

Transfusion in ACS Patients Has Unexpected Risks

BY BRUCE JANCIN
Denver Bureau

CHICAGO — American physicians are quick to order blood transfusions—and a growing body of evidence indicates that is not necessarily a good thing, Dr. Sunil V. Rao said at a satellite symposium held in conjunction with the annual meeting of the Society for Cardiovascular Angiography and Interventions.

"In the U.S., we're just very, very transfusion happy. We have a very quick transfusion trigger. And I think there are some compelling data in the acute coronary syndrome population that [suggest it] may not be such a good idea," added Dr. Rao of Duke University Medical Center, Durham, N.C.

Indeed, his recent analysis of three large international clinical trials, totaling more than 24,000 acute coronary syndrome (ACS) patients in 30 countries, concluded that patients outside the United States were 76% less likely to get a blood transfusion. After adjusting for differences in baseline patient characteristics, procedures, and bleeding severity, non-U.S. ACS patients were still 24% less likely to get a transfusion than were comparable Americans.

The 10% of patients who received one or more blood transfusions during their hospitalization had an unadjusted 30-day mortality of 8%, significantly greater than

the 3% rate in ACS patients who weren't transfused. After statistical adjustment for the transfused patients' greater age and more baseline comorbidities, transfusion was associated with a fourfold increased risk for mortality at 30 days.

In the setting of a nadir hematocrit of 25% or less, transfusion was beneficial. However, with a hematocrit above 25%, transfusion was associated with increased 30-day mortality (JAMA 2004;292:1555-62).

It is noteworthy that the adjusted odds ratio for 1-year mortality was also increased fourfold in transfused patients who underwent percutaneous coronary intervention in the Randomized Evaluation of PCI Linking Angiomax to Reduced Clinical Events (REPLACE-2) trial, most of whom had stable ischemic heart disease, Dr. Rao continued.

"That's close to what we found in our study of ACS patients. It suggests the effect may be real," the cardiologist said at the symposium, sponsored by The Medicines Company.

Much the same appears to be true in patients without ischemic heart disease. A Cochrane Collaboration meta-analysis of 10 randomized clinical trials in which the majority of participants didn't have ischemic heart disease concluded that a restrictive transfusion strategy was associated with a 20% reduction in the relative risk of mor-

tality, a 51% decrease in heart failure, and a 56% reduction in acute MI.

The notion that blood transfusion can be bad for patients in ways beyond the common concerns regarding disease transmission and acute immune reactions runs counter to conventional thinking. But packed RBCs possess several negative properties: They have a high affinity for oxygen and are severely depleted of nitric oxide, which plays an essential role in oxygen exchange.

In fact, packed RBCs function as nitric oxide sinks. They cause platelet aggregation and vasoconstriction. And in one study, administration of packed RBCs was associated with increased C-reactive protein and interleukin-6, important markers of inflammation.

If bleeding is bad for patients and transfusion often is, too, it's clear that the key is to prevent bleeding problems in the first place. Today the safety-efficacy equation has shifted such that a greater focus on safety will pay dividends in terms of efficacy. In contemporary practice, as shown in a recent 40,000-patient analysis from the CRUSADE National Quality Improvement Registry, the most common in-hospital adverse outcome in ACS patients is no longer ischemic complications but severe bleeding, Dr. Rao said.

Dr. Rao is a consultant to the Medicines Company, which funded ACUTY. ■

Gender, Racial Gaps in Post-MI Care Persist Since 1980s in U.S.

BY BRUCE JANCIN
Denver Bureau

ATLANTA — Women with acute MI are roughly one-third less likely than are men to undergo cardiac catheterization and coronary revascularization procedures, a trend that has persisted since the mid-1980s, William J. Kostis, Ph.D., said at the annual meeting of the American College of Cardiology.

Similarly, African Americans with an MI—men as well as women—are roughly one-quarter less likely than are whites to get a revascularization procedure. And again, that trend has held constant since the mid-1980s, said Dr. Kostis of Robert Wood Johnson Medical School, Piscataway, N.J.



These were among the provocative findings of an analysis of nearly 248,000 first MIs in New Jersey during 1986-2002. The data were collected through the state's Myocardial Infarction Data Acquisition System (MIDAS), which includes information on all patients admitted with acute MI to nonfederal hospitals in New Jersey.

