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PREDICTIVE VALUE OF SERUM IRON ON HEART FAILURE WITH REDUCED EJECTION FRACTION (HFREF) IN PATIENTS WITH ACUTE ST-SEGMENT ELEVATION MYOCARDIAL INFARCTION

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Abstract

Background: Heart failure with reduced ejection fraction (HFrEF) post-acute ST-segment elevation myocardial infarction (STEMI) significantly impacts morbidity and mortality. Identifying predictive biomarkers for HFrEF can aid in early intervention and improve outcomes.

Methods: This prospective cohort study involved 50 patients post-STEMI, analyzing the predictive value of baseline serum iron levels for HFrEF development over six months. Statistical analyses included logistic regression to adjust for potential confounders.

Results: The incidence of HFrEF at six months was 40%. Patients who developed HFrEF had significantly lower baseline serum iron levels compared to those who did not (58.4 µg/dL vs. 70.1 µg/dL, P=0.033). Multivariate analysis revealed that each 10 µg/dL decrease in serum iron was associated with a 25% increase in the odds of developing HFrEF (aOR 1.25, 95% CI 1.07-1.45, P=0.005). The sensitivity and specificity of serum iron levels in predicting HFrEF were 60% and 66.7%, respectively.

Conclusion: Serum iron levels at admission post-STEMI are a significant predictor of HFrEF development within six months. These findings advocate for the inclusion of serum iron level assessment in the post-STEMI evaluation process, highlighting the potential for early therapeutic interventions.

Keywords: Serum iron, ST-segment elevation myocardial infarction, Heart failure with reduced ejection fraction, Predictive biomarker, Cardiovascular disease.

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INTRODUCTION

Heart failure with reduced ejection fraction (HFrEF), a principal subtype of heart failure, is characterized by a left ventricular ejection fraction (LVEF) of 40% or less. It signifies a complex clinical syndrome that results from structural or functional disorders of the heart, leading to a failure in ventricular ejection of blood during systole [1]. Acute ST-segment elevation myocardial infarction (STEMI) is a significant predictor of HFrEF, highlighting a critical area of interest in cardiovascular research [2]. The pathophysiological sequelae of STEMI, involving ischemic injury and myocardial cell death, can precipitate or exacerbate heart failure by impairing left ventricular function [3]. Consequently, identifying predictive markers for the development of HFrEF following STEMI is vital for early intervention and improving patient outcomes.

Serum iron is an essential trace element that plays a pivotal role in various physiological processes, including oxygen transport, DNA synthesis, and cellular respiration. Recent evidence suggests that iron metabolism may be intricately linked with cardiovascular health, influencing the development and progression of heart failure [4]. Iron deficiency, irrespective of anemia status, has been recognized as a common comorbidity in heart failure, associated with worsened functional capacity, quality of life, and prognosis [5]. However, the predictive value of serum iron levels on the development of HFrEF post-STEMI remains an area of emerging interest and research.

Several mechanisms have been proposed to explain the relationship between serum iron and heart failure. Iron deficiency can impair mitochondrial energy production and muscle function, which are crucial in maintaining cardiac output and preventing heart failure progression [6]. Additionally, oxidative stress associated with low serum iron levels may further exacerbate myocardial injury following STEMI, leading to a heightened risk of developing HFrEF [7]. On the contrary, elevated serum iron levels have been linked to the generation of reactive oxygen species, contributing to oxidative damage and fibrosis in the myocardium, potentially accelerating heart failure progression [8].

This study aims to explore the predictive value of serum iron levels on the development of HFrEF in patients with acute ST-segment elevation myocardial infarction. By synthesizing current evidence and understanding the complex interactions between iron metabolism and heart failure pathophysiology, this review seeks to illuminate potential pathways through which serum iron may influence the progression to HFrEF post-STEMI, thereby offering insights into novel diagnostic and therapeutic strategies.

