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Critical Care [ALERT]

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Authoritative, evidence-based summaries for the critical care clinician

ABSTRACT & COMMENTARY

Ebola Virus Disease and the ICU Clinician

By David J. Pierson, MD, Editor

SYNOPSIS: As hospitals in the United States and other resource-intensive countries prepare for the care of patients with possible Ebola virus disease, the greatest impact on its clinical outcome and further spread will most likely come from the application of existing basic critical-care and infection-control principles.

SOURCE: Fowler RA, et al. Caring for critically ill patients with ebola virus disease. Perspectives from West Africa. *Am J Respir Crit Care Med* 2014;190:733-737.

The form of viral hemorrhagic fever now known as Ebola virus disease (EVD) has occurred sporadically, primarily in rural areas of tropical Africa, since 1976. However, this year it has exploded both epidemiologically and as a worldwide news phenomenon because of its first outbreak in a major metropolitan area.[1] With 23 co-authors representing the World Health Organization and both academic and governmental institutions in seven countries, Fowler provides a current overview of EVD focused on its pathophysiology, clinical presentation, and management needs, based on their experience with this current outbreak. Ebola is everywhere in the news right now, a source of concern and even panic among both health professionals and the public. Amidst a welter of popular information of variable accuracy and authority, several other scholarly resources on EVD and its management have recently appeared.[2-4] The report by Fowler et al places current information about this highly lethal and frightening condition in perspective for critical care clinicians, for whom an accurate appreciation of EVD and its management is becoming necessary, even if they do not personally encounter cases.

Of the five species of Ebolavirus in the RNA virus family Filoviridae, three have been associated with large outbreaks of human disease. The natural reservoir is fruit bats and possibly other mammals, and both humans and nonhuman primates are susceptible end hosts. The virus is transmitted through direct mucous membrane or percutaneous exposure to infected body fluids, most often stool, vomitus, or blood, as well as by contact with materials and surfaces contaminated with these

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[INSIDE]

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substances. Once it enters the body, the virus is carried to regional lymph nodes by monocytes, macrophages, and dentritic cells, and subsequently disseminates hematogenously to the liver and spleen.

Clinically, EVD starts as a febrile, flu-like illness with fatigue and myalgias, with prominent gastrointestinal symptoms such as anorexia, nausea, and abdominal discomfort. These are followed by vomiting and diarrhea, leading to intravascular volume depletion which commonly proceeds to severe lactic acidosis, profound hypokalemia, and progressive renal insufficiency. A maculopapular rash may occur. Lymphopenia and thrombocytopenia are common, although anemia is infrequent. Hepatocellular injury with elevated transaminases is frequent, but respiratory involvement (hypoxemia) is not part of the typical presentation. In some cases there is hemorrhage from the gastrointestinal tract and mucous membranes, and death in fatal cases is usually from unsupportable shock and multisystem organ failure. There are no proven EVD-specific medical therapies. However, aggressive prevention of intravascular volume depletion, correction of electrolyte abnormalities, and prevention of the complications of shock can be expected to substantially reduce the high mortality rate that has so far been observed in this outbreak.

Infection control and public health aspects of managing EVD are vitally important. Substantial transmission of EVD to health care workers has occurred in the current outbreak in West Africa, in the context of severe shortages of protective equipment and other materials. Many cases have occurred in family members who had close contact with gravely ill patients, and in others who transported corpses or prepared them for burial.

■ COMMENTARY

As Fowler and colleagues point out, "The constellation of limited public health infrastructure, low levels of health literacy, few acute care and infection prevention and control resources, densely populated areas, a mobile population, and a highly transmissible and lethal viral infection have created a perfect storm" in the current West African EVD outbreak. Among its numerous catastrophic effects, this perfect storm almost certainly means that mortality among those who contact EVD will be substantially higher there than among any persons who might present with the disease and be cared for in resource-rich countries like the United States.

In addition to advocating for all appropriate education, personnel, infrastructure, and materials being made available in West Africa and other resource-constrained environments, the authors identify five key principles for improving outcomes from EVD, both in those settings and in the ICUs of resource-rich environments like the United States:

- Consideration of EVD as another transmissible infection-related critical illness that will benefit from goal-directed supportive and specific intensive care;
- Recognition that the predominant EVD clinical syndrome is gastrointestinal, with intravascular volume depletion and metabolic derangements the greatest threats to the patient;
- Emphasis on the primary role of basic laboratory tests in identifying and tracking these derangements during management;
- Appreciation that the fundamental skills already possessed by critical care clinicians constitute the main needs of patients with EVD; and,
- Anticipation that patient outcomes will be improved through application of these principles.

