SURVIVAL DIFFERENCES IN HEART FAILURE PATIENTS WITH AND WITHOUT IRON DEFICIENCY OR ANEMIA AND BY IRON TREATMENT

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OBJECTIVES

• Iron deficiency/anemia (ID/A) are frequent comorbidities in heart failure (HF) and associated with increased morbidity.1-3
• Treatment of ID/A includes oral and intravenous iron, but little is known about the effect of different treatments on mortality.
• The aim of this study was to determine survival differences between HF patients without ID/A and with untreated ID/A and differences between various iron treatments in a real-world setting, stratified by New York Heart Association (NYHA) classes.

METHODS

• A retrospective, matched cohort analysis was conducted from the statutory health insurance (SHI) perspective.
• Therefore, data from the InGef research database (Institut für angewandte Gesundheitsforschung Berlin) containing German claims data of over 4 million covered lives were used.
• HF patients within this database were identified using the International Statistical Classification of Diseases and Related Health Problems, 10th revision, German Modification (ICD-10-GM) Code I50.- in the inpatient setting (main or secondary diagnoses) or outpatient setting (verified diagnoses) in 2013.
• These patients were stratified by ID/A using the ICD-10-GM Codes D50, D50.0, D50.8, D50.9, or E61.1 or using the Anatomical Therapeutic Chemical Code B03A for prescribed iron medication.
• Patients with the need of dialysis in the baseline period were excluded before matching, as dialysis-dependent ID/A was not the subject of this study.
• HF patients without ID/A and HF patients with untreated incident ID/A were matched 1:1. Incident ID/A was determined applying a 1-year diagnosis-free period before the ID/A diagnosis in 2013.
• HF patients with untreated ID/A, HF patients with ID/A starting oral iron treatment, and HF patients with ID/A starting intravenous iron treatment were matched 1:1:1.
• An exact, direct matching approach on age/age group, gender, and NYHA class was applied. Additionally, baseline healthcare costs were matched using an optimization algorithm that minimized the cost difference over all matched pairs.
• All-cause mortality was analyzed in a 1-year time frame and tested with the McNemar test.
• Survival was analyzed in a 1-year time frame using Kaplan-Meier curves and logrank tests.
• The data analysis was performed in cooperation between Xcenda GmbH and Elsevier Health Analytics.

RESULTS

Study Cohorts
• In total, n=3,048 HF patients with untreated incident ID/A were matched to HF patients without ID/A (1:1 matching).
• The matching of HF patients with ID/A without iron treatment, with oral iron treatment, or with intravenous iron treatment resulted in n=352 triplets (1:1:1 matching).

Baseline Characteristics – 1:1 Matching
• HF patients without ID/A and HF patients with untreated incident ID/A were on average 79.9 years old (±10.1 years) and 58.1% were female.
• The majority of patients in both cohorts (44.6%) were classified as NYHA n/a due to unspecified ICD-10-GM Codes, while 2.9% belonged to NYHA 1, 12.2% to NYHA 2, 20.1% to NYHA 3, and another 20.1% to NYHA 4.
• The annual baseline healthcare costs averaged €24,574.56 (±€32,832.12) in HF patients without ID/A and €25,858.74 (±€39,819.91) in HF patients with untreated incident ID/A.
• The standardized differences ranging from 0 to 3.5 showed that the matching parameters were balanced between the cohorts after matching.

Baseline Characteristics – 1:1:1 Matching
• HF patients with untreated ID/A were on average 79.3 years old (±8.7 years), HF patients with ID/A starting oral iron treatment 79.4 years old (±8.6 years), and HF patients with ID/A starting intravenous iron treatment 79.3 years old (±8.5 years), due to matching on age groups.
• Among all three matched cohorts, 58.2% were female.
• The majority of patients in all three cohorts (61.1%) was classified as NYHA n/a, 1.4% as NYHA 1, 12.2% as NYHA 2, 16.8% as NYHA 3, and 8.5% as NYHA 4.
• The mean annual baseline healthcare costs reached €20,581.20 (±€34,734.89) in HF patients with untreated ID/A, €19,124.46 (±€23,364.10) in HF patients with ID/A starting oral iron treatment, and €19,252.00 (±€23,693.26) in HF patients with ID/A starting intravenous iron treatment.
• The standardized differences ranging from 0 to 4.9 showed that the matching parameters were balanced between the three cohorts after matching.

Survival – 1:1 Matching
• In a 1-year time frame, 33.1% of the HF patients with untreated incident ID/A died, as opposed to 24.1% of HF patients without ID/A (P<0.01).

