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THE IMPORTANCE OF HEMATOLOGICAL PARAMETERS IN HEART FAILURE PROGNOSIS - EVIDENCE FROM THE REFERENCE STUDY

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BACKGROUND: In patients with heart failure (HF), anemia and iron deficiency are predictors of poor long-term outcome.

OBJECTIVE: The purpose of this study was to examine the association of anemia, iron deficiency, and related hematological parameters with early (defined as the period of 90 days post-discharge) rehospitalization due to HF and all-cause mortality, and long-term all-cause mortality in HF patients.

METHODS: Anemia, iron deficiency, red cell distribution width (RDW) and erythropoietin (EPO) were assessed in patients hospitalized with acute decompensated heart failure in class III or IV of New York Heart Association (NYHA) to an Internal Medicine ward. Comparison between patients with and without each of the events was performed for all variables using t test or Wilcoxon Rank test as applicable. Categorical variables were summarized by relative and absolute frequencies, and compared using chi-squared test or Fisher's Exact test as applicable. Univariate Cox proportional hazard model was used to assess the relationship between variables and outcomes.

RESULTS

N=65 HF patients
Mean age: 79.2 (SD 10.8)

Median follow-up : 13.7 months
[Q1: 6.7 to Q3: 18.9]

Table 1 – General baseline characteristics

Characteristics	Patients (n=65)
Age, mean (SD)	79.2 ± 10.8
Female Gender, n (%)	37 (56.9)
Hypertension, n (%)	58 (89.2)
Type 2 Diabetes, n (%)	25 (38.5)
Dyslipidemia, n (%)	41 (63.1)
Obesity, n (%)	17 (26.2)
Atrial Fibrillation, n (%)	28 (43.1)
Family History of CVD, n (%)	31 (47.7)
Tabagism, n (%)	21 (32.3)
Chronic Kidney Disease, n (%)	34 (52.3)
GFR (Baseline), median	57.8 (43.8 - 82.2)
GFR (Admission), median	47.9 (33.2 - 68.1)
Previous Acute Myocardial Infarction, n (%)	27 (41.5)
Hypertensive Cardiomyopathy, n (%)	44 (67.7)
Ischemic Cardiomyopathy, n (%)	22 (33.8)
Valvular Cardiomyopathy, n (%)	56 (86.2)
LVEF, mean (SD)	50.38 ± 19.07
NYHA class III, n (%)	43 (66.2)
ACE Inhibitor, n (%)	43 (66.2)
Beta Blocker, n (%)	38 (58.5)
Mineralocorticoid Receptor Antagonists, n (%)	19 (29.2)
Angiotensin II Receptor Blocker, n (%)	11 (16.9)
Loop Diuretic, n (%)	54 (83.1)
Digoxin, n (%)	8 (12.3)

Values are median (IQR), n (%), or mean±SD. IQR: interquartile range and minimum/maximum, SD: standard deviation, CVD: cardiovascular disease, GFR: glomerular filtration rate, ACE: Angiotensin-Converting-Enzyme.

Table 2 – Hematological parameters baseline characteristics

Characteristics	Patients (n=65)
Hemoglobin, mean (SD)	11.7 ± 1.9
Red Blood Cell Distribution Width, median	15.0 (13.8 - 16.2)
Transferrin Saturation, median	14.0 (10 - 21)
Total Iron-Binding Capacity, mean (SD)	281.5 ± 76.1
Serum Iron, median	40.1 (27.6 - 60.1)
Serum Ferritin, median	149.1 (52.3 - 350.9)
Iron Deficiency, n (%)	30 (46.2)
Anemia, n (%)	38 (58.5)
Anemia with Iron Deficiency, n (%)	17 (26.2)
Absolute Iron Deficiency, n (%)	20 (30.1)
Functional Iron Deficiency, n (%)	10 (15.4)
Anemia without Iron Deficiency, n (%)	15 (23.0)
Iron Deficiency without Anemia, n (%)	13 (20.0)
Absolute Iron Deficiency without Anemia, n (%)	6 (9.2)
Functional Iron Deficiency without Anemia, n (%)	7 (10.8)

Values are median (IQR), n (%), or mean±SD. IQR: interquartile range and minimum/maximum, SD: standard deviation.