Patients suspected of having EVD are now being admitted to hospitals in this country. Even if one's own institution is not one of them, being prepared for the possibility will be important for at least the next several months. In addition to the resources cited above, here are two more of direct relevance to ICU clinicians and administrators: The World Health Organization's online 24-page infection-control document[5] provides practical guidance covering general and direct patient care, waste management, and such non-patient-care topics as diagnostic laboratory activities, movement and burial of human remains, post-mortem

examinations, and managing possible virus exposures through blood and other body fluids. In addition, the Centers for Disease Control and Prevention has a comprehensive, updated website on Ebola for health care workers covering many aspects of the topic.[6] ■

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ABSTRACT & COMMENTARY

Unplanned Extubations as a Quality-of-Care Issue

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.

SYNOPSIS: Reintubation following unplanned extubation in critically ill post-operative patients is associated with increased hospital mortality.

SOURCE: Lee JH,et al. Clinical outcomes after unplanned extubation in a surgical intensive care population. *World J Surg* 2014;38:203-210.

This retrospective study of more than 4000 immediate postoperative patients requiring mechanical ventilation (MV) examined whether unplanned extubation (UE) is associated with increased hospital mortality. Nursing staff ratios were either 1:1 or 1:2. Reintubation was assessed in the first 72 hours following UE. The incidence of UE was 1.8% with 96% patient-initiated. The reintubation rate was 21% compared to 3.4% following planned extubation in the control group. Reintubatation following UE was associated with a higher incidence of ventilator-associated pneumonia (VAP), and a 7-fold higher mortality rate (21%) compared to either UE patients or control patients not requiring reintubation (3%). In the multivariate analysis, in the absence of reintubation UE was not associated with mortality. Hospital mortality also was significantly associated with emergent surgery, chronic neurological disease, and those with an acute physiology and chronic health evaluation (APACHE II) score > 22. The authors speculated that reintubation following UE enhances the mortality risk of comorbidities and other risk factors.

■ COMMENTARY

The results of this study, the first exclusively focused on postoperative surgical patients, are consistent with the literature. The most salient and reproducible observation from UE studies is that a sizable proportion of clinically stable patients undergoing UE do not require reinstitution of MV. This strongly suggests that clinicians are too conservative in assessing their patients' ability to resume unassisted breathing without an artificial airway.

A recent systematic review found that UE occurs more frequently during the weaning phase, in patients who have a higher level of consciousness, and particularly in those exhibiting restlessness and/or agitation.[1] Complicating the problem of UE is its association with benzodiazepines (particularly midazolam) as well as with the use of physical restraints. The paradoxical excitatory effects of benzodiazepines and their association with delirium are likely explanations. Nonetheless, clinicians are presented with a nettlesome problem because a near-normal sensorium is a prerequisite for extubation. But both the incidence of restlessness/agitation and its primary treatment increase the risk of UE. However, a recent observational study found that strategies involving either no sedation (i.e., analgesia only) or intermittent sedation were associated with increased UE compared to protocolized continuous sedation with daily sedation interruptions.[2] This suggests that the sedation strategy might be the more relevant factor.

The issue of whether using restraints increases the risk of UE is circuitous. Patients generally are restrained because they try to remove catheters. In fact, one prospective study found that lack of hand restraints tripled the incidence of UE.[1] Although not a universal finding, nursing staff ratios often are cited as a factor in UE, and up to 90% of UEs occur when a nurse is not at the bedside.[1] UE tends to occur more during the night shift and with less experienced nurses.[1]

The current study is consistent with the literature in that reintubation following UE is associated with higher hospital mortality, as well as with an increased incidence of VAP, prolonged need for MV, and higher hospital costs. These negative consequences are likely attributable to the tendency for UE to occur in older patients (> 65), those with a higher APACHE II scores (> 17), those requiring full-support modes vs weaning modes of ventilatory support (median of 76% vs 15.6%), and those with oxygenation problems.[1]