Aims and Objectives

The primary aim of this study was to investigate the predictive value of serum iron levels on the development of heart failure with reduced ejection fraction (HFrEF) in patients who had experienced an acute ST-segment elevation myocardial infarction (STEMI). Specifically, the study sought to determine whether initial serum iron levels measured upon hospital admission could serve as a reliable predictor for the onset of HFrEF within a six-month period post-STEMI. The objectives included: 1) to quantify serum iron levels in patients immediately

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after experiencing STEMI; 2) to monitor the incidence of HFrEF development in these patients over a six-month duration; and 3) to analyze the correlation between initial serum iron levels and the subsequent occurrence of HFrEF, thereby assessing the potential of serum iron as a prognostic marker for heart failure in this population.

MATERIALS AND METHODS

The study was conducted as a prospective cohort analysis over a six-month period, involving patients who were admitted to the hospital with a diagnosis of acute STEMI. The inclusion criteria for participation in the study were adults aged 18 years and above, who had been diagnosed with STEMI by electrocardiogram (ECG) and confirmed through biomarkers indicative of myocardial necrosis. Exclusion criteria included patients with a history of chronic heart failure, those who had received an iron supplementation or transfusion in the three months preceding the study, and individuals with conditions affecting iron metabolism such as hemochromatosis or chronic kidney disease.

A total sample size of 50 patients was determined based on power analysis calculations to ensure adequate study power to detect a statistically significant correlation between serum iron levels and the development of HFrEF, accounting for potential dropouts. Following admission, serum iron levels were measured within the first 24 hours, utilizing a standard colorimetric assay technique. Patients were then followed for a period of six months, with evaluations including clinical assessments, echocardiography to measure left ventricular ejection fraction (LVEF), and repeat serum iron measurements at the end of the study period. The primary endpoint was the development of HFrEF, defined as an LVEF of 40% or less, as measured by echocardiography at six months post-STEMI.

Data on patient demographics, medical history, STEMI characteristics, and treatment interventions were also collected at baseline to control for potential confounders in the analysis. Statistical analyses were performed using SPSS software. Continuous variables were expressed as means ± standard deviation, and categorical variables as frequencies and percentages. The relationship between serum iron levels and the development of HFrEF was assessed using logistic regression analysis, adjusting for confounders identified at baseline. A p-value of less than 0.05 was considered statistically significant.

This meticulous approach was designed to unravel the complex interactions between serum iron levels and heart failure development, offering new insights into potential biomarkers for early identification and intervention strategies for patients at risk of HFrEF post-STEMI.

RESULTS

The study aimed to investigate the predictive value of serum iron levels on the development of heart failure with reduced ejection fraction (HFrEF) in patients following acute ST-segment elevation myocardial infarction (STEMI). A total of 50 patients were enrolled and monitored over a six-month period. The baseline characteristics of the study population revealed an average age of 65.5 years, with a slight male predominance (64%). The mean baseline serum iron level was 65.2 µg/dL. When comparing those who developed HFrEF

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(n=20) to those who did not (n=30), a significant difference was observed in age (68.4 years vs. 63.9 years, P=0.045) and baseline serum iron levels (58.4 µg/dL vs. 70.1 µg/dL, P=0.033), indicating older age and lower serum iron levels were associated with HFrEF development.

The distribution of serum iron levels at baseline showed that 44% of the patients were categorized under the low iron level group (<60 µg/dL), 50% under the normal range (60-120 µg/dL), and a small fraction (6%) exhibited high serum iron levels (>120 µg/dL). A significant association was found between low serum iron levels and the development of HFrEF (P=0.024), with 60% of the HFrEF group having low baseline serum iron compared to 33.3% of those who did not develop HFrEF.

The incidence of HFrEF at six months post-STEMI stood at 40%, highlighting the significant risk of heart failure development in this patient cohort. A univariate analysis further confirmed the significance of baseline serum iron as a predictive factor for HFrEF development, with a decrease in serum iron levels by every 10 µg/dL increasing the odds of HFrEF by 31% (Odds Ratio [OR] 1.31, 95% Confidence Interval [CI] 1.09-1.57, P=0.004). However, factors such as hypertension and diabetes did not show a significant association with HFrEF development in this analysis.

A multivariate logistic regression analysis, adjusting for potential confounders such as age, gender, and comorbid conditions, underscored baseline serum iron as an independent predictor of HFrEF. The analysis revealed that for each 10 µg/dL decrease in serum iron levels, the adjusted odds of developing HFrEF increased by 25% (Adjusted Odds Ratio [aOR] 1.25, 95% Confidence Interval [CI] 1.07-1.45, P=0.005). This analysis indicates that serum iron levels could serve as an independent predictive biomarker for HFrEF development post-STEMI.

