Iron Deficiency and Anemia in Heart Failure Patients, a Quality Improvement Project

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Abstract:

Background: Iron deficiency is an independent predictor of impaired functional capacity and decreased survival in patients with congestive heart failure (CHF). IV iron administration has been associated with improvement of functional capacity in CHF regardless of whether or not anemia is present. However, the frequency of IV iron utilization in iron-deficient CHF patients has not been well studied.

Methods: We conducted a retrospective analysis of consecutive patients admitted to a single tertiary medical center between May 2019 – May 2021 with the primary diagnosis of CHF exacerbation.

Results: The study cohort included 2,069 individual patients (44% females) who had 2,732 visits during the study period. Iron studies results with both ferritin and transferrin saturation were available in 579 visits (21.2%). Of these, in 250 patient visits ferritin was <100 and in 84 patient visits ferritin level was 100-300 with transferrin saturation < 20%. Overall, indications for iron replacement were met during 334 admissions, however the IV therapy was prescribed in only 82 (25.1%) patient visits.

Conclusion: Despite known benefits of IV iron replacement in CHF patients, only a minority of in-patients admitted for CHF exacerbation are being evaluated for iron deficiency and/or receive indicated IV iron replacement therapy. Interventions to increase the awareness on this subject are warranted.

Introduction:

Iron deficiency is an independent predictor of impaired functional capacity and decreased survival in patients with congestive heart failure (CHF). IV iron administration has been associated with improvement of functional capacity in CHF regardless of whether or not anemia is present. [i] However, the frequency of IV iron utilization in iron-deficient CHF patients has not been well studied. Almost 50% of Congestive Heart Failure (CHF) patients suffer from iron deficiency. Intravenous Iron (IV) utilization in iron deficient CHF patients has been recently studied and seen as an improvement in symptoms and functional capacity. Many studies have been done comparing the results of oral iron, but there is a conclusive result of unsuccessfulness. Oral iron provides little to no improvement of symptoms or functional capacity. [ii] The ACCESS-HF suggested that all patients admitted for CHF exacerbated should be screened and treated appropriately if iron deficiency is identified. Importantly, multiple quality improvement projects have demonstrated a significant time gap between the clinical trials and the implementation of their protocols into everyday clinical practice. We conducted a retrospective analysis of single tertiary medical center to characterize real-life recognition of iron-deficiency and utilization of intravenous iron. We created the following objectives to achieve this goal: first, to identify a retrospective cohort of patients with the primary medical problem being sudden worsening of heart failure among thousands of admitted to a tertiary medical center. We selected a recent timeframe 2019 – 2021, so the study could be relevant to contemporary clinical practice. The second objective was to identify a subgroup of patients who were tested for iron deficiency during the index hospitalization from the overall HF cohort. Importantly, because iron deficiency was shown to be a negative prognostic marker independently of the presence of anemia, we didn't use hemoglobin level as an identifier at this step. [iii] Further,

based on the prior experience with quality improvement projects in CHF, we expected less than 50% of patients in this subgroup. The third objective was to identify patients that met the definition of iron deficiency among all CHF patients tested. The fourth step was to identify the proportion of Iron deficient patients which had received appropriate therapy with IV iron during the index hospitalization. Teleologically, because the indications for iron replacement in CHF are different from these used in general medical practice for iron deficiency anemia, we expected that the minority of the patient would receive guideline-directed therapy, instead of i.e., oral iron preparations or no therapy at all. The fifth objective was to identify the potential barriers towards better implementation of Iron protocols in heart failure.

Methods:

We selected a cohort of consecutive patients admitted with the primary diagnosis of Heart Failure exacerbation (ICD code I-50) to Albany Medical Center (AMC). AMC is a 700+ beds tertiary medical facility and has been recognized for exceptional CHF care with "Gold +" award from the American Heart Association, and a prestigious The Advanced Heart Failure Certificate by the Joint commission since 2010. We used well-established parameters of absolute and functional iron deficiency to identify study participants from a cohort of patients admitted between May 2019 and May 2021. Specifically, absolute iron deficiency was defined by ferritin level < 100 ng/ml, functional by a combination of transferrin saturation < 20% and ferritin level between 100 and 300 ng/ml. [iv] We extracted the unique medical record number, discharge date, ferritin level, admission Hgb, and transferrin saturation values (% iron saturation) from electronic medical records.