Risk for early rehospitalization

RDW — [HR: 1.35, 95% CI: 1.16-1.5, P<0.05]

Anemia — [HR 3.81; 95% CI 1.29-11.28, P<0.05]

Anemia with iron deficiency — [HR 3.50; 95% CI 1.30-9.38, P<0.05]

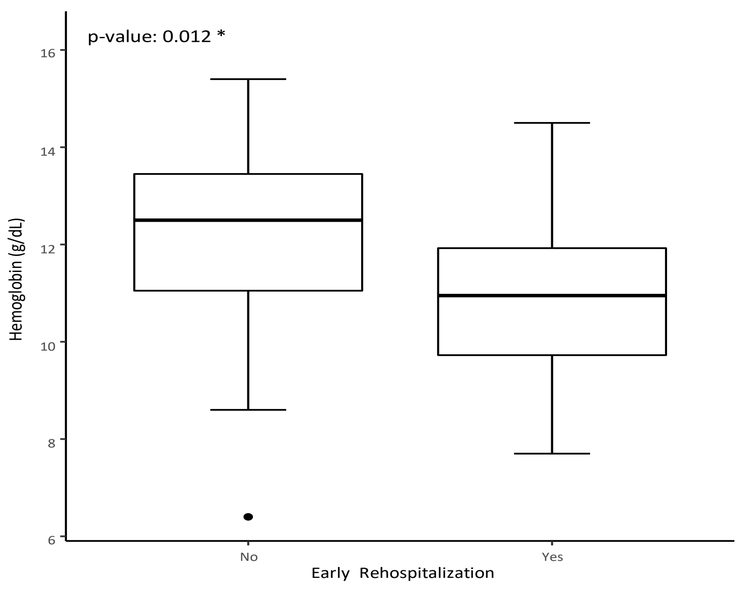
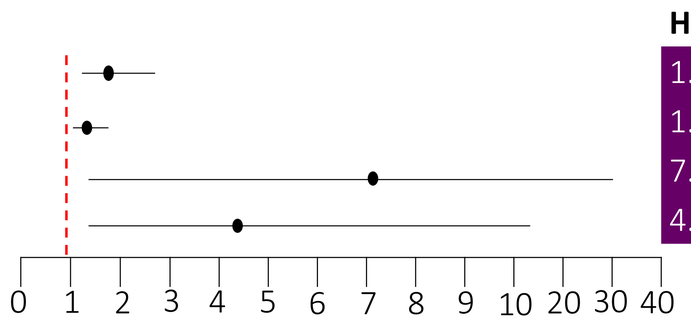


Figure 1- Baseline comparison of subjects by early rehospitalization status: Anemia

Increased risk for early mortality

Forest Plot of Hazard Ratios by Patient Subgroups

Characteristic	HR	95% CI	P value
RDW	1.83	1.29-2.59	<0.05
EPO	1.38	1.04-1.82	**<0.05**
Absolute Iron Deficiency	7.22	1.50-34.81	**<0.05**
Anemia with iron deficiency	4.48	1.26-15.88	**<0.05**



HR, Hazard ratio.

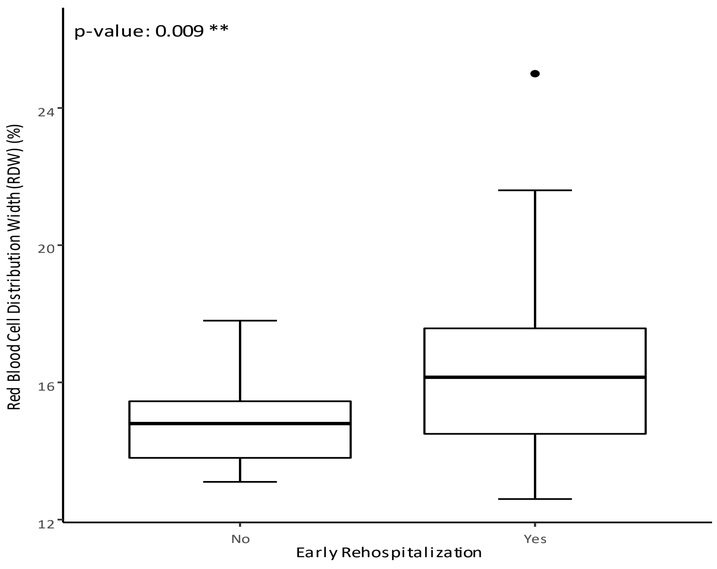


Figure 2 - Baseline comparison of subjects by early rehospitalization status: RDW

