Researchers Probe Anemia–Heart Failure Link

Mike Mitka

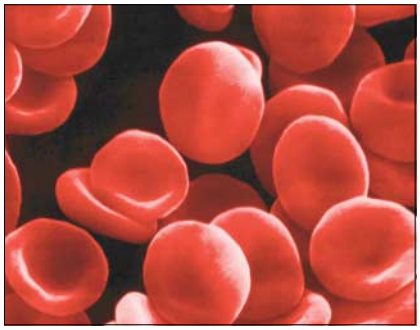
VIENNA—For years, physicians have noticed that patients with congestive heart failure who have anemia fare less well than those with a normal hematocrit, but the link was largely dismissed as a mere association. In recent years, however, researchers have begun to question whether anemia is only a marker for the problem or whether it may cause or exacerbate heart failure—and if treating anemia will improve outcomes.

"We have had a whole series of studies allowing us to recognize that anemia is a problem [for those with congestive heart failure]," said Justin Ezekowitz, MD, of the University of Alberta, Edmonton.

A COMMON PROGNOSTIC FACTOR

In a study published earlier this year, Ezekowitz and colleagues demonstrated that anemia is a common and independent predictor of mortality in patients with congestive heart failure (*Circulation*. 2003;107:223-225). Analyzing a population-based cohort of patients with new-onset congestive heart failure discharged from 139 acute-care hospitals in Alberta between April 1993 and March, 2001, the investigators found that 1-year and 5-year mortality rates were 38% and 59% in those with anemia compared with 27% and 50% in those without the condition.

That mortality trend was confirmed in a study presented here last month during the European Society of Cardiology Congress. Using a Scottish national database of hospital discharge statistics, Simon Stewart, PhD, of the University of South Australia in Adelaide and John J. V. McMurray, MD, of the University of Glasgow in Scotland examined 42 713 discharges between 1990 and 1995 where heart failure was the primary diagnosis. Stewart and colleagues found that for patients with non–iron deficiency anemia, long-term mortality (30 days to 2 years) was



James A. Sullivan

Researchers are exploring whether anemia causes or worsens congestive heart failure or is merely a marker for the condition.

66% for men and 61% for women compared with 53% and 54%, respectively, for men and women without anemia (all comparisons were statistically significant). Stewart speculated that anemia-associated mortality could be even higher, as anemia is often underreported on hospital charts of patients with heart failure.

Barry Massie, MD, of the University of California, San Francisco, said the cause-and-effect question needs to be answered next. "The most important question is whether heart failure causes anemia or if anemia affects heart failure," Massie said.

If the latter is the case, interventions to treat anemia may benefit patients with congestive heart failure. Preliminary studies suggest this strategy may indeed help. The initial thrust in the research has centered around increasing hemoglobin levels with erythropoietin or its derivatives.

BOOSTING BLOOD CELLS

In one study of 26 patients with anemia and persistent, severe congestive heart failure, researchers at Tel Aviv Medical Center in Israel found that treatment with subcutaneous erythropoietin and intravenous iron was associated with improvement in cardiac function (*J Am Coll Cardiol*. 2000;35:1737-1744). In another study involving 26 anemic patients with chronic heart failure randomized to receive erythropoietin or placebo for 3 months, researchers at Columbia Presbyterian Medical Center in New York found patients who received erythropoietin had significantly enhanced exercise capacity—increases in hemoglobin, peak oxygen consumption, and exercise duration—compared with patients who received a placebo (*Circulation*. 2003;107:294-299).

While researchers are now calling for larger trials to explain the relationship between anemia and heart failure, several issues need to be addressed, said Ezekowitz.

"We need to define what we mean by 'anemia'—the studies so far have not used set definitions of anemia and its severity, so it's hard to compare results," Ezekowitz said. "Also, we know there's a number of other links associated with anemia in patients with heart failure: renal dysfunction, medications, and so on. We need to see how these relate."

