ECG gating of myocardial perfusion images provides the additional ability to assess the severity of the infarction using wall motion and wall thickening, while also providing information regarding the remaining ischemic territories and global as well as regional LV systolic function. The combination of all these data can augment the clinical value of perfusion imaging, and can result in more precise diagnostic and prognostic information without the added expense of additional imaging studies and with no additional time or radiation exposure to the patient. The simultaneity of a single resting gated SPECT scan image in a postinfarct patient can give information regarding both infarct size, as well as regional and global systolic function, as demonstrated in the study by Lapeyre et al.

The addition of data on regional ejection fraction in patients following thrombolytic therapy for infarction can provide valuable clinical information for the prediction of future events in this population of patients. Regional function is another clinical marker, in addition to perfusion defect size, that can determine the success of reperfusion therapy and can contribute to the long-term prognostic data in these patients.

The quantitative assessment of regional contraction and wall thickening by gated SPECT imaging can assist in the follow-up of patients with myocardial dysfunction and contributes to the ongoing evaluation of medical or invasive therapy in these patients.

LIMITATIONS OF SPECT IMAGING

Despite the tremendous clinical advantages of gated SPECT imaging, there are limitations to the technique that must be considered when acquiring and interpreting the images. Most errors in gated SPECT can images can be attributed to the following:

1. In small hearts the end systolic dimension can effect the reconstructed spatial resolution resulting in an artificially high ejection fraction. The method described here continues to have this limitation.
2. In the presence of an extensive perfusion defect or when a part of the myocardium is missing, it is difficult to delineate the myocardium using epicardial contours or edge-detection methods.
3. There is no compensation for translational or rotational heart motion during the cardiac cycle. This makes it unlikely for the same region of the myocardium to lie within the same region of interest in the end-systolic and end-diastolic phases. In turn, this can result in the overestimation of ejection fraction.

CONCLUSION

Gated SPECT imaging has developed to provide useful functional information. It has evolved into a valuable clinical adjunct to SPECT imaging. It not only improves the test specificity but also adds incremental clinical value to the study. Lapeyre et al have demonstrated the additional benefit of SPECT imaging in evaluating infarct size and regional function in patients following thrombolytic therapy.

The gated perfusion images are easy to obtain, reliable, and highly reproducible without incurring significant additional cost or patient risk. They provide information about the global function and regional contraction simultaneously with perfusion imaging with minimal limitations, and increase the ability to provide accurate diagnostic imaging in healthy and ischemic patients, as well as in patients who have experienced myocardial infarction.

Maryam Afshar, MD
Peter Tilkemeier, MD
Providence, RI

Dr. Afshar is a Clinical Instructor of Medicine, Brown University. Dr. Tilkemeier is Associate Professor of Medicine, Brown University, and Director of Nuclear Cardiology, Miriam Hospital. Reproduction of this article is prohibited without written permission from the American College of Chest Physicians (e-mail: permissions@chestnet.org).
Correspondence to: Peter Tilkemeier, MD, The Miriam Hospital, 164 Summit Ave, Providence, RI 02906

REFERENCE


Transfusion Practice in the ICU
When Will We Apply the Evidence?

Anemia is a common problem in the ICU. The vast majority of patients are anemic on admission to the ICU. Among the few patients who have normal hemoglobin levels at presentation, nearly all become anemic during the course of their ICU stay. The causes for anemia in critically ill patients are manifold. In some instances, anemia results from acute blood loss after trauma, GI hemorrhage, or surgery. For other individuals, anemia arises because of earlier treatment
with chemotherapeutic agents or because of the patient’s chronic medical conditions. All patients, however, are exposed to the risk of frequent phlebotomy. Some estimates have suggested that we remove nearly 60 mL blood per day from those in the ICU.

Blunted erythropoiesis also contributes to the development of anemia in the ICU. For example, despite anemia and adequate iron stores, Bogiers and colleagues demonstrated that critically ill individuals fail to produce appropriate levels of erythropoietin (EPO). Although one would expect an inverse correlation between the hematocrit and EPO measurements, these investigators found no such relationship in a mixed ICU cohort. Furthermore, when compared to non-acutely ill individuals, critically ill subjects have a relatively limited reticulocytosis in response to their anemia. These observations have led to the development of the concept of “anemia of critical illness.” Physiologically, this phenomenon appears to result from the inhibition of the gene regulating EPO production. Elevated levels of proinflammatory cytokines suppress not only the transcription of a key sensor of tissue hypoxemia, but also limit the endogenous production of EPO. These cytokines further contribute to anemia by directly hindering the production of RBCs in the bone marrow and altering iron metabolism.

