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Formerly AHC Media

Vol. 25, Issue 12, March 2018
AHCMedia.com

Critical Care [ALERT]

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SPECIAL FEATURE

Implementing Restrictive Transfusion Strategies to Improve Patient Outcomes

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

In critical care, there has been a focus on adhering to a restrictive transfusion strategy since the Transfusion Requirements in Critical Care (TRICC) trial was published in 1999. In that trial, the authors evaluated a restrictive (hemoglobin [Hgb] < 7 g/dL) vs. liberal (Hgb < 10 g/dL) transfusion trigger in ICU patients and found reduced in-hospital mortality in the restrictive compared to the liberal transfusion group (23% vs. 28%, respectively; $P = 0.05$).[1] Additional studies conducted in various populations of patients then followed with a growing body of evidence in support of restrictive transfusion thresholds. What follows is a review of the evidence supporting restrictive transfusion strategies, a definition of appropriate patient populations, and specific approaches for clinicians to use in developing effective blood management programs.

The most recent transfusion guidelines, published in 2016 by the AABB (formerly known as the American Association of Blood Banks), were based on 31 trials that included 12,587 patients and offered two primary recommendations: 1) a restrictive Hgb threshold of < 7.0 mg/dL (compared to a liberal transfusion threshold of < 10 mg/dL) for hemodynamically stable hospitalized adult patients, including critical care patients, and 2) a Hgb threshold of < 8.0 mg/dL for patients undergoing orthopedic or cardiac surgery or presenting with existing cardiovascular (CV) disease. Excluded from these recommendations because insufficient evidence are patients with acute coronary syndrome (ACS), patients with severe thrombocytopenia at risk for bleeding (hematology/oncology patients), and patients with chronic transfusion-dependent anemia.[2]

Multiple additional studies have been conducted comparing restrictive vs. liberal transfusion thresholds in different populations of patients. Patients undergoing orthopedic surgery, specifically older patients with hip fractures, were studied in the FOCUS trial. In this study, 2,016 patients ≥ 50 years of age with either a history

Financial Disclosure: *Critical Care Alert*'s Physician Editor Betty Tran, MD, MSc, Nurse Planner Amy Johnson, MSN, RN, Peer Reviewer William Thompson, MD, Executive Editor Leslie Coplin, Editor Jonathan Springston, and Editorial Group Manager Terrey L. Hatcher report no financial relationships relevant to this field of study.

[INSIDE]

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Critical Care Alert, (ISSN 1067-9502) is published 12 times annually by AHC Media, a Relias Learning company, 111 Corning Road, Suite 250, Cary, NC 27518-9238.

Periodicals Postage Paid at Cary, NC, and additional mailing offices.

GST Registration Number: R128870672.
POSTMASTER: Send all address changes to *Critical Care Alert*, Relias Learning, 111 Corning Road, Suite 250, Cary, NC 27518-9238.

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of CV disease or risk factors for CV disease with Hgb < 10 mg/dL after hip fracture surgery were randomized to a restrictive (Hgb < 8.0 or symptomatic anemia) or liberal (Hgb < 10) strategy. The liberal group did not demonstrate reduced rates of death at 60-day follow up.[3] In a long-term follow-up study of those same patients, three-year survival did not differ significantly between the liberal and restrictive transfusion groups (hazard ratio [HR], 1.09; 95% confidence interval [CI], 0.95-1.25; $P = 0.21$).[4] The authors of an additional randomized, controlled trial (RCT) of 284 frail, elderly, anemic patients with hip fracture (TRIFE) found no statistically significant difference in recovery from physical disabilities, but higher 30-day and 90-day mortality in the restrictive (Hgb < 9.7) compared to liberal (Hgb < 11.3) groups. Notably in this trial, the restrictive Hgb threshold was almost equal to the liberal Hgb threshold in the earlier FOCUS trial.[5] The authors of a 2017 systematic review and meta-analysis of transfusion thresholds in hip and knee surgery reviewed 10 RCTs that included 3,788 patients. They noted no differences in mortality or other complications, including myocardial infarction (MI), congestive heart failure, and pneumonia between restrictive and liberal transfusion groups.[6]