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Researchers are currently enrolling patients in a double-blind, placebo-controlled, randomized trial that may help clarify the link between anemia and heart failure and whether treating anemia improves outcome for patients. In the Studies of Anemia in Heart Failure Trial (STAMINA HeFT), about 250 congestive heart failure patients with anemia (defined as having a hemoglobin level < 12 g/dl) will be randomized to treatment (subcutaneous injections every 2 weeks for 1 year) with darbepoetin alfa (Aranesp) or placebo. Exercise treadmill tests will be performed at baseline and again at 13 and 27 weeks. Change in functional status will be the main end point.

Beat Knusel, PhD, global study manager for the trial's sponsor, Amgen Inc of Thousand Oaks, Calif, said the trial is being conducted in 65 centers in 8 countries from the United States, Canada, Australia, and Europe and is expected to conclude in the second quarter of 2005.

"In general, anemia is something that's underappreciated by physicians, and, cardiologists in particular," said Paul Burton, MD, associate medical director with Amgen. "There [are] provocative data from small, limited studies saying that improving anemia may improve outcomes of heart failure. Our goal is to answer that question."

Ezekowitz, who is enrolling patients in STAMINA HeFT, said that while the trial will not be the final word on the subject, he hopes results will guide the science in the right direction.

"What [STAMINA HeFT] is going to do is show the feasibility of performing clinical trials in this area," Ezekowitz said. "While it is not powered to show mortality per se, it can show improvement in functional status, which is a good surrogate for mortality and a good launching pad for further research." □

Breast Cancer Racial Gap Examined

No Easy Answers to Explain Disparities in Survival

Brian Vastag

WASHINGTON, DC—The problem is clear: white women diagnosed as having breast cancer tend to outlive black women with the disease. The dynamics driving this disparity, however, are much cloudier.

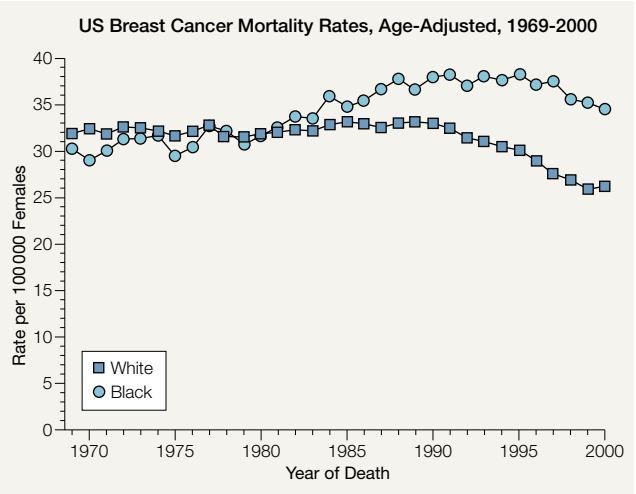
According to a recent report, breast cancer mortality rates decreased 2.5% a year for white women during the 1990s. In contrast, mortality rates decreased only 1% a year for black women (*J Natl Cancer Inst*. 2003;95:1276-1299).

In search of an explanation for the lower survival rates among black women, researchers have cited a range of potential causes, including variations in treatment, high prevalence of comorbid conditions, poor eating habits, lower rates of screening, and late diagnosis. Published studies tend to wrap many of these factors into a meta-indicator—socioeconomic status—and point to it as the essential variable.

But a closer examination of the phenomenon has teased out a single demographic curiosity driving the disparity: black women aged 50 years and younger diagnosed as having breast cancer tend to present with aggressive, hard-to-treat tumors. In fact, breast cancer survival rates are nearly identical for black and white women aged 65 years and older, possibly because Medicare provides similar treatment options across all populations.

Harold Freeman, MD, director of the Center to Reduce Cancer Health Disparities at the National Cancer Institute (NCI) and a coauthor of the latest report to confirm the lower survival rates among black women (*Cancer*. 2003;97:2853-2860), opened a recent meeting by calling the problem a "moral and ethical dilemma for our nation."

"We are not delivering all we know about cancer prevention, early detection, and treatment to everyone," said Freeman at the conference, which was sponsored by the NCI and the George Washington University (GWU) Medical Center.



Source: Surveillance, Epidemiology, and End Results Program/US National Center for Health Statistics

Recent reports indicate that mortality rates for black women with breast cancer are higher than those for white women with the disease. Researchers are trying to determine what factors may play a role in this disparity.

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