Imbalance of iron needs and supply in patients with acute and chronic heart failure

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Background: Iron deficiency (ID) is frequent in patients with chronic and acute heart failure (CHF, AHF) associated with morbidity and mortality. ID can be absolute, defined as depleted iron stores (also named true ID), or functional describing hypoferremia despite adequate iron stores as a result of inflammation-related reduced iron mobilization and restriction in mononuclear cells. Empty iron stores can also be found simultaneously to inflammation-related reduced iron mobilization (combined ID).

Purpose: We aimed to better characterize ID and iron homeostasis in HF patients applying different biomarkers and to evaluate the accuracy of current ID definition by the ESC to indicate actual tissue iron needs and supply.

Methods: We performed a retrospective cohort study including 277 AHF and 476 CHF patients treated between 02/2021–05/2022 at the Medical University of Innsbruck.

Results: AHF patients had higher iron needs and lower iron supply than CHF patients, reflected by increased soluble transferrin receptor (sTfR) and sTfR-Ferritin (sTfR-F) index, and lower ferritin, serum iron, transferrin saturation (TfS), hepcidin and reticulocyte hemoglobin (Ret-Hb). Only 28.0% of CHF and 81.4% of AHF patients with absolute ID as well as 10.5% of CHF and 50.0% of AHF patients with combined ID based on the current ESC definition presented with an elevated sTfR-F index (>2.0 without and >3.2 with inflammation) and/or reduced Ret-Hb (<28pg), being indicative for tissue iron needs. Suppressed hepcidin expression (<8.6ng/mL) as early marker of iron depletion was found in 80% of CHF and 91% of AHF patients with absolute ID and only in 19% of CHF and 32% of AHF patients with combined ID based on the current ESC definition.

When breaking down the ID definition into ferritin and TfS, in AHF an elevated sTfR-F index was found in patients with inflammation and associated with lower ferritin (<200 ng/mL), while a reduced Ret-Hb was primarily found in patients with inflammation, TfS <20% and ferritin <100 ng/mL. In CHF an elevated sTfR-F index and a reduced Ret-Hb were primarily present in patients with ferritin <30 ng/mL and TfS <20% as well as in patients with inflammation, TfS <20% and ferritin <100 ng/mL. (Figure 1) Specificity for defining true ID and reducing the upper limit of ferritin for defining true ID in the setting of inflammation (Figure 2).

Conclusion: A substantial proportion of patients with ID defined by the current ESC definition, had normal tissue iron supply with no increased tissue iron needs. In accordance with previous studies, results from our study suggest that the current ESC definition might overestimate true ID especially in CHF. A more accurate definition of ID may help to identify those patients with AHF and CHF who truly benefit from intravenous iron supplementation.