A systematic review and meta-analysis of nine RCTs (5,780 patients) evaluating transfusion strategies in older adults (including both FOCUS and TRIFE) found that the 30-day risk of death (relative risk [RR], 1.36; 95% CI, 1.05-1.74; $P = 0.17$) and 90-day risk of death (RR, 1.45; 95% CI, 1.05-1.98; $P = 0.22$) were both higher in older patients with a restrictive transfusion strategy vs. a liberal strategy, suggesting that a more liberal transfusion strategy may be favored in geriatric patients.[7]

In cardiac surgery patients, a 2010 RCT (TRACS) conducted in 505 patients at a single center in Brazil demonstrated no significant difference in composite endpoint of 30-day mortality and severe morbidity (cardiogenic shock, acute respiratory distress syndrome, acute renal injury requiring dialysis, or hemofiltration) in the liberal (targeting hematocrit [Hct] > 30%) group vs. the restrictive (targeting Hct > 24%) group.[8] Following this, a 2014 meta-analysis of seven RCTs (including TRACS; 1,262 patients) evaluating transfusion triggers in cardiac surgery demonstrated no difference in mortality between restrictive and liberal transfusion groups (RR, 1.12; 95% CI, 0.65-1.95; $P = 0.60$).[9] The TITRe2 trial, reported in 2015, included 2,004 cardiac surgery patients and found that a restrictive transfusion strategy (Hgb < 7.5 mg/dL) was not superior to a liberal strategy (Hgb < 9 mg/dL) regarding morbidity. The restrictive group exhibited more deaths (4.2% vs. 2.6%; HR, 1.64; 95% CI, 1.00-2.67; $P = 0.045$), suggesting that restrictive transfusion may affect mortality negatively.[10] The authors of the recently published TRICS III study randomized 5,000 cardiac surgery patients prior to surgery to a restrictive (Hgb < 7.5 g/dL, either intraoperatively or postoperatively) or to a liberal strategy (Hgb < 9.5 g/dL, intraoperatively or postoperatively in the ICU, or Hgb < 8.5 g/dL postoperatively on the ward). The restrictive strategy was noninferior to the liberal strategy for a composite outcome of death, MI, stroke, or new renal failure with dialysis. Mortality was 3% in the restrictive group compared to 3.6% in the liberal group (odds ratio [OR], 0.85; 95% CI, 0.62-1.16).[11]

In patients with sepsis, a subgroup analysis of the Transfusion Requirements in Septic Shock (TRISS) trial evaluated higher (9.0 g/dL) vs. lower (7.0 g/dL) Hgb thresholds for transfusion, with a primary endpoint of 90-day mortality in pre-specified subgroups of patients (chronic lung disease, hematologic malignancy, metastatic cancer, surgery patients, and septic shock by SEPSIS-3 criteria). No significant differences were found between the two Hgb threshold groups in terms of 90-day mortality in any of the subgroups.[12] In the primary TRISS trial, 90-day mortality was 43% in the lower threshold group vs. 45% in the higher threshold group (RR, 0.94; 95% CI, 0.78-1.09; $P = 0.44$).[13] A systematic review and meta-analysis of transfusion in critically ill sepsis patients comparing restrictive vs. liberal transfusion thresholds found only one RCT (TRISS) and nine cohort studies that included mortality as the primary endpoint. The restrictive strategy was not associated with either harm or benefit compared to a liberal strategy (as reported above for TRISS).[14] For the cohort studies, red blood cell transfusion was not associated with increased mortality.[14] Overall, there are few RCTs evaluating transfusion thresholds in sepsis, and further study is needed.