Irrespective of the cause of anemia, physicians must determine if and how to treat this problem. Despite the frequency of anemia in the ICU, no recent, formal guidelines exist to help the clinician. The recommendations made in older position statements suggest that transfusion is rarely indicated when the hemoglobin concentration is > 10 g/dL but may be indicated when the level falls below this threshold, especially if surgery is planned. However, such recommendations stem more from tradition rather than from the results of clinical trials. These guidelines also fail to acknowledge the evidence that certain patients tolerate severe anemia so long as they received adequate fluid resuscitation.

This lack of strong data results in variable practice styles and certainly helps to explain the frequency of blood transfusion in the ICU. For example, a Canadian survey revealed that many intensivists perform transfusions at hemoglobin levels of approximately 9 g/dL. Moreover, this study noted a wide variability in practice. A more recent European prospective, observational study of 3,534 patients documented that anemia was common in critically ill patients, with nearly one third of subjects having hemoglobin concentrations of < 10 g/dL. Approximately 40% of the cohort received transfusions during the course of their ICU stay, and the mean pretransfusion hemoglobin level was 8.4 g/dL. A similar study in the United Kingdom confirmed these observations. In both reports the most common reason for transfusion was “low hemoglobin.” In other words, patients did not receive transfusions in response to acute hemorrhage or as part of resuscitation for shock. Rather, the intensivist determined that the degree of anemia posed a threat to the patient’s health and that this necessitated a response.

In this issue of CHEST (see page 928), Levy and colleagues describe the results of a subgroup analysis of US patients who were enrolled in the CRIT study. The CRIT study initially represented a large multicenter observational investigation into transfusion practices in the ICU. In their report, Levy et al focus on subjects requiring mechanical ventilation (MV). Appreciating process of care and outcomes in the mechanically ventilated patient is a crucial aspect of health services research in critical care, since MV disproportionately contributes to cost and length of stay in the ICU. MV also represents a technology that is unique to the ICU environment. Not surprisingly, Levy et al found that individuals requiring MV were more severely ill than those not requiring MV and more often received transfusions while in the ICU. Strikingly, though, MV patients accounted for > 75% of all the units of blood administered, and the typical MV subject received nearly 5 U packed RBCs during care in the ICU. One might expect that this disproportionate use of transfusion reflects the higher severity of illness among patients receiving MV. However, when queried as to the reason for transfusion, the most common reason for transfusion in those patients who were receiving MV was not hemodynamic instability but, rather, low hemoglobin. How low was the hemoglobin level that triggered transfusion, and the attendant costs and risks of transfusion? The mean ± SD pretransfusion hemoglobin level was 8.4 ± 1.4 g/dL. Furthermore, 40% of the transfusions performed in the MV population were done after day 4 of an ICU stay (ie, during the extended phase of the patient’s illness).

These results from the CRIT investigators are particularly distressing, since the trial was conducted between August 2000 and April 2001. The findings from the Transfusion Requirements in Critical Care (TRICC) study were published in 1999. In that landmark trial, Hebert et al randomized critically ill patients either to a liberal transfusion strategy, with a hemoglobin level goal of 10 g/dL, or to a restrictive protocol, with a hemoglobin level goal of 7 g/dL. The study included > 800 persons, many of whom required MV. At 30 days post-study enrollment, the mortality rate was similar between the two arms of the study, indicating that a restrictive transfusion strategy was at least as safe as a liberal approach. More importantly, the results from this project suggested that the greater use of transfusion might
actually result in harm to our patients. The hospital mortality rate was higher in those persons randomized to the liberal transfusion strategy arm (28.1% vs 22.2%, respectively; p = 0.05). In both younger patients (ie, those <55 years) and in less severely ill subjects (ie, acute physiology and chronic health evaluation [APACHE] II score, <20), mortality was significantly lower in the restrictive transfusion cohort. Because of continuing controversy regarding the “optimal hemoglobin” level that would facilitate liberation from MV, Hebert and coworkers14 separately analyzed outcomes in subjects requiring MV. Although not designed to expressly explore transfusion and MV, the study by Hebert et al14 reported that the higher hemoglobin goal did not result in shorter durations of MV. In short, nearly a year after the publication of a well-done clinical trial that provided important insight into the management of ICU patients, Levy et al reveal that few intensivists had modified their clinical practice. Failure to alter our treatment algorithms despite clinical studies focused on our patients only underscores the amount of work that remains to be done if critical care is to become an evidence-based specialty.

It is important to note that the TRICC trial13 only enrolled hemodynamically stable patients. The findings from the TRICC trial cannot and should not be applied to individuals undergoing short-term resuscitation. The goals and objectives of resuscitation are unique, and hence the decision to transfuse in this scenario must be based on how the patient responds to other interventions, including early, aggressive fluid resuscitation. Nonetheless, more liberal transfusion criteria during acute resuscitation cannot fully explain the significant transfusion rates documented by Levy et al. For example, the vast majority of the blood given to those needing MV was given after what many would consider to have been the acute phase of the subject's illness.