• The all-cause mortality increased with HF severity indicated by NYHA classes but was always higher among HF patients with untreated incident ID/A than among HF patients without ID/A (**Figure 1**).
• The time-to-death analysis revealed that HF patients with untreated incident ID/A had a significantly lower 1-year survival probability than patients without ID/A (P<0.01) as displayed in **Figure 2**.
• This was observed for all NYHA classes except for NYHA class 1 where the same trend did not reach statistical significance (P=0.74).

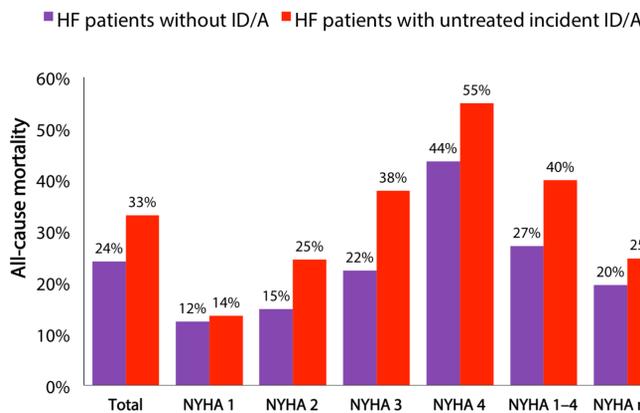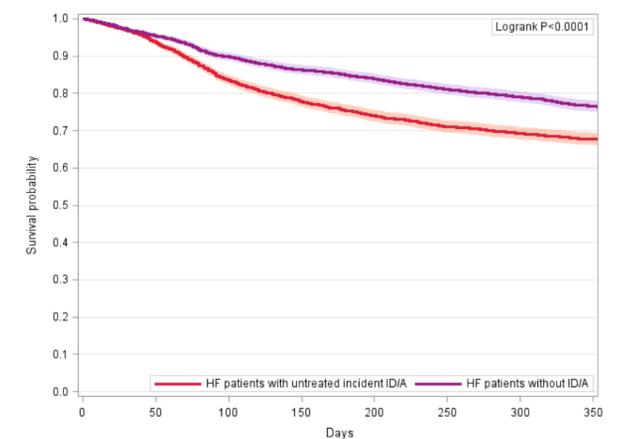*Figure 1. All-cause mortality rates in the 1:1 matched cohorts*

■ HF patients without ID/A   ■ HF patients with untreated incident ID/A

Figure 2. Kaplan-Meier curves comparing the 1:1 matched cohorts

Survival – 1:1:1 Matching
• In total, 18.5% of the HF patients with ID/A starting intravenous iron treatment died in a 1-year time frame, as opposed to 22.4% of HF patients with ID/A starting oral iron treatment and 23.6% of HF patients with untreated ID/A (P>0.05 for all comparisons).
• Survival was not analyzed separately for NYHA class 1, as patient counts were too low.
• Looking at the time-to-death analysis, only NYHA 3 patients starting oral iron treatment showed a significantly higher survival probability than patients without iron treatment (P=0.02) as displayed in **Figure 3**.
• Comparing HF patients with ID/A starting intravenous iron treatment to those without iron treatment revealed significant differences in favor of intravenous iron treatment for NYHA classes 2 (P=0.01), 3 (P=0.01) and pooled 1-4 (P<0.01), as shown in **Figure 4**.

