Patients with ischemic heart disease have always been of special concern for transfusion therapy. There are a number of observational studies showing that moderate to severe anemia in patients with cardiac disease is associated with adverse outcomes, including higher mortality rates. While most tissues have the ability to extract more oxygen from the blood when demand increases, the heart muscle extracts near-maximal concentrations of oxygen under resting conditions. For that reason, the primary adaptive response to increased oxygen demand or decreased oxygen supply is to increase coronary artery blood flow. However, this adaptive response is impaired in patients with abnormal coronary circulation, such as atherosclerosis, leading to critical oxygen delivery levels at lower hemoglobin levels than in patients with "normal" coronary circulation. For these reasons, patients with ischemic heart disease have traditionally been transfused at higher hemoglobin levels than other patients with the assumption that blood transfusions improve outcomes.

The Transfusion Requirements in Critical Care (TRICC) Trial compared a liberal transfusion strategy (transfusion trigger of 10 gm/dL) to a restrictive strategy (transfusion trigger of 7 gm/dL) in 838 critically ill patients. The conclusion was that patients did not benefit from a more liberal strategy, and most had better outcomes being transfused more conservatively (less is
more). However, patients with severe cardiac disease were specifically excluded from the recommendation that “a restrictive strategy of red cell transfusions is at least as effective as and possibly superior to a liberal strategy in critically ill patients, with the possible exception of patients with acute myocardial infarction or unstable angina.” Furthering the concern about patients with ischemic heart disease was the criticism that some physicians had refused to enroll high risk cardiac patients in the TRICC trial, lowering the number of cardiac patients that were studied. This issue was addressed in a post-hoc analysis of cardiac patients in the TRICC trial, which still concluded that “most hemodynamically stable, critically ill patients with cardiovascular disease may receive a transfusion safely when hemoglobin concentrations decrease below 7.0 g/dL and may be maintained at hemoglobin concentrations between 7.0- 9.0 g/dL.” However, the possible exception to conservative therapy remained patients with acute coronary syndromes (ACS).

**JAMA 2004**

Rao was the first investigator to scientifically question the logic of anemia and transfusions in patients with ischemic cardiac disease. In a 2004 study published in JAMA, he reviewed 24,000 patients enrolled in FDA trials for acute coronary syndromes. Using this comprehensive data set and a variety of sophisticated statistical tools, including multivariate analysis and propensity scoring, he came to a shocking conclusion: patients with acute coronary syndromes get worse with blood transfusions, not better. In fact, his conclusion was that heart attack patients transfused at a hematocrit above 25% (or a hemoglobin of 8 gm/dL) were more likely to have a second heart attack and were four times more likely to die within a month. A study of 2400 myocardial infarction patients in Israel demonstrated remarkably similar findings to the Rao study, and an analysis of over 4100 patients with ST-elevation MI (STEMI) using propensity scoring concluded that mortality rates in transfused patients were three to four times higher at 30 days, six months and one year. The conclusion of the latter study was “blood transfusion is associated with increased short- and long-term mortality in the setting of STEMI.”

**OTHER RECOMMENDATIONS**

There are a growing number of transfusion trials in high risk patients noting that restrictive transfusion thresholds for red blood cells are at least as effective, if not superior, to more liberal strategies, and the AABB recently published a nice consensus document summarizing the evidence. There is growing evidence from observational studies that liberal transfusions may increase mortality in patients with acute coronary syndromes (ACS), and there is a pilot study of transfusion strategies in ACS patients currently underway known as the MINT trial. While we await the results of the MINT trial, we should certainly be cautious about reflexively transfusing patients with ACS given the pro-inflammatory and pro-coagulant effects of stored blood. A single unit approach in non-bleeding patients is warranted, when transfusion is necessary.