Since this is a nonselected patient population, it seems highly likely that the observed trends regarding gender and racial disparities in invasive cardiac procedures are generalizable to the rest of the country, he said. Lower rates of invasive procedures in women and African Americans have been reported previously in several other studies. Where MIDAS breaks new ground is in providing a picture of trends over a lengthy 17-year period.

MIDAS documented a marked increase in cardiac catheterization in MI patients during the study period. Among men, the rate

climbed from 23% in 1986 to 70% in 2002. In women, it rose from 13% to 52%.

The rate of revascularization by percutaneous coronary intervention or coronary artery bypass surgery was less than 10% in both men and women with acute MI in 1986. In men, the rate climbed steadily to 54% by 2002, but in women it reached 34% in the mid-1990s and then leveled off.

Both African Americans and whites with acute MI underwent cardiac catheterization

about 20% of the time in 1986. The rates of the diagnostic procedure rose comparably in the two racial groups over time.

Coronary revascularization, however, was a different story. The revascularization rate was less than 10% in both groups in 1986, but

by 2002 it rose to 46% among whites, and to 38% in African Americans, Dr. Kostis continued.

To learn whether these differences in procedure rates influence clinical outcome, Dr. Kostis and coinvestigators looked at 30-day mortality following a first MI, adjusting for age, comorbid conditions, site and severity of MI, and complications during hospitalization. Adjusted mortality was significantly greater in women than in men, and in African Americans than in whites.

But after further adjustment for rates of invasive cardiac procedures, the increased mortality risk in women and African Americans was diminished; it became statistically nonsignificant in African Americans. This implies the lesser use of procedures in these groups is causally related to their higher mortality, he said.

Dr. Kostis said that he plans next to look at the impact of disparities in procedure rates on longer-term mortality. ■

African Americans with an MI are roughly one-quarter less likely than whites to undergo revascularization.

DR. KOSTIS

Ischemic Symptoms Prior to MI Missed in Primary Care Settings

BY JANE NEFF ROLLINS
Contributing Writer

LOS ANGELES — Nearly one in nine patients admitted with an acute myocardial infarction were seen shortly before their MI in the primary care setting with symptoms suggestive of acute cardiac ischemia Dr. Thomas D. Sequist reported at the annual meeting of the Society of General Internal Medicine.

"We know from our own experience in Boston that missed diagnosis of MI in this setting is a rising source of malpractice claims," said Dr. Sequist of Brigham and Women's Hospital, Boston.

The investigators identified 966 admissions for acute MI, of whom 106 (11%) had complained of symptoms typical of potential heart disease at their last outpatient visit. During the outpatient visit prior to the MI, chest pain and dyspnea accounted for more than three-quarters of all chief complaints. Other complaints included thoracic or epigastric pain, dizziness, weakness, or nausea.

This population-based case-control study used billing claims to identify admissions for acute MI from 2000 to 2004 among patients with no prior history of coronary heart disease (CHD). The 318 control patients were matched to cases on chief complaint and date of outpatient visit, but had no diagnosis of MI within the next 30 days.

Compared with controls, cases were older and were more likely to be male and to have diabetes or dyslipidemia. Approximately 50% of both cases and controls received an

electrocardiogram (ECG). Not surprisingly, among those who had an ECG, the rates of normal results were much lower in cases than controls. Despite having symptoms of possible CHD, few study participants in both groups received cardiac medications (aspirin, 11%; beta-blockers, 7%). "There was a significant opportunity for more aggressive evaluation and treatment of these symptomatic patients," Dr. Sequist said.

The Framingham Risk Score (FRS) predicts risk for developing CHD using information about coronary risk factors readily available in the outpatient setting, and may be used with asymptomatic individuals. In contrast, the Diamond and Forrester Probability (DFP) and the Goldman Prediction Tool (GPT), which calculate risk scores that predict either CHD or MI, can only be used with individuals who have chest pain.

Cases had a nearly 20-fold greater likelihood of having a FRS greater than or equal to 10%, compared with controls (odds ratio, 19.5). Among patients whose FRS was greater than or equal to 10%, more than 30% were diagnosed with angina. Higher DFP and GPT scores were also associated with MI (odds ratio of 8.3 with a DFP score of 10% or more, and OR of 12.1 with a GPT greater than 7%). However, the FRS had the best sensitivity (85%) and specificity (75%) combination in those individuals at moderate risk.

"This study documents the very substantial role of primary care clinicians in the early evaluation of acute cardiac ischemia," Dr. Sequist said. ■