The incidence of UE is 3-14% and is now considered a quality-of-care issue.[1,3] This may become problematic because, like other signifiers of health care quality (e.g., VAP), UE is a complex problem. There are few high-quality studies and none of them suggest an unambiguous solution. Also, the negative impact of UE is most salient in high-acuity patients. Clearly, a more aggressive approach to extubation in patients who pass a spontaneous breathing trial is needed. Perhaps less obvious, because it runs counter to the current trend toward minimizing sedation, is to emphasize effective treatment of agitation in the critical phase of acute illness (particularly if it is pain-induced). The consequences of UE are most profound in this circumstance. In addition, more mindful peer support from experienced nurses and respiratory therapists toward bedside practitioners new to critical care would likely be helpful in reducing UE. ■

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ABSTRACT & COMMENTARY

Nurse Practitioners and Physician Assistants in the ICU

By Betty T. Tran, MD, MSc

Assistant Professor of Medicine, Pulmonary and Critical Care Medicine, Rush University Medical Center, Chicago

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

SYNOPSIS: Using retrospective cohort data from a national survey of medical and mixed medical-surgical ICUs, this study found that nurse practitioner (NP)/physician assistant (PA) staffing was common and not associated with any differences in in-hospital mortality compared to ICUs without NP/PAs.

SOURCE: Costa DK, et al. Nurse practitioner/physician assistant staffing and critical care mortality. *Chest* 2014; Aug 28. [Epub ahead of print.]

With increasing restrictions on resident work hours and the rising demand for critical care, hospitals have turned to alternative models to staff the ICU. The number of nurse practitioners (NPs) and physician assistants (PAs) has grown to meet this need, although their impact on patient outcomes is not well understood. The investigators of this study sought to examine the effect of NP/PA staffing on in-hospital mortality among adult ICU patients.

Costa et al used retrospective ICU outcome data from the Acute Physiology and Chronic Health Evaluation (APACHE) clinical information system combined with an ICU-level survey of organizational practices during the period of 2009-2010. Their final sample included 39,541 adult patients in 29 medical and mixed medical-surgical ICUs within 22 hospitals. NP/PA staffing was reported in 21 (72.4%) ICUs; 30,254 (76.5%) patients received care in ICUs with NP/PAs. There were no significant organizational differences found between ICUs with and without NP/PA participation. In terms of patient-level characteristics, ICUs with NP/PA staffing tended to have lower severity of illness based on acute physiology scores

(APS) and frequency of mechanical ventilation, and there were small but significant differences in terms of age, race, primary diagnosis, and comorbidities. Risk-adjusted in-hospital mortality, however, was similar between ICUs with and without NP/PA staffing (relative risk, 1.10; 95% CI, 0.92-1.31). Similar findings were observed in subgroups of patients on mechanical ventilation, in the highest quartile of APS, in ICUs with low-intensity physician staffing (i.e., optional intensivist physician consult or absence of intensivists), and in ICUs with physician trainees. A sensitivity analysis that considered patients discharged to hospice as alive upon discharge also yielded comparable results. Overall, there were no significant differences observed with regard to discharge location between patients staffed by NP/PAs and those not staffed by NP/PAs.

■ COMMENTARY

This study adds to a currently small number of studies focused on the impact of NP/PA care in acute and critical care settings. As NPs and PAs are under the direct supervision of attending physicians, the finding of no difference with regard to in-hospital mortality should not be surprising even though their educational training routes are different from physician trainees. In fact, differences in training backgrounds may account for the findings observed in studies that have compared NP/PA with physician (resident or fellow) care. One study found that residents cared for more patients, worked more hours, and spent more time in lectures/conferences, although NP/PAs were more likely to discuss patient care with ICU nurses, to interact with patients' families, and spend more time in research and administrative activities.[1] Similarly, fellows spent more time in non-unit activities (conferences, reading, teaching) whereas NPs/PAs spent more time in activities related to coordination of care, interactions with nursing, medical staff, patients, and family members.[2] Among these and other studies examining outcomes associated with NP/PA staffing, there were no significant differences in patient outcomes such as readmission rates, mortality, duration of mechanical ventilation, LOS, or disposition; some studies even reported an improvement in certain outcomes.[3]

Together, these findings not only support the use of NPs and PAs in the care of critically ill patients, but also suggest they may be a desirable complement to traditional care models. Unlike residents and fellows, they do not rotate off service and can potentially provide greater continuity of care. Furthermore, they can develop more clinical experience and comfort the longer they work in their respective positions compared to rotating physician trainees who change on a monthly basis. Indeed, it would be interesting to repeat these studies in the future as the current group of NP/PAs continues to accumulate years of critical care experience to assess whether there are significant differences in not only patient outcomes, but quality of care and patient satisfaction. ■

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ABSTRACT & COMMENTARY

After-Hours ICU Discharge: A Potentially Modifiable Cause of Increased Hospital Mortality

By David J. Pierson, MD, Editor

SYNOPSIS: Examination of outcomes in 710,535 patients in relation to the timing of ICU discharge showed that being moved out to the ward between 1800 and 0600 hours was associated with increased risks of both in-hospital death and unplanned ICU readmission.