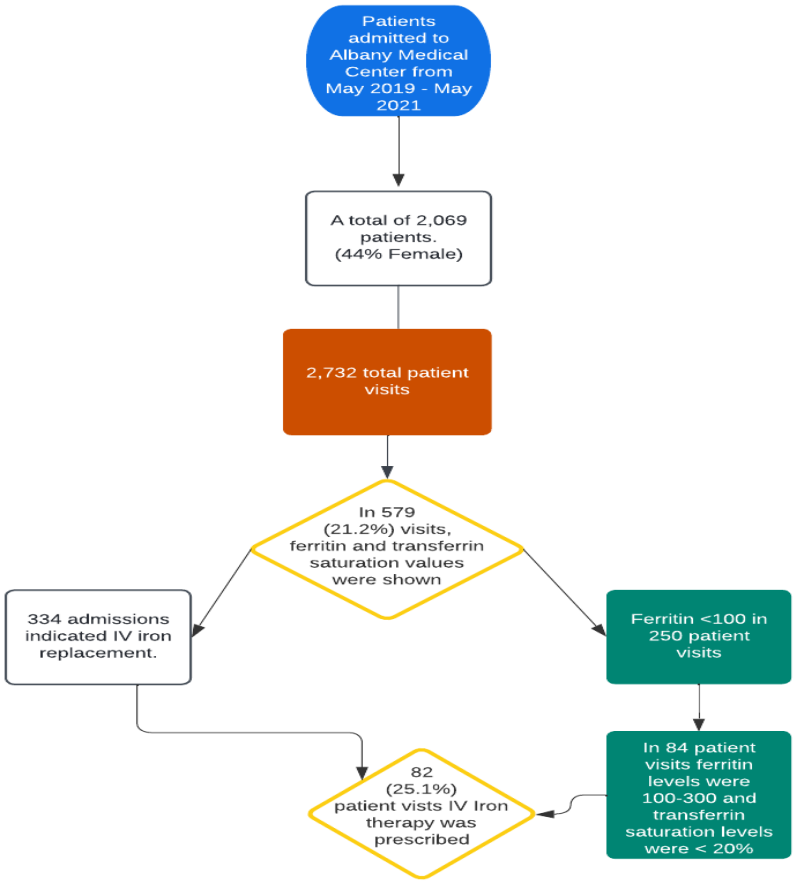
Following the extraction, patient identifiers were removed according to the Health Insurance Portability and Accountability Act and AMC Institutional Review Board Recommendations The statistics was calculated in Excel software (Microsoft Corporation, 2018), and the final results are expressed as a percentage.

Purpose:

Our hypothesis was that physicians have poor awareness to the recent scientific studies and updates regarding iron deficiency, a recently emerged modifiable CHF prognostic marker. To test this hypothesis, we conducted a quality improvement project, with the aim to evaluate the recognition and management of iron deficiency in patients with decompensated CHF admitted to a tertiary care facility.

Results:

The study cohort included 2,069 individual patients (44% females) who had 2,732 visits during the study period. Iron studies results with both ferritin and transferrin saturation were available in 579 visits (21.2%). Of these, in 250 patient visits ferritin was <100 and in 84 patient visits ferritin level was 100-300 with transferrin saturation < 20%. Overall, indications for iron replacement were met during 334 admissions, however the IV therapy was prescribed in only 82 (25.1%) patient visits.



Discussion:

Despite known benefits of IV iron replacement in CHF patients, only a minority of in-patients admitted for CHF exacerbation are being evaluated for iron deficiency and/or receive indicated IV iron replacement therapy. Obviously, these findings from a CHF tertiary center of excellence, require further systematic and thorough analysis, due to the

known delay that exists between clinical trial results and their implementation as a standard of care. For example, famous studies have previously demonstrated that a significant proportion of patients hospitalized with CHF hadn't lost weight, leading to a transformative change.

An estimated 6.5 million adults are currently living with CHF in the United States. CHF is a dreadful diagnosis, with only 57% and 35% of people diagnosed with this condition will survive for 5 and 10 years (Jones Nicholas, 2019 Eur J Heart Fail). Equally important, shortness of breath, edema, exercise intolerance and other manifestations of this disease severely and drastically impair the quality of everyday life for a lot of people. Expectedly, attempts to alleviate CHF symptoms lead to high number of hospital admission (809,000 in 2016). Up to a quarter of such patients have been readmitted within 30 days of discharge, reflecting not only the malignant course of the disease, but the lack of adherence to current guideline recommendations, social and community support, and or appropriate medical follow up. It was shown recently, addressing several comorbidities of CHF, namely iron deficiency, sleep disorders could be highly beneficial. [v]

From a biochemical standpoint, iron's ability to bind oxygen makes it an instrumental component for oxygen carrying by blood and, also for an aerobic energy generation through the cytochrome system. Having a deficit in one of these oxygen-related pathways creates a supply and demand mismatch, leading to a compensatory hyperfunction of the heart to maintain steady oxygen flow to the organs. This seemingly appropriate compensatory response to increased metabolic demands leads to decompensation in CHF patients with poor functional reserve. In addition, low iron level

could directly impede energy production in the skeletal and cardiac muscles, switching toward anaerobic glycolysis, and leading to decreased contraction strength. Due to the role Iron plays in human's physiology, it seems biologically plausible, that the deficiency of this crucial element in CHF was found to be associated with worse survival (Okonko et al., JACC 2011), poor exercise capacity (Anand, I. S., & Gupta, P. 2018) or worsening of CHF symptoms.