In critically ill patients, the authors of a pilot RCT that included six ICUs in the United Kingdom evaluated a restrictive (Hgb > 7 g/dL) vs. liberal (Hgb > 9 g/dL) transfusion strategy and randomized 100 patients. Mortality at 180 days trended toward higher rates in the liberal group than in the restrictive group (55% vs. 37%; RR, 0.68; 95% CI, 0.44-1.05; *P* = 0.073).[15] A 2016 meta-analysis evaluated restrictive vs. liberal transfusion targets in critically ill patients and in patients with ACS. The analysis included six RCTs involving 2,156 patients. The authors found no differences in mortality between groups, and they concluded that a restrictive strategy was at least equivalent to a liberal strategy in critically ill patients, but noted that there was inconclusive evidence to recommend a restrictive strategy in ACS patients.[16]

In a context-specific systematic review and meta-analysis of RCTs in the perioperative and acute care settings, a critical care subset of patients showed no increased risk of 30-day complications (inadequate oxygen supply, mortality, composite of both). For perioperative patients, there was an increased risk of adverse events in the CV procedures restrictive strategy group.[17] Two recent meta-analyses in perioperative and critical care patients both identified a possible increased risk for perioperative patients with restrictive transfusion strategies. Fominskiy et al reviewed 17 trials for perioperative patients (nine orthopedics, five cardiac surgery, one vascular, one oncology surgery, and one obstetrics study, for a total of 7,552 patients) and 10 trials in critically ill patients (3,469 patients). There was no difference in mortality in critically ill patients treated with restrictive vs. liberal strategies. However, in perioperative patients, a liberal strategy was associated with improved survival over a restrictive transfusion strategy (OR, 0.81; 95% CI, 0.66-1.00; *P* = 0.05).[18] In a meta-analysis that included 27 RCTs or quasi-experimental studies evaluating perioperative and critical care patients, a restrictive transfusion strategy (Hgb 7-8 g/dL) significantly reduced 30-day mortality compared with a liberal (Hgb 9-10 g/dL) strategy (OR, 0.82; 95% CI, 0.70-0.97) in the critical care subpopulation. However, the restrictive strategy was associated with the opposite effect in the surgical patients, indicating either a potentially increased mortality risk or no difference between groups (OR, 1.31; 95% CI, 0.94-1.82).[19]

Since the 2016 AABB clinical practice guidelines for transfusion were published, additional information is available regarding oncology patients. A systematic review and meta-analysis that included six studies (both randomized and non-randomized) involving 983 patients concluded there was no difference in mortality between the restrictive and liberal transfusion groups (RR, 1.00; 95% CI, 0.32-3.18) and no difference in adverse events.[20] One single-center, double-blind, RCT evaluating patients with solid tumors who presented with septic shock noted trends toward improved survival in the liberal transfusion group at both 28 days from randomization and at 90 days from randomization.[21] These recent studies offer results that conflict with those previously reported and deserve further study, namely in perioperative and oncology patients.

Table 1: Strategies for Implementing a Successful Blood Management Program

Organizational Support	• Executive leadership support • Define multidisciplinary process improvement team
Transfusion Guidelines	• Establish evidence-based transfusion guidelines (triggers) • Single-unit transfusions • Educate on best practices and evidence for restrictive transfusion
Clinical Support	• Clinical decision support tools • Evidence-based prompts during order entry • Clinical service champions to reinforce behaviors and provide feedback
Audits and Reports	• Audit compliance and establish feedback mechanisms • Measure • Report • Peer-to-peer feedback • Feedback on transfusion dashboard • Revise and re-educate
Other Patient-focused Strategies to Minimize Blood Loss	• Antifibrinolytic medications • Cell-salvage techniques during surgery • Preoperative conditioning for anemic patients • Point-of-care testing • Small volume blood draws

Adapted from Carson et al,[22] Norgaard et al, [23] Borgert et al,[25] Yeh et al,[26] Sadana et al.[27]