The analysis by Levy et al has several limitations. First, they did not provide sufficient data regarding the physician's reasoning as to why he/she chose to transfuse. “Low hemoglobin” as a potential choice on a list of options may not adequately capture more nuanced features in the decision-making process. Second, Levy et al did not describe the incidence of ongoing shock in the cohort or the number of persons who initially received therapy with vasopressors. They opted not to perform any multivariate analyses to explore the relationships among transfusion, MV, and other confounders such as severity of illness. The connection between greater lengths of stay in the ICU and more transfusions in the MV cohort may reflect only an association, and not necessarily a causative relationship.

Beyond health services research and descriptive analyses like that presented by Levy and colleagues, another area of active investigation in transfusion and intensive care medicine has been an effort to better understand the risks related to transfusion in the critically ill patient. Several research teams have noted that transfusion is immunomodulatory, and increases the production of proinflammatory cytokines and alters T-cell function both in vitro and in vivo. Correspondingly, transfusion heightens the potential for nosocomial infection. Similarly, there is now greater appreciation of the potential for transfusion-related acute lung injury (TRALI). TRALI represent a form of acute lung injury that is thought to arise from the activation of primed neutrophils and is the third most common cause of transfusion-related death. Epidemiologic reviews have suggested that subclinical forms of TRALI exist but that these cases may not be appreciated by the clinician. Hence the true incidence of the disease is unknown because of underreporting.

Thus, in the last 5 years the potential benefits of transfusion have come into question, while the impact of the relative dangers of transfusion have become more evident. Nonetheless, it remains unclear whether we have made any effort to reevaluate the balance of these risks and benefits in our practice.

It is important to note that issues of benefit and harm do not necessarily provide insight into what represents the “optimal” hemoglobin level. Needless to say, that will be a function of a patient’s clinical status at the time that one considers whether to perform the transfusion. As newer alternatives to transfusion become available, though, we will have to reexamine our transfusion goals. The opportunity to raise a patient’s hemoglobin level without exposing them to the risks of transfusion remains appealing. At present, multiple phase III trials are underway investigating the role for both artificial hemoglobins and exogenous EPO. Although the early results of investigations employing these products have been encouraging, as clinicians we should demand that future studies be well designed and target important clinical end points such as survival, rates of nosocomial infection, and length of stay.21,22 Showing that any new approach only alters some surrogate or laboratory marker without a commensurate improvement in outcomes should not prompt us to modify our practice. However, let us hope that if such trials are successful, we adopt those evidence-based interventions more rapidly than we have responded to the current data regarding the value and role for transfusion.

Andrew F. Shorr, MD, MPH
Washington, DC

William L. Jackson, MD
Dr. Shorr is affiliated with the Pulmonary, Critical Care, and Sleep Medicine Service, Department of Medicine and the Critical Care Medicine Service, Walter Reed Army Medical Center, and Dr. Jackson is affiliated with the Department of Surgery, Walter Reed Army Medical Center.

The opinions expressed herein are not to be construed as official or as reflecting the policies of either the Department of the Army or the Department of Defense.

Reproduction of this article is prohibited without written permission from the American College of Chest Physicians (e-mail: permissions@chestnet.org).

Correspondence to: Andrew F. Shorr, MD, MPH, Pulmonary, Critical Care, and Sleep Medicine, Walter Reed Army Medical Center, Washington, DC 20307; e-mail: afshorr@dnamail.com

REFERENCES

5 Fink MP. Pathophysiology of intensive care unit-acquired anemia. Crit Care 2004; 8(suppl):S9–S10
16 Vamvakas EC, Blajchman MA. Deleterious clinical effects of transfusion-associated immunomodulation: fact or fiction? Blood. 2001 1; 97:1180–1195

Referral for Lung Transplantation

A Moving Target

S

c

uccessful human lung transplantation has evolved significantly since 1963, when the first lung transplant recipients lived only a few days after transplantation. Changes in surgical techniques and advances in immunosuppressive therapy have been credited with the advancing lung transplantation, making it an invaluable tool for the management of advanced respiratory diseases. This is apparent by the growing number of patients listed for transplantation. A gross disparity exists, however, between the number of potential recipients and the number of donor organs available, resulting in many patients dying while on the waiting list. Due to long wait times, transplant physicians are no longer just faced with trying to improve survival after transplantation, but are now facing the challenge of improving a patient’s chances of survival while on the waiting list for transplantation. As a further challenge, the natural history of various advanced lung diseases vary and are somewhat unpredictable. This is especially true of diseases for which we do not have adequate prognostic scales, unlike cystic fibrosis or idiopathic pulmonary fibrosis. As a result, predicting survival in specific advanced pulmonary diseases is one of the major issues confounding referral for transplantation. As waiting list times appear to be increasing from 24 months to a median of 46 months, questions are now being raised regarding the appropriate disease-specific time for referral to ensure maximum survival before and after transplantation.

Much attention has been given to better defining lung transplant candidacy guidelines in order to