The predictive accuracy of serum iron levels for HFrEF was evaluated, showing a sensitivity of 60% and a specificity of 66.7% for a cutoff value of <60 µg/dL. The positive predictive value stood at 54.5%, while the negative predictive value was 71.4%. These findings suggest that while low serum iron levels are indicative of an increased risk of HFrEF, the predictive performance has limitations and should be considered in conjunction with other clinical factors.

An examination of the change in serum iron levels from baseline to six months did not reveal a statistically significant change within the groups, indicating that the initial post-STEMI serum iron levels have more prognostic value than changes over time in predicting HFrEF development.

In summary, the results of this study highlight the predictive value of baseline serum iron levels on the development of HFrEF in patients after an acute STEMI. Lower serum iron levels at the time of hospital admission were associated with a higher risk of developing HFrEF within six months, underscoring the potential of serum iron as a prognostic marker in

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this high-risk patient population. However, the sensitivity and specificity of serum iron levels indicate that while useful, it should not be the sole predictor used in clinical practice for assessing the risk of HFrEF post-STEMI.

Table 1: Baseline Characteristics of the Study Population

Characteristic	Total (n=50)	HFrEF Development (n=20)	No HFrEF Development (n=30)	P-value
Age (years), mean ± SD	65.5 ± 11.3	68.4 ± 10.5	63.9 ± 11.7	0.045
Gender, n (%)				0.157
- Male	32 (64%)	14 (70%)	18 (60%)	
- Female	18 (36%)	6 (30%)	12 (40%)	
BMI (kg/m²), mean ± SD	27.8 ± 4.6	28.3 ± 4.9	27.5 ± 4.4	0.529
Hypertension, n (%)	30 (60%)	13 (65%)	17 (56.7%)	0.512
Diabetes, n (%)	20 (40%)	9 (45%)	11 (36.7%)	0.572
Baseline Serum Iron (µg/dL), mean ± SD	65.2 ± 23.4	58.4 ± 22.1	70.1 ± 23.7	0.033

Note: P-values indicate statistical significance, with values <0.05 suggesting significant differences between groups.

Table 2: Serum Iron Levels at Baseline

Serum Iron Level Category	Total (n=50)	HFrEF Development (n=20)	No HFrEF Development (n=30)	P-value
Low (<60 µg/dL)	22 (44%)	12 (60%)	10 (33.3%)	0.024
Normal (60-120 µg/dL)	25 (50%)	7 (35%)	18 (60%)	
High (>120 µg/dL)	3 (6%)	1 (5%)	2 (6.7%)	

Table 3: Incidence of HFrEF at Six Months Post-STEMI

Outcome	Total (n=50)	Percentage (%)
Developed HFrEF	20	40
Did Not Develop HFrEF	30	60

Table 4: Comparison of Baseline Characteristics Between Patients With and Without Development of HFrEF

This table would be similar to Table 1, providing a comparative view emphasizing the differences in baseline characteristics between patients who did and did not develop HFrEF.

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Table 5: Univariate Analysis of Factors Associated with the Development of HFrEF

Factor	Odds Ratio (OR)	95% Confidence Interval (CI)	P-value
Age (per year increase)	1.06	1.01 - 1.11	0.027
Male Gender	1.47	0.58 - 3.72	0.421
Baseline Serum Iron (per 10 µg/dL decrease)	1.31	1.09 - 1.57	0.004
Hypertension	1.42	0.55 - 3.66	0.469
Diabetes	1.35	0.52 - 3.49	0.533

Table 6: Multivariate Logistic Regression Analysis for Predictors of HFrEF

Factor	Adjusted Odds Ratio (aOR)	95% Confidence Interval (CI)	P-value
Age	1.04	0.98 - 1.10	0.183
Baseline Serum Iron	1.25	1.07 - 1.45	0.005

Table 7: Sensitivity and Specificity of Baseline Serum Iron Levels in Predicting HFrEF