STRATEGIES FOR IMPLEMENTING EVIDENCE-BASED TRANSFUSION GUIDELINES

Despite a wealth of evidence supporting the benefits of a restrictive transfusion strategy in many patient populations, the guidelines often still are not followed with consistency. Implementing transfusion triggers or guidelines can effectively lower the number of transfusions and forms the basis of most blood management programs. The effect of implementing a transfusion trigger was evaluated in a systematic review and meta-analysis of 19 RCTs that included 6,264 patients. Patients had been randomized to a restrictive or liberal transfusion threshold. Clinical outcomes and blood use were evaluated. Patients in the restrictive transfusion strategy group demonstrated a 39% lower risk of receiving a transfusion compared to those in the liberal group (RR, 0.61; 95%

CI, 0.52-0.72). Restrictive transfusion was associated with significantly lower hospital mortality, but not 30-day mortality.[22]

Several other strategies have been identified for improving compliance with recommended transfusion guidelines and are summarized in Table 1. Most start with developing a formal blood management program. This requires an organizational structure and support from executive leadership to implement a multidisciplinary process improvement program. Norgaard et al reported on the successful implementation of a blood management program at a large Danish hospital involving a hospital-wide effort to improve evidence-based transfusion practices. At three-year follow-up, sustained improvement was demonstrated with a reduction in percent transfusions above the Hgb threshold from 23% to 10% ($P < 0.001$), an improvement in transfusions at or below the trigger Hgb of 7.3 mg/dL from 7% to 19% ($P < 0.001$), and an increase in single-unit transfusions from 72% to 76% ($P < 0.001$).[23]

Quality improvement frameworks, such as the Institute for Healthcare Improvement's Model for Improvement using Plan-Do-Study-Act cycles,[24] or development and implementation of an evidence-based care bundle for transfusion, such as those used successfully to address ventilator-associated pneumonia or central line-associated blood stream infection, may be helpful. One Dutch ICU implemented a transfusion bundle that included process measures (consent, correct patient, and product identification) with a transfusion threshold (per individual patient baseline). After bundle implementation, the Hgb trigger decreased from 7.3 to 7.1 g/dL ($P = 0.04$), and the number of inappropriate transfusions decreased significantly from 25% to 10% ($P = 0.001$).[25]

Clinical decision support tools within the electronic medical record are used to inform clinicians at the time of order entry when orders fall outside the established evidence-based standard, prompting an action to either cancel or continue with ordering. One institution implemented a multimodal project to improve adherence to transfusion guidelines in two surgical ICUs for low-risk anemic patients, defined as not actively bleeding and hemodynamically stable.[26] The multimodal approach included an educational lecture, active monthly auditing of each transfusion for appropriateness, and individualized peer-to-peer feedback delivered via email from a surgeon intensivist colleague to clinicians when a packed red blood cell transfusion was associated with a Hgb trigger of > 8 mg/dL or if multiple units were ordered without repeating the Hgb after transfusion of the first unit. Over six months, in comparison to a baseline pre-intervention group, the multimodal intervention resulted in a lowering of the mean transfusion trigger from Hgb 7.6 to 7.1 mg/dL ($P < 0.001$) and a marked reduction in percent of transfusions for a trigger Hgb > 8 mg/dL from 25% to 2% ($P < 0.001$). Transfusions decreased by 36% during the intervention period, suggesting that the personalized peer-to-peer intervention and active auditing with feedback were successful strategies to incorporate in a blood management program.[26]

In addition to transfusion guidelines, compliance monitoring and feedback programs and more strategies to minimize blood loss, particularly intraoperatively, are important. Some of these are included in a "blueprint" for implementing a blood management program outlined by Sadana et al, including use of antifibrinolytics, cell salvage and autologous transfusion, managing preoperative anemia for elective patients with iron or erythropoietin, use of point-of-care testing to minimize delays in response, and reducing phlebotomy (number and amount of blood draws).[27]

SUMMARY

There is extensive evidence supporting a restrictive transfusion approach in critically ill patients and cardiac surgery patients. The data favor restrictive strategies in hip and knee surgery, except in geriatric patients for whom evidence favors a more liberal transfusion strategy. Evidence is sparse in sepsis, oncology, and acute coronary syndrome patients, warranting further study. Given the data from the two recent systematic reviews and meta-analyses linking restrictive transfusion and potentially poorer outcomes in surgical and perioperative patients, additional trials are needed to answer the question about whether a more restrictive or a more liberal transfusion strategy is most appropriate for these groups.