Therapy with IV Iron in Heart Failure Reduced Ejection Fraction (HFrEF) reduces symptoms, improves exercise capacity, quality of life and CHF-related admissions. Consequently, both current American and European HF guidelines recognize Iron deficiency as an attractive therapeutic target. Similarly, both guidelines emphasize that oral iron products (because of their unpredictable absorption due to ie. intestinal edema) should not be used in CHF patients. Despite these similarities, the documents endorse different pathways for diagnosing this condition. The European HF guidelines provide more discrete recommendations, including initial, *periodic* as well as predischarge assessment of iron status. However, no specific description is provided on which periods Iron stores should be reevaluated. Contrary, the American guidelines endorses iron studies *only* at the time of the initial evaluation. At the same time, this should be emphasized, both the American and European guidelines endorse only IV Iron with the goal to reduce HF symptoms and risk of CHF-related hospitalizations, and to improve exercise capacity and quality of life.

We found the following potential explanations for the suboptimal adherence to the guideline-recommended treatment of CHF patients with Iron deficiency: 1. It is missing from the ACC/HFSA guidelines about when to test. While the guidelines describe the benefits of treatment, it fails to describe who and when to treat. 2. Unawareness of the physicians on the significance of iron deficiency in CHF patients with or without anemia. It is common that even mild-to-moderate anemia is perceived as an insignificant finding deserving only an outpatient evaluation in a patient improving with diuretics. 3. The recommendations for iron replacement in CHF patients are more inclusive, then for the general population. This could lead to a wrong diagnosis that the patient is not iron deficient. 4. Health care providers mistakenly assume that oral iron therapy is sufficient in CHF patients. Oral iron products are mistakenly assumed to be a less-invasive, more convenient and chipper option. 5. The unavailability of Ferric Carboxymaltose, the product which is currently endorsed by European HF society. It should be noted that the maximal single dose of Iron Carboximaltose (1 g) conveniently corresponds well with an average iron deficiency observed in CHF patients. A more commonly used Iron Sulfate would require 10 days to replenish the same amount of iron.

We would like to recommend the following interventions based on our findings: 1. The creation of a local, institutional guide to improve care of Iron Deficient CHF patients, while the current ACC/HFSA guidelines remain outdated as per 2022. Several studies have validated such local guidelines effectiveness to improve the quality of care. In addition, the appropriate administration of IV Iron would reduce the 30 day readmission rate, counterintuitively making it cost-effective. 2. It is vitally necessary to educate hospitalists

and general cardiologists about Iron deficiency in CHF patients. This intervention should focus on the importance of the routine evaluation of Iron Status, the awareness of the different diagnostic standards and the benefits of IV therapy in CHF patients. 3. We believe that ferric carboxymaltose should be available for use for all CHF patients with iron deficiency, until head-to-head clinical studies prov it's therapeutic equivalence with other iron products.

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[i] Walther, C. P., Triozzi, J. L., & Deswal, A. (2020). Iron deficiency and iron therapy in heart failure and chronic kidney disease. Current Opinion in Nephrology & Hypertension, Publish Ahead of Print. https://doi.org/10.1097/mnh.0000000000000630

[ii] Anand, I. S., & Gupta, P. (2018). Anemia and Iron Deficiency in Heart Failure. Circulation, 138(1), 80–98. https://doi.org/10.1161/circulationaha.118.030099

[iii] Nairz, M., Theurl, I., Wolf, D., & Weiss, G. (2016). Iron deficiency or anemia of inflammation? Wiener Medizinische Wochenschrift, 166(13-14), 411–423. https://doi.org/10.1007/s10354-016-0505-7

In-text citation: (Nairz et al., 2016)

[iv] Docherty, Kieran F., et al. "Iron Deficiency in Heart Failure and Effect of Dapagliflozin: Findings from DAPA-HF." Circulation, vol. 146, no. 13, 27 Sept. 2022, pp. 980–994, https://doi.org/10.1161/circulationaha.122.060511. Accessed 13 Mar. 2023.

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