Figure 3. Kaplan-Meier curves comparing the 1:1:1 matched cohorts – No iron treatment vs oral iron treatment
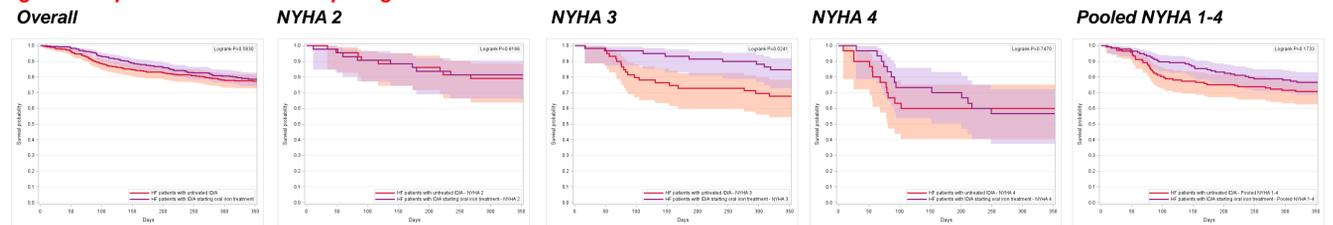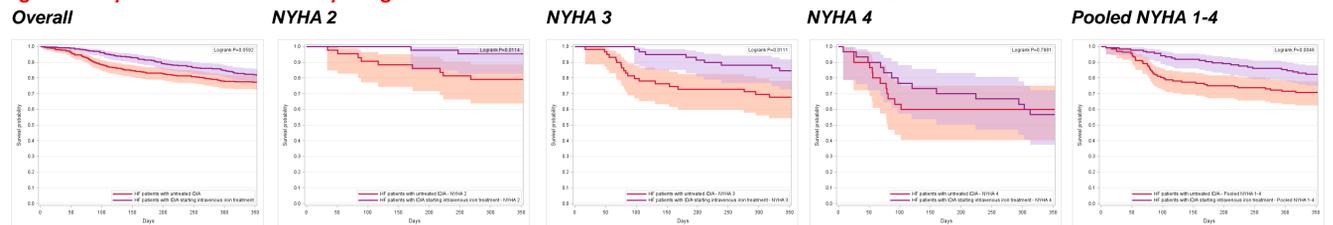

Figure 4. Kaplan-Meier curves comparing the 1:1:1 matched cohorts – No iron treatment vs intravenous iron treatment

• Direct comparison of oral iron treatment and intravenous iron treatment favored intravenous iron treatment in NYHA 2 patients (P=0.02) and revealed the same trend for pooled NYHA 1–4 patients (P=0.13), as displayed in **Figure 5**.

Figure 5. Kaplan-Meier curves comparing the 1:1:1 matched cohorts – Oral iron treatment vs intravenous iron treatment
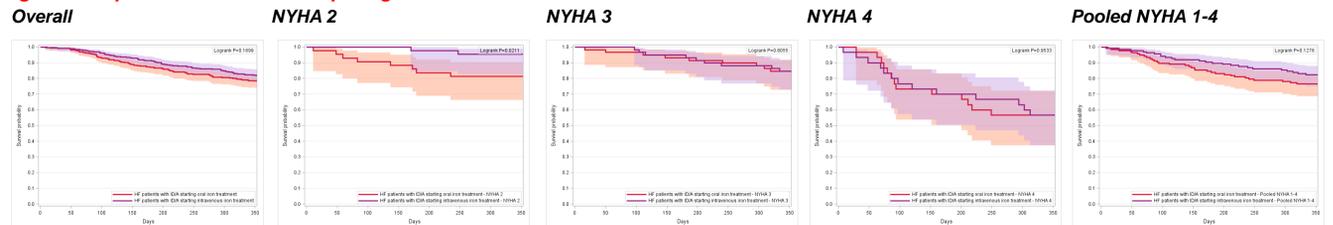
CONCLUSIONS

• This matched cohort study using real-world data from the SHI in Germany revealed that HF patients with comorbid ID/A had a lower 1-year survival probability than HF patients without ID/A, irrespective of NYHA class.
• Similar implications are found in the literature which highlights the need to prevent or treat ID/A among HF patients.1,2,4
• Additionally, the study showed that iron treatment is associated with an improved survival probability.
• This trend was particularly evident in HF patients with ID/A starting intravenous iron treatment. They had a significantly higher 1-year survival probability than untreated patients in most NYHA classes.
• Intravenous iron treatment was also associated with survival advantages when compared to oral iron treatment, especially among NYHA class 2 patients.

LIMITATIONS

• In general, claims data analyses are subject to limitations as they are primarily collected for accounting purposes, and therefore clinical parameters are not covered.

REFERENCES

1. Jankowska EA, Rozentryt P, Witkowska A, et al. Iron deficiency: an ominous sign in patients with systolic chronic heart failure. *Eur Heart J*. 2010;31(15):1872-1880.
2. Ezekowitz JA, McAlister FA, Armstrong PW. Anemia is common in heart failure and is associated with poor outcomes: insights from a cohort of 12 065 patients with new-onset heart failure. *Circulation*. 2003;107(2):223-225.
3. Comin-Colet J, Enjuanes C, Gonzalez G, et al. Iron deficiency is a key determinant of health-related quality of life in patients with chronic heart failure regardless of anemia status. *Eur J Heart Fail*. 2013;15(10):1164-1172.
4. Groenveld HF, Januzzi JL, Damman K, et al. Anemia and mortality in heart failure patients: a systematic review and meta-analysis. *J Am Coll Cardiol*. 2008;52(10):818-827.