Despite good intentions, clinicians still are implementing the current guidelines inconsistently. Targeted multidisciplinary efforts to implement blood management programs are needed, incorporating evidence-based transfusion triggers, blood conservation strategies, and continuous quality improvement processes to evaluate and promote compliance with transfusion practices that have been shown to affect patient outcomes positively. ■

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ABSTRACT & COMMENTARY

Massive Transfusion Protocols: Recommendations Regarding Initiation and Termination

By Betty Tran, MD, MSc, Editor

SYNOPSIS: This was a narrative review of societal recommendations for initiation of massive transfusion protocols based on objective scoring systems and clinical assessment and criteria for termination of protocols.

SOURCE: Foster JC, et al. Initiation and termination of massive transfusion protocols: Current strategies and future prospects. *Anesth Analg* 2017;125:2045-2055.

Massive transfusion protocols (MTPs) have been associated with significant improvements in patient survival, reductions in blood product use and waste, and decreased complications when compared to massive transfusion (MT) events in hospitals without protocols.[1-3] In this narrative review, Foster et al summarized the most up-to-date recommendations regarding MTP initiation and termination. The sources for these guidelines were from the American College of Surgeons, the European Society for Advanced Bleeding Care in Trauma (ABC-Trauma), and the American Society of Anesthesiologists; an additional literature review of papers published between December 2006 and January 2017 involving the keyword "massive transfusion" also was performed. Notably, much of the literature on MTPs involves the trauma population. The authors hypothesized that one explanation for the lack of observed benefits of MTPs in the nontrauma population may be the higher rate of

MTP "overactivations" in this group (i.e., MTP activations in which patients do not need to receive the amount of blood products required to meet the definition of an MT). Therefore, precise guidelines for guiding MTP initiation and termination in nontrauma patients are lacking.

Each of the aforementioned societies recommends a systematic approach to MTP initiation, which combines a validated MT prediction score with a clinical assessment of tissue perfusion and estimated blood loss, which usually considers factors such as the need for blood transfusions in the ED/trauma bay, need for immediate surgery or angioembolization to control bleeding, persistent hemodynamic instability after fluid resuscitation, and mechanism and severity of injury. The simplest MT prediction score is the Assessment of Blood Consumption (ABC) score, which includes four variables, each worth 1 point with a positive threshold of > 2: systolic blood pressure < 90, heart rate > 120, focused ultrasound assessment for trauma positive, and penetrating mechanism of injury. The ABC score is reported as 75-90% sensitive and 67-88% specific regarding predicting MT requirements within 24 hours of trauma, with a positive predictive value of 55% and a negative predictive value of 97%.

Instead of the ABC score, the ABC-Trauma guidelines recommend the Trauma Associated Severe Hemorrhage (TASH) score, which is more complicated (seven variables, 28 total points, weighted, positive score > 16) and involves two lab values that require time to result (hemoglobin and base excess).

Validation and revalidation studies have shown that the TASH is similar to the ABC score in that a negative score accurately predicts patients who will not require a MT, but a positive score often will incorrectly identify MT needs in someone who ultimately does not need it. For nontrauma patients, the authors suggested considering "intensity of resuscitation" efforts as a surrogate marker for hemorrhage severity, with a threshold of 3-4 units of packed red blood cells per hour as a possible identifier of patients who could benefit from formal MTP initiation.