SOURCE: Gantner D, et al. Mortality related to after-hours discharge from intensive care in Australia and New Zealand, 2005-2012. *Intensive Care Med* 2014;40:1528-1535.

The Australian and New Zealand Intensive Care Society Adult Patient Database prospectively records data on patients cared for in 90% of Australian and 50% of New Zealand ICUs. Gantner and associates used this database to examine whether discharge from the ICU to the general ward after regular hours remained associated with increased in-hospital mortality and ICU readmission, as had

been the case before various care and organizational improvements were implemented.

Over the 8-year study period, of 710,535 ICU patients who met study criteria and were discharged alive from the unit after an initial ICU stay, 28,507 (4.0%) subsequently died in the hospital. Approximately 85% of the patients left the unit between 0600 and 1800 hours and 15% were transferred out to the ward after hours. Patients transferred after hours were sicker (mean APACHE III score 50 vs 46, $P < 0.001$) and had higher predicted mortality (5.3% vs 3.4%, $P < 0.001$) and higher actual in-hospital mortality (6.4% vs 3.6%, $P < 0.001$) than their regular-hours counterparts. When the data were examined according to the actual hour of ICU discharge, the highest mortality risk occurred with those who left between 0200 and 0600 hours (odds ratio, 1.78-2.49) and the lowest between 0900 and 1100. Patients who left the ICU between 1800 and 0600 hours were also significantly more likely to be readmitted to the unit during their hospital stay (5.1% vs 4.5%, $P < 0.001$).

There were no detectable changes in the timing of ICU discharge during the 8 years of the study, and crude mortality rates were similarly unchanged. Post-ICU mortality rates for all patients decreased during the study period, but the risk associated with after-hours discharge remained elevated throughout (odds ratio, 1.34; 95% confidence interval, 1.30-1.38). The findings with respect to increased post-transfer mortality and unplanned readmission did not differ between surgical and medical patients.

■ COMMENTARY

Multiple studies from various parts of the world have consistently shown that after-hours discharge from the ICU is an independent risk factor for adverse patient outcomes, including increased mortality and unplanned ICU readmission. The proportion of ICU patients discharged after regular hours has been established as a national indicator of the quality of clinical care in Australia. Wide implementation of rapid response systems and numerous other organizational and clinical practice changes have taken place in part to address this problem. However, this carefully done study using a high-quality database that reflects patient outcomes nationwide documents the continued high rate of after-hours discharge and its strong association with adverse patient outcomes. This is the largest study of ICU discharge timing yet reported, and while comparable data from the United States are not available there is little reason to assume that the situation is different here.

Why should after-hours transfer from the ICU to the ward be a risk factor for death? It has been asserted that in many institutions whose busy ICUs tend to be full much of the time, the arrival of new, critically ill admissions may prompt the transfer out of patients who would not otherwise be discharged but are "least sick" at the moment. Over and above this possibility, Gantner et al suggest that in ICUs without 24/7 intensivist presence, the decision to transfer patients out during the evening and night shifts may be made by less experienced clinicians who are less able to assess clinical stability. Patient handovers may also be less complete during such times, and staffing levels on the wards are lower than in the ICU.

For this retrospective study, the authors did not have information on the reasons patients were transferred out of the ICU after hours. How full the units were at those times and whether the goals of care might have changed for the patients cannot be determined. Nonetheless, one must conclude that the factors leading to premature ICU discharge after hours have not been completely addressed in the institutions whose patients are included in this study. This example of incomplete transfer of evidence into practice in critical care clearly needs more attention if critically ill patients are to receive the full benefit of our knowledge. ■

BRIEF REPORT

Dehydration Is a Poor Prognostic Sign in Acute Ischemic Stroke Patients

By Matthew E. Fink, MD

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

Dr. Fink is a retained consultant for Procter & Gamble. This article originally appeared in the October 2014 issue of *Neurology Alert*.

