Vitamin D, Heart Dysfunction Tied in Thalassemia

BY FRAN LOWRY
Orlando Bureau

ATLANTA — Vitamin D deficiency was strongly associated with high cardiac iron and increased ventricular dysfunction in a retrospective review of 24 young thalassemia major patients.

A review of their medical records showed levels of vitamin D(25[OH]D), the predominant circulating form of vitamin D, were "markedly depressed" in 13 patients and borderline depressed in the remaining patients, said Dr. John C. Wood of Children's Hospital Los Angeles and Keck School of Medicine at the University of Southern California, Los Angeles. There were 11 girls and 13 boys; mean age was 15 years.

Vitamin D(25[OH]D) levels less than 20 ng/mL are considered deficient and D(25[OH]D) levels 20-30 ng/mL are borderline or insufficient, Dr. Wood said in a presentation at the annual meeting of the American Society of Hematology. In this study, the mean D(25[OH]D) was 17 ng/mL.

The vitamin D levels were then compared with cardiac R2*—a surrogate MRI measure of the amount of iron in the heart—and left ventricular ejection fraction (LVEF) from each patient's most recent cardiac MRI. As vitamin D levels decreased, cardiac R2* increased. Vitamin D(25[OH]D) levels below 13 ng/mL were associated with severe cardiac iron loading. LVEF also decreased as D25-OH decreased.

Vitamin D might be worsening the cardiac iron overload and dysfunction by modulating calcium signaling.

DR. WOOD

"In our MRI laboratory, an ejection fraction less than 56% is considered abnormal and indicates poor pump function. In these patients, there was a proportional association between vitamin D(25[OH]D) levels and cardiac function. The four patients with the lowest D(25[OH]D) had an LVEF between 50% and 54%," he said.

The population also was moderately iron overloaded, with mean ferritin levels of 2,089 ng/mL, liver iron 14 mg/g dry weight, transferrin saturation 84%, and cardiac R2* 65 Hz. The normal R2* should not exceed 50 Hz. "Vitamin D deficiency … is extremely common in thalassemia. Twenty-three of the 24 patients in our study had levels that are considered inadequate to ensure optimal calcium absorption and bone mineralization," he said in an interview. Low vitamin D is linked to decreased cardiac function, muscle weakness, glucose insensitivity, and refractory congestive heart failure.

Increased iron in the heart becomes evident in children with thalassemia major around the age of 9 years. Two-thirds of adults with thalassemia have cardiac iron deposition. Iron cardiomyopathy is the leading cause of death in thalassemia. "Our study describes an association between low vitamin D, high cardiac iron, and increased ventricular dysfunction. We cannot prove [cause and effect], but vitamin D might be worsening the cardiac iron overload and the cardiac dysfunction through its modulation of calcium signaling in these patients."

"Vitamin D deficiency is extremely common in thalassemia, and since osteoporosis is ubiquitous in this disease, vitamin D screening and replacement are probably indicated regardless of the heart findings," Dr. Wood said.

He added that low vitamin D produces secondary hyperparathyroidism, which exacerbates heart failure of any etiology. Because of this, thalassemia patients with ventricular dysfunction should have their vitamin D levels assessed, and replacement should be started if these levels are low.

The National Heart, Lung, and Blood Institute, the Centers for Disease Control and Prevention, and Novartis Pharma funded the study. Dr. Wood disclosed he receives research funding and honoraria from Novartis and Apotex, and is a consultant to Novartis. ■

Steps Taken to Avert Pending Shortage of Cardiac Surgeons

BY BRUCE JANCIN
Denver Bureau

SNOWMASS, COLO. — The pipeline of future cardiac surgeons is "essentially nonexistent," which will have serious consequences not only for the surgical specialty but for cardiologists and all others who provide care for patients with heart disease.

"When I began my cardiac surgical training, there were roughly 10 applicants per available position. Today there are basically more positions than applicants. So anyone who has reasonable qualifications will be accepted by a program somewhere," said Dr. Andrew S. Wechsler, professor of cardiothoracic surgery at Drexel University, Philadelphia.

Surveys indicate only one-quarter of practicing cardiac surgeons would advise medical students to enter the field.

DR. WECHSLER

Last year, there were only 97 applicants for the 130 U.S. training positions, and only 68 of whom were graduates of American medical schools. The quality of the applicants has dropped off, he said at a conference sponsored by the Society for Cardiovascular Angiography and Interventions.