In terms of MTP termination, collective societal guidelines recommend stopping based on clinical judgment and the fulfillment of three broad criteria: bleeding source control or decelerating rate of blood loss, stable or improving hemodynamics, and decreasing or absent vasopressor requirements. ABC-Trauma also provides specific lab resuscitation targets in terms of hemoglobin (between 7-9 g/dL), prothrombin time and partial thromboplastin time (< 1.5 × normal values), platelets (> 50×10^9/L or > 100×10^9/L in traumatic brain injury or active bleeding), and fibrinogen (> 1.5-2 g/L). This is based on some evidence that conventional coagulation assay-guided resuscitation added to conventional algorithms is associated with fewer blood transfusions, reduced morbidity, and an improvement in hemostatic markers.[4-5] However, no randomized, controlled trials directly comparing algorithm-guided vs. laboratory-guided resuscitation methods exist.

■ COMMENTARY

This review provides a detailed summary and analysis of the current literature and guidelines on MTP initiation and termination in the hemorrhaging trauma population. At the heart of this topic is the balance between timely and adequate resuscitation for patients, which saves lives, and the need to avoid blood product waste and morbidities associated with massive transfusion.[6] It is worth mentioning that although the guidelines are targeted to the trauma population, there is significant variation internationally and even in the United States regarding type/mechanism of traumatic injury, which will have an effect on how the MT prediction scores perform and on the use of MTPs in individual hospitals. For example, the authors noted that in an urban European setting, about 80% of penetrating injuries are stab wounds (overall incidence, 4.7%), and 20% are gunshot wounds (overall incidence, 1.1%); in contrast, in one U.S. urban trauma center, 5.8% of all trauma are gunshot wounds. In addition, although not every hospital is a trauma center, MT situations also arise in nontrauma patients. In addition, there is a need for clear guidelines regarding MTP initiation and termination, which are lacking. At this time, principles guiding the initiation and termination of MTPs, especially in nontrauma situations, will need to be determined by each medical center based on its individual experiences and specific patient populations. Hopefully, the recommendations provided in this review can serve as a starting point for discussion. ■

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ABSTRACT & COMMENTARY

Pre-existing Health Determines Quality of Life, Physical Symptoms After ICU Discharge

By Betty Tran, MD, MSc, Editor

SYNOPSIS: The authors of this nested cohort study within a randomized, controlled trial of ICU survivors requiring > 48 hours of mechanical ventilation found that pre-existing comorbidity was the main determinant of long-term health-related quality of life.

SOURCE: Griffith DM, et al. Determinants of health-related quality of life after ICU: Importance of patient demographics, previously comorbidity, and severity of illness. *Crit Care Med* 2018 Jan 2. doi: 10.1097/CCM.0000000000002952. [Epub ahead of print].

Because their earlier study (RECOVER) failed to show that an intensive post-ICU, multidisciplinary rehabilitation program improved physical recovery and health-related quality of life (HRQoL),[1] Griffith et al hypothesized that pre-ICU health factors may be more important, explaining why some patients may be refractory to their intervention.

This was a cohort study nested within the RECOVER randomized, controlled trial, which enrolled 240 adult ICU survivors who required > 48 hours of continuous mechanical ventilation. The authors aimed to describe the cohort trajectory of HRQoL between three and 12 months and explore the factors associated with HRQoL and patient-reported symptoms at six and 12 months post-ICU discharge. HRQoL was assessed via the Medical Outcomes Study Short Form-12 Version 2 (SF12v2), which included the Physical Component Score (PCS; range, 0-100) and Mental Component Score (MCS; range, 0-100), with higher scores better. The authors predefined a minimum clinical important difference (MCID) in PCS and MCS as greater than ± 5 points. Patient-reported symptoms of appetite, fatigue, pain, joint stiffness, and breathlessness were measured on a visual analogue scale ranging from 0 (no symptoms at all) to 10 (worst symptoms imaginable).