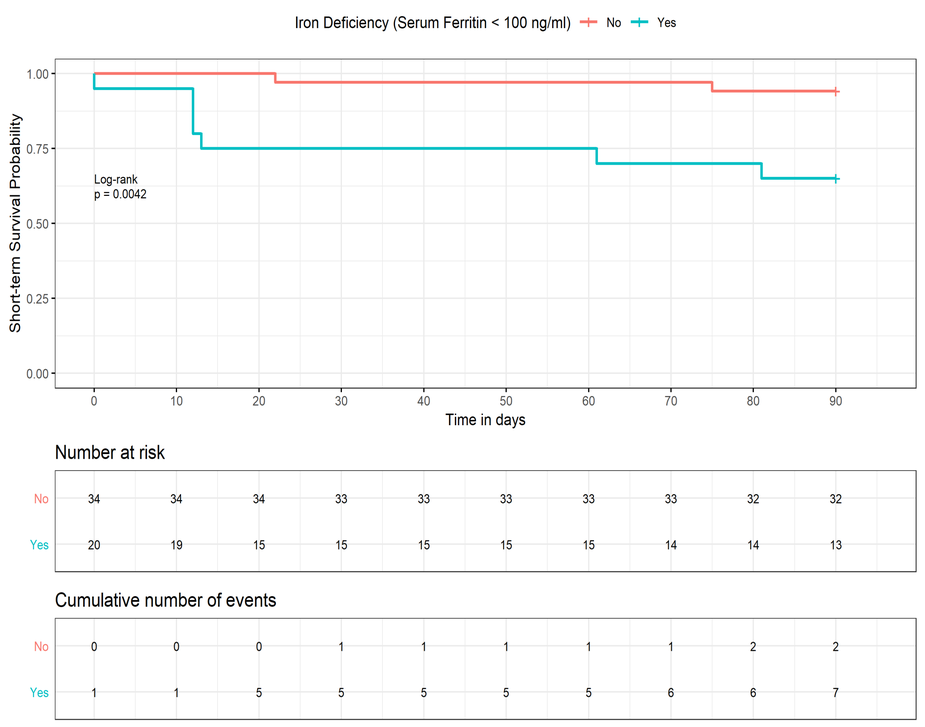
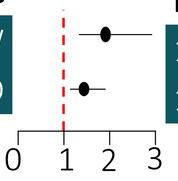


Figure 3 - Short-term mortality - Kaplan Meier: Serum ferritin <100 ng/mL

Increased risk for long-term mortality

Forest Plot of Hazard Ratios by Patient Subgroups

Characteristic	HR	95% CI	P value
RDW	1.31	1.12-1.54	<0.05
EPO	1.29	1.11-1.9	**<0.05**



HR, Hazard ratio.

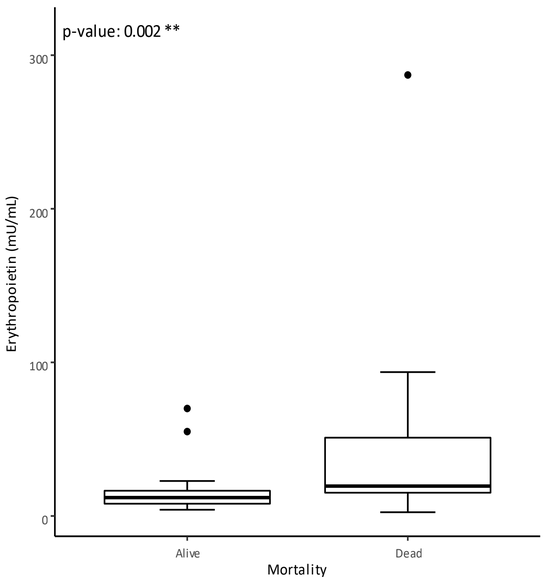


Figure 4 - Baseline comparison of subjects by long-term mortality status: EPO

CONCLUSION:

- Anemia, iron deficiency, RDW and EPO were associated with early rehospitalization, early mortality, and long-term mortality.
- Our findings may provide insight into HF prognosis and may raise the interest in some neglected hematological parameters.
- The recognition and treatment of risk factors that influence HF outcome, beyond HF specific therapy, may further contribute to ameliorate HF prognosis.