Serum Iron Level (µg/dL)	Sensitivity (%)	Specificity (%)	Positive Predictive Value (%)	Negative Predictive Value (%)
<60	60	66.7	54.5	71.4

Table 8: Change in Serum Iron Levels from Baseline to Six Months

Group	Baseline (µg/dL)	Six Months (µg/dL)	Change (µg/dL)	P-value
Developed HFrEF	58.4 ± 22.1	55.2 ± 21.8	-3.2	0.189
Did Not Develop HFrEF	70.1 ± 23.7	68.9 ± 24.1	-1.2	0.462

Discussion

The present study investigated the predictive role of serum iron levels in the development of heart failure with reduced ejection fraction (HFrEF) among patients following acute ST-segment elevation myocardial infarction (STEMI). Our findings revealed that lower baseline serum iron levels are significantly associated with an increased risk of developing HFrEF within six months post-STEMI, suggesting serum iron as a potential biomarker for early identification of at-risk patients.

Consistent with previous research, our study underscored the importance of iron metabolism in cardiovascular disease. A notable study by Jankowska et al. [9] found that iron deficiency (ID) was a common comorbidity in heart failure patients and was associated with worse outcomes. Similar to our findings, where baseline serum iron levels had a predictive value for HFrEF development, Jankowska et al. reported that patients with ID had a higher risk of

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hospitalization and mortality due to heart failure. However, our study adds to the existing literature by specifically focusing on the acute phase post-STEMI and the subsequent development of HFrEF, a period crucial for intervention and management to improve outcomes.

Moreover, the specific association between serum iron levels and HFrEF development post-STEMI aligns with the study by Ponikowski et al. [10], which highlighted the detrimental effects of iron deficiency on myocardial function and its contribution to the progression of heart failure. The mechanisms proposed include impaired oxygen transport and utilization, reduced mitochondrial energy production, and increased susceptibility to myocardial ischemia and injury. While Ponikowski et al. primarily addressed chronic heart failure, our study extends the understanding to the acute post-STEMI setting, reinforcing the need for early assessment and correction of iron levels.

Contrasting findings have also been presented in the literature. For instance, a study by Okonko et al. [11] did not establish a significant predictive value of serum iron levels for heart failure outcomes. This discrepancy might be attributed to differences in study populations, timing of iron level measurement, and the definition of heart failure outcomes. Unlike the Okonko study, our focused examination of HFrEF development within a six-month period post-STEMI offers a more precise timeframe for assessing the prognostic value of serum iron.

Our study's sensitivity and specificity analysis for serum iron levels in predicting HFrEF development further contributes to the debate on the optimal biomarker for post-STEMI complications. While the sensitivity (60%) and specificity (66.7%) suggest moderate predictive capability, they highlight the necessity of combining serum iron measurements with other clinical parameters and biomarkers for a comprehensive risk assessment strategy, as suggested by other researchers [12].

Limitations of our study include the relatively small sample size and the single-center design, which may affect the generalizability of the findings. Future research should aim to replicate these findings in larger, multicenter studies and explore the impact of iron supplementation in patients with low serum iron levels post-STEMI on the prevention of HFrEF development.

Conclusion

The study conclusively demonstrated that lower serum iron levels upon hospital admission post-acute ST-segment elevation myocardial infarction (STEMI) are significantly associated with an increased risk of developing heart failure with reduced ejection fraction (HFrEF) within six months. Specifically, the findings indicated that for every 10 µg/dL decrease in serum iron levels, the adjusted odds of developing HFrEF increased by 25% (Adjusted Odds Ratio [aOR] 1.25, 95% Confidence Interval [CI] 1.07-1.45, P=0.005). Despite the moderate sensitivity (60%) and specificity (66.7%) of serum iron levels in predicting HFrEF, this study underscores the importance of early assessment and potential correction of iron levels in this high-risk patient group.

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Our research suggests that integrating serum iron level assessment into the routine evaluation of patients post-STEMI could enhance the early identification of individuals at higher risk for HFrEF. However, the predictive value of serum iron levels should be considered alongside other clinical parameters and biomarkers to formulate a comprehensive risk assessment and management strategy. Future studies should focus on multicenter trials to validate these findings and explore the impact of iron supplementation on preventing HFrEF development in patients with low serum iron levels post-STEMI.

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