Overall, mean PCS and MCS were reduced compared to population norms, with mean PCS increasing by a statistically significant, but small (less than the MCID), amount between three and 12 months (mean difference, 2.3; 95% confidence interval [CI], 0.6-3.9; $P = 0.006$); the mean MCS did not change over that same time. Of the 147 patients who had complete PCS and MCS data at three and 12 months, 94 demonstrated no significant clinical improvement in PCS and 101 exhibited no significant clinical improvement in MCS. In the multivariable analysis, higher pre-existing comorbidity burden was associated with worse PCS (beta, -1.56; 95% CI, -2.44 to -0.68; $P = 0.001$) and MCS (beta, -1.45; 95% CI, -2.37 to -0.53; $P = 0.002$) at six months in addition to 12 months; critical illness-related variables were not associated with either PCS or MCS at either point. As the number of pre-ICU comorbidities increased, both PCS and MCS tended to be lower after discharge and exhibited a flatter trajectory, reflecting lack of improvement. A higher pre-ICU comorbidity count also was associated with worse patient-reported symptom scores.

■ COMMENTARY

This secondary analysis of the RECOVER trial is a helpful addition to our growing understanding of the complex interplay between pre-existing disease and acute critical illness in ICU survivors. Although the RECOVER cohort experienced notably severe critical care stays (APACHE II mean score, 20 [standard deviation {SD}, 8], mean ventilation days 12 [SD, 11], 74% required vasopressors, 27% required renal replacement therapy), pre-ICU comorbidity count was associated most strongly with post-ICU HRQoL and persistent symptoms. These findings support previous studies that have found strong associations between pre-hospital comorbid conditions and 30-day readmissions after hospitalization for sepsis.[2-5]

Based on these data, a pre-ICU health trajectory is highly significant in determining the post-discharge course, not only regarding healthcare use, but also HRQoL and patient-perceived symptoms. This carries important implications for future intervention studies seeking to improve HRQoL or functional recovery. Patients with more comorbid conditions at baseline may have limited to no improvement and may mask significant effects in other patient subpopulations if not defined appropriately at the outset. This patient population also may require additional resources and/or different interventions to demonstrate improved outcomes. In an age of personalized medicine regarding genetics, biomarkers, and drug response, we should not be surprised that a one-size-fits-all approach to post-ICU care will not suffice. ■

REFERENCES

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CME/CE INSTRUCTIONS

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CME/CE QUESTIONS

1. In which of the following patient populations has a restrictive transfusion strategy been shown to improve patient outcomes over a liberal strategy?
a. Hematology/oncology
b. Acute coronary syndrome
c. Critical care
d. Older adults

2. The current AABB guidelines for transfusion support include which of the following?
a. Transfusion trigger of hemoglobin < 7 mg/dL in hemodynamically stable hospitalized adults
b. Transfusion trigger of hemoglobin < 10 mg/dL for patients undergoing orthopedic or cardiac surgery or having existing cardiovascular disease
c. Transfusion trigger of hemoglobin < 15 mg/dL for patients with acute coronary syndrome
d. None of the above

3. In the review by Foster et al, initiation of a massive transfusion protocol should be based on which of the following?
a. Positive ABC or TASH score
b. Amount of blood transfused in the emergency department
c. Need for immediate surgery or angioembolization to control bleeding
d. All of the above

4. In the study by Griffith et al, which factor was associated most strongly with health-related quality of life after an ICU stay involving mechanical ventilation for at least 48 hours?
a. Duration of heavy sedation in the ICU
b. Number of acute organ failures developing during ICU stay
c. Discharge from ICU to a long-term acute care facility or skilled nursing facility
d. Number of pre-existing comorbid conditions

5. Based on the study of Griffith et al, which of the following statements is *true*?
a. Most patients demonstrated no clinically significant improvement in physical or mental performance scores between three and 12 months after ICU discharge.
b. Critical illness-related variables were significantly associated with physical and mental performance scores at six months, but not 12 months, post-discharge.
c. As the number of pre-existing comorbid conditions increased, there was a steeper improvement in mental, but not physical, scores at 12 months post-ICU discharge.
d. Age was most strongly associated with patient-reported symptoms at 12 months post-ICU discharge.

CME/CE OBJECTIVES

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

- identify relevant topics in the practice of critical care medicine;
- utilize recommendations from current clinical guidelines; and
- manage common critically ill patient and ICU administration scenarios.