Heart failure (HF) is a leading cause of morbidity and mortality around the world. Despite recent progress in both pharmacological and non-pharmacological interventions, mortality among patients with HF remains very high. This is in part because HF is often accompanied by other ailments that can adversely affect patient outcome. One such ailment is anemia, which is common among patients with chronic HF (CHF) and is associated with poor outcomes.

Potential explanations of this association include adverse left ventricular (LV) remodeling effects, increased expression of neurohumoral and inflammatory cytokines, adverse cardiorenal effects and poor nutritional status. A better understanding of the association between anemia and outcome in patients with CHF would likely enable more accurate risk profiling and better selection of therapeutic options (eg, erythropoietin or iron therapy). Although there are many unanswered questions about anemia in CHF, of particular interest to us is the interaction between the prognostic impact of anemia and patient characteristics.

In this issue of the Journal, Yamauchi et al address the prognostic impact of anemia with reference to the clinical characteristics of CHF patients registered in the Chronic Heart Failure Analysis and Registry in the Tohoku District-2 (CHART-2) study, one of the largest prospective cohort studies in Japan. They show that 35% of CHF patients have anemia and, consistent with a previous report, the anemia was associated with an increased incidence of all-cause death and hospitalization for HF. Furthermore, subgroup analysis demonstrated that the prognostic impact of anemia varied in relation to LV ejection fraction (LVEF) and CHF etiology; that is, anemia was significantly associated with a worse outcome in CHF patients with preserved LVEF and those with hypertension (HT). In addition, there was a significant interaction...
between anemia and LVEF in CHF patients with ischemic heart disease. These results highlight the importance of taking clinical background into account when managing anemia in patients with CHF.

On the other hand, several earlier studies have reported that there is no interaction between LVEF and outcome related to anemia. The reason for the difference in the interaction of the prognostic impact of anemia and LVEF between the earlier studies and the present study by Yamauchi et al is unknown at present, but may be attributable to differences in the patients’ clinical characteristics, including regional differences in comorbidity prevalence among the study population. Patients with HF with preserved EF (HFpEF) reportedly have a higher number of non-cardiac comorbidities than patients with HF with reduced EF (HFrEF). Several studies that examined the causes of death in patients with HF suggested a higher proportion of non-cardiovascular deaths among patients with HFpEF than with HFrEF. In the study by Yamauchi et al, the incidence of non-cardiovascular death increased as Hb levels decreased. It would be interesting to compare the incidence of non-cardiovascular deaths among patients with HFpEF and HFrEF and the relationship to anemia in this study population.

Another important question that remains unanswered is whether correction of anemia leads to improved outcomes in patients with HFpEF or HT. A recent trial investigating the effect of darbepoetin alfa in patients with HFpEF failed to show improvement of clinical outcomes. In addition, although erythropoietin may be beneficial for some patients with HFpEF or HT, a recent small trial of epoetin alfa in older patients with HFpEF and mild anemia did not find significant beneficial effects on LV structure, functional capacity or quality of life. Iron replenishment using intravenous ferric carboxymaltose in patients with HFpEF and iron deficiency, with or without anemia, improved symptoms, functional capacity and quality of life, though these beneficial effects appear to be independent of anemia.

More research is thus needed into the therapeutic options for treating anemia in these patient populations.

References