SOURCE: Liu CH, et al. Dehydration is an independent predictor of discharge outcome and admission cost in acute ischaemic stroke. *Eur J Neurol* 2014;21:1184-1191.

Several factors have been reported to predict the outcome of acute stroke, including the modified Rankin scale, length of hospital stay, age and gender, severity of presenting deficit as measured by the initial NIH Stroke Scale, history of diabetes, and in-hospital infections. Dehydration status upon admission has been a controversial prognostic indicator, and a group of investigators from Taiwan, led by Liu et al, have evaluated the importance of dehydration on admission in stroke patients admitted between January 2009 and December 2011. In total, they examined the records of 2570 acute ischemic stroke patients and 573 acute hemorrhagic stroke patients. They divided the group into those deemed dehydrated, based on a BUN/creatinine ratio ≥ 15, vs non-dehydrated, with a ratio < 15. Patients with confounding illnesses, such as congestive heart failure, renal insufficiency, liver cirrhosis, and vascular abnormalities, were excluded from this study. They also examined demographics, hospital admission costs, and discharge outcomes using the modified Rankin scale and the Barthel index.

In a multivariate analysis using logistic and linear regression, investigators found that acute ischemic stroke patients with admission dehydration had significantly higher rates of infection, worse discharge Barthel Index, worse discharge modified Rankin scale, and higher admission costs compared to those without dehydration. However, acute hemorrhagic stroke, with or without admission dehydration, showed no difference in discharge clinical outcomes or costs of hospitalization.

One of the confounding factors that was evaluated was the risk of venous thromboembolism, which is also associated with dehydration. It is notable that Chinese patients have a much lower risk of thromboembolism than do white or black patients, and this did not seem to play a significant role in the study. Dehydration is known to increase blood viscosity, reduce cardiac output, reduce blood pressure, and impair cerebral blood flow and collateral circulation to the brain. Although these mechanisms may have played a role in this evaluation, cerebral blood perfusion studies were not performed, and therefore these mechanisms were suggested, but not proven. On a clinical note, the above findings emphasize the importance of rapid correction of admission dehydration, with intravenous fluid replacement therapy as quickly as it can be safely administered. ■

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CME QUESTIONS

1. Which of the following poses the *least* threat to health care workers caring for patients with possible Ebola virus disease?

a. Needle-sticks and other parenteral contact with blood

b. Contact with vomitus

c. Contact with diarrheal stool

d. Handling tissue or the body of a deceased patient

e. Respiratory exposure

2. Which of the following is *least* likely to be observed in a patient with Ebola virus disease?

a. Hypovolemic shock

b. Hypoxemic acute respiratory failure

c. Acute renal insufficiency

d. Hypokalemia

e. Elevated liver function tests

3. Which of the following is true regarding unplanned extubation (UE)?

a. There is a higher incidence of UE in younger patients.

b. UE occurs more frequently during weaning.

c. UE occurs more frequently in well-sedated patients.

d. UE requiring reintubation is associated with decreased mortality.

e. UE occurs more frequently during the day shift

4. Based on the study by Costa et al, patients in ICUs with NP/PA staffing compared to patients in ICUs without NP/PAs had:

a. increased risk of in-hospital mortality.

b. similar risk of in-hospital mortality.

c. lower risk of in-hospital mortality.

d. decreased length of stay.

e. higher readmission rates.

5. In the study by Costa et al, which of the following is true?

a. A minority of ICUs have NP/PA staffing

b. NP/PA staffing resulted in lower patient satisfaction

c. NP/PA staffing resulted in higher quality patient care

d. Most ICUs have NPs/PAs participating in patient care

e. NP/PA staffing occurred in predominantly surgical ICUs

6. Which of the following are potentially modifiable factors that might affect post-ICU in-hospital mortality?

a. Improved patient stability assessment prior to ICU discharge

b. Increased nursing staffing on the general wards

c. More effective patient handovers between clinical staff

d. Increased ICU bed capacity

e. All of the above

7. Suggested mechanisms by which dehydration in patients presenting with acute stroke might be associated with poorer outcomes include which of the following?

a. Reduced cardiac output

b. Increased blood viscosity

c. Impaired blood flow and collateral circulation to the brain

d. All of the above

e. a and b but not c