Low Iron Is Biomarker, Treatment Target in HF

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STOCKHOLM – Iron deficiency in patients with heart failure is common, occurs independently of anemia, and is strongly associated with exercise intolerance and increased risk of death or need for heart transplantation.

Moreover, iron deficiency in heart failure is not merely an independent predictor of poor outcomes, it's also emerging as an attractive target for treatment, Dr. Piotr Ponikowski said at the congress.

"Iron deficiency is pretty new stuff for cardiologists," he observed in at a press conference. "Cardiologists should start to become more aware of the importance of iron deficiency in chronic heart failure patients and be able to evaluate iron status using a combination of simple, clinically applicable biomarkers of iron metabolism."

Dr. Ponikowski, president of the Heart Failure Association of the European Society of Cardiology, was senior author of a prospective observational study in which 546 patients with stable systolic heart failure were tested for iron deficiency.

Thirty-seven percent of subjects were found to be iron deficient based on either a serum ferritin level below 100 mcg/L, or 100-300 mcg/L with a transferrin saturation below 20%. One-third of the iron-deficient patients were nonanemic. Iron deficiency was significantly more common in women, in subjects with C-reactive protein or plasma N-terminal pro type B natriuretic peptide levels above the median values, and in those with New York Heart Association (NYHA) class III-IV heart failure, although it was also found in 31% of patients who were class I-II (Eur. Heart J. Aug. 2010; 31:1872-80).

The mean 2-year survival rate free of heart transplantation was 53% in iron-deficient patients, significantly worse than the 67% in non–iron-deficient patients. In a multivariate analysis, the adjusted risk of death or heart transplantation in nonanemic heart failure patients with iron deficiency was 60% greater than in subjects without iron deficiency, noted Dr. Ponikowski, professor of cardiology at Wroclaw (Poland) Medical University.

It's safe to treat iron deficiency in patients with symptomatic heart failure, but it's 'not in the guidelines yet.'

DR. PONIKOWSKI

He was also a coauthor of the first major treatment study, the Ferinject Assessment in Patients With Iron Deficiency and Chronic Heart Failure (FAIR-HF). In that double-blind, placebo-controlled, randomized trial, intravenous iron repletion of patients with heart failure resulted in significant improvement of all primary and secondary study end points, including exercise tolerance, self-reported patient global assessment scores, quality of life, and NYHA functional class (N. Engl. J. Med. 2009;361:2436-48). The improvement was apparent early, after two of the biweekly injections.

Asked whether it is now appropriate to prescribe iron therapy in iron-deficient patients with symptomatic heart failure, Dr. Ponikowski replied that he routinely screens symptomatic heart failure patients for iron deficiency and treats those who are deficient. "It's fairly safe and fairly straightforward. But we in the ESC [European Society of Cardiology] are very guideline-oriented people, and it's not in the guidelines yet," he added.

He recommended intravenous iron over oral formulations. The bioavailability of iron from oral intake is poor, only 3-4 mg per dose. He and his colleagues have estimated that the total amount of iron that needs to be replaced in iron-deficient heart failure patients is on average 800-1,200 mg. That would require close to a year of daily oral therapy, which would be poorly tolerated gastrointestinally.

Dr. Ponikowski has received lecture and consulting fees from Vifor Pharma, which sponsored the FAIR-HF trial, as well as from Amgen. ■