathogens. This likely distorts the literature by exaggerating the risks associated with HCAP. Indeed, the excess mortality in HCAP is more likely caused by advanced age and co-morbidities than MDR organisms. Given the risks of broad-spectrum antibiotics (e.g. *Clostridium difficile* infection, promoting antibiotic resistance) and the lack of high-quality evidence that such therapy improves outcomes in HCAP, a re-examination of this practice seems warranted.

There are some limitations to the study that need to be mentioned. As with all meta-analyses, the conclusions reached are only as valid as the quality of the source studies. Overall the general quality of the studies included in the analysis was poor. Only a few applied strict criteria for classification of the isolates as true pathogens and the higher-quality ones reported lower frequencies of such pathogens. Another limitation was that Enterobacteriaceae were rarely subdivided into extended-spectrum β-lactamase (ESBL) producing organisms which require different antibiotic therapy (i.e. carbapenems) than non-ESBL producers. Finally, the authors could have selected additional clinical measures such as length of stay and re-admission rates that compared HCAP and CAP.

How do the findings from this meta-analysis potentially impact clinical practice? The data make a strong argument for needing to understand the local prevalence of MDR pathogens and creating appropriate treatment algorithms in regions where such prevalence is high. As noted in an accompanying editorial, we also need to elucidate the risk factors for MDR pathogens in individual patients.[2] One way could be the utilization of MDR pathogen risk scores which help clinicians objectively quantify the risk for these organisms in order to select appropriate antibiotic therapy. The results from this meta-analysis raise important questions about the validity of the current ATS/IDSA guidelines and support the need for a re-evaluation of the HCAP concept.

References

1. American Thoracic Society/Infectious Diseases Society of America. Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. *Am J Respir Crit Care Med* 2005; 171:388-416.

2. Restrepo MI, et al. Healthcare-associated pneumonia: Where do we go next? *Clin Infect Dis* 2014; 58:340-341. ■

ABSTRACT & COMMENTARY

An Evidence-Based Extubation Bundle Improved Care Outcomes in Mechanically Ventilated Brain-Injured Patients

By Leslie A. Hoffman, RN, PhD

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Leslie A. Hoffman reports no financial relationships in this field of study.

This article originally appeared in the March 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: Implementation of an evidence-based extubation-readiness bundle was associated with a decrease in mechanical ventilation days and pneumonia in brain-injured patients.

SOURCE: Roquilly A, et al. Implementation of an evidence-based extubation readiness bundle in 499 brain-injured patients. A before-after evaluation of a quality improvement project. *Am J Respir Crit Care Med* 2013;188:958-966.

Brain injury is a frequent cause of prolonged mechanical ventilation. The authors hypothesized that use of a systematic management protocol, termed an extubation-readiness bundle, could reduce the duration of mechanical ventilation for brain-injured patients. Patients were required to have: 1) evidence of acute neurological injury, e.g., extradural hematoma, subarachnoid hemorrhage, brain contusion, brain edema, skull fracture, stroke, or abscess, 2) require mechanical ventilation for > 24 hours, and 3) Glasgow Coma Score of ≤ 12. Patients were excluded if there was a decision to limit care within 24 hours of ICU admission or if they died within 24 hours of admission. The study used a before-after design. The control phase included all patients (n = 299) admitted to the two study ICUs over a 3-year period. The intervention was then introduced over a 12-month period (no data collected). The intervention phase included all patients (n = 200) who met entry criteria during the following 22-month period. The bundle included four components: 1) lung protective ventilation (tidal volume 6-8 mL/kg of ideal body weight; PEEP > 3 cm H_20; respiratory rate set to achieve normocapnia or moderate hypocapnia), 2) early enteral nutrition (Day 1), 3) optimized antibiotic therapy (predefined criteria), and 4) a systematic approach to extubation. Sedation management was not included in the bundle because it was already standardized.

Patients enrolled in the bundle experienced fewer days of mechanical ventilation (12.6 ± 10.3) compared to control (14.9 ± 11.7 days; $P = 0.02$). At day 28 and day 90, the intervention group also experienced more ventilator-free days ($P = 0.01$), with no difference in mortality in the ICU ($P = 0.51$) or at day 90 ($P = 0.22$). The rate of hospital-acquired pneumonia declined from 57.5% in the control phase to 47.5% in the intervention phase ($P = 0.03$). There was a nonsignificant increase in reintubation for intervention vs control patients (13.8% vs 9%; $P = 0.11$). Unplanned extubation decreased from 9.4% (control) to 4.5% (intervention) ($P < 0.01$).

■ COMMENTARY

Commonly, patients with an acute brain injury are explicitly excluded from clinical trials. Therefore, guidance regarding weaning from mechanical ventilation is limited. This is concerning, as brain injury is a frequent cause of prolonged mechanical ventilation. The protocol tested in this study consisted of four components: lung protective ventilation, early enteral nutrition, protocolized antibiotic therapy, and a standardized extubation protocol. Lung protective ventilation was included based on two rationales: lung compliance of brain-injured patients is frequently not altered and hypercapnia can be easily prevented by increasing respiratory rate instead of increasing tidal volume. Early enteral nutrition was included because a prior study, conducted by the authors, suggested early enteral nutrition was a protective factor in regard to the risk of hospital-acquired pneumonia. International guidelines, adapted to local epidemiology, were used to guide antibiotic therapy. Criteria used to indicate extubation readiness included tolerance

of inspiratory support < 10 cm H_2O or spontaneous breathing and $FIO_2 \leq 40\%$ for ≥ 30 minutes. Tube removal occurred if the Glasgow Coma Score was ≥ 10 and the patient had a cough that was spontaneous or caused. Full awakening was not required. These criteria were selected based on findings from prior studies that suggested a low risk of extubation failure when the Glasgow Coma Score was between 8 and 10, provided patients can cough.

Using these criteria, 13.8% of patients required reintubation in the intervention phase, a percentage slightly higher than goal (≤ 10% in neurological patients). However, there were significantly fewer unplanned extubations. As with all before-after studies, the study design prevents attributing causality to positive outcomes. Notably, the authors included several statistical procedures designed to exclude the possibility that extraneous factors caused their results in their analytic strategy. These included a time series analysis to rule out changes due to improvements in patient care and two sensitivity analyses designed to balance covariates in the two phases and reduce bias. Future studies are needed to confirm findings. In the interim, study findings suggest ways to potentially speed weaning of this complex and challenging patient population. ■

CME INSTRUCTIONS

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CME QUESTIONS

1. Patients with chronic kidney disease are at increased risk for of the following:

a. Atherosclerotic disease
b. Thromboembolic disease
c. Increased bleeding
d. All of the above

2. In the study by Bougouin and colleagues, the prognosis for patients with in-hospital ventricular fibrillation after an acute MI have the following prognosis:

a. A higher in-hospital, short-term mortality
b. A higher long-term all-cause mortality
c. A higher long-term rate of sudden cardiac death
d. All of the above

3. In the LINC trial, the use of a mechanical chest compression device for out-of-hospital CPR led to the following outcome:

a. Earlier delivery of the first defibrillation in the mechanical chest compression group.
b. No significant difference in 4-hour survival.
c. A significant improvement in 4-hour survival but no difference in survival to hospital discharge.
d. A significantly increased rate of serious adverse events.

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.