The fall-off in the applicant pool began about 4 years ago. It's a trend of particular concern because of the projected increasing demand for cardiac surgical services as the population ages and the fact that one-half of practicing cardiac surgeons are above the age of 53 years. Many are contemplating retirement because of decreasing reimbursement, mounting malpractice insurance costs, and declining job satisfaction.

Reimbursement for cardiac surgery today is, in real dollars, about 30% of what it was 15 years ago. Cases have become more complex, with a huge increase in the number of reoperations. The average yearly cost of malpractice insurance for cardiac surgeons in Pennsylvania is $125,000. Surveys indicate only one-quarter of practicing cardiac surgeons would advise medical students to enter the field, Dr. Wechsler said at the conference, cosponsored by the American College of Cardiology.

Cardiac surgery is currently performed at more than 1,400 U.S. hospitals, many of which have small-volume programs. Dr. Wechsler predicted that one result of the looming shortage will be governmental pressure to reconsolidate cardiac surgical services to high-volume centers, with resultant closure of many smaller programs. Referring physicians are likely to find excellent-quality cardiac surgeons becoming less readily available.

Cardiac surgical educators have launched a number of initiatives to address the predicted shortage. Paid internships are being offered to medical students in an effort to capture their attention early in their education in the hope of steering them into this challenging field. New integrated training programs have been approved, including a 6-year program in cardiac surgery beginning right out of medical school. It is no longer required that trainees complete the chief resident year and take the board exam in general surgery before entering cardiac surgical training. And vascular surgery is now accepted as a pathway to cardiac surgical training, noted Dr. Wechsler. ■

Heart Failure Deemed Driving Force in Excess Mortality in RA

BY BRUCE JANCIN
Denver Bureau

SNOWMASS, COLO. — Heart failure is a major contributor to the excess mortality in patients with rheumatoid arthritis, Dr. Sherine E. Gabriel said at a symposium sponsored by the American College of Rheumatology.

Rheumatoid arthritis (RA) patients have twice the risk of developing heart failure (HF) compared with the general population, and its lethality is markedly greater, said Dr. Gabriel, the William J. and Charles H. Mayo Professor of Medicine and Epidemiology at the Mayo Clinic, Rochester, Minn.

Regular monitoring of erythrocyte sedimentation rate and inflammatory markers might help identify patients at risk of HF.

DR. GABRIEL

These are among the recent findings of the Rochester Epidemiology Project, an ongoing, primarily National Institutes of Health–funded longitudinal project drawing on the inpatient and outpatient medical records of the populace of Olmsted County, Minn. Dr. Gabriel presented highlights from published and not-yet-published studies from the project.

In 575 Rochester patients with no history of HF at the time of diagnosis with RA and 583 no-RA controls, the relative risk of new-onset HF during the subsequent 30 years was 1.9-fold greater in the RA group after adjustment in a multivariate analysis for age, gender, standard cardiovascular risk factors, and the presence of ischemic heart disease. In the subset of rheumatoid factor–positive RA patients, the relative risk climbed to 2.6 (Arthritis Rheum. 2005;52:412-20).

Another distinguishing feature of HF in RA patients is that it is far more likely to involve diastolic dysfunction with preserved left ventricular ejection fraction. Rochester patients with RA were an adjusted 2.6-fold more likely than were non-RA subjects to have a preserved ejection fraction at the time they developed HF. This is problematic because treatment options for isolated diastolic dysfunction are limited. Medications that have improved survival and quality of life in HF (ACE inhibitors, angiotensin receptor blockers, and β-blockers) have been studied almost exclusively in patients with left ventricular systolic dysfunction, and that's the HF population in which those drugs are approved.

The most likely explanation for the increased risk of HF in RA is the persistent inflammatory state that characterizes the rheumatic disease. Dr. Gabriel cited a study of 575 Rochester patients free of HF at the time of diagnosis with RA. During 15 years of follow-up, 172 patients had new-onset HF. The proportion with an elevated erythrocyte sedimentation rate of 40 mm/hour or greater was higher during the 6-month period before diagnosis of HF than in any other period during the 15 years (Ann. Rheum. Dis. 2007;66:76-80).

This suggests that regular monitoring of erythrocyte sedimentation rate and other inflammatory markers might help identify RA patients at increased near-term risk of developing HF, she noted. ■