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ORIGINAL ARTICLE

Thrombocytopaenia as a Prognostic Indicator in Heart Failure with Reduced Ejection Fraction

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Background Studies suggest that thrombocytopaenia is associated with a higher mortality in several diseases. Little is known about the effect of low platelet count on mortality in patients with heart failure with reduced ejection fraction (HFrEF). The aim of this study was to determine the prognostic value of thrombocytopaenia in these patients by assessing all-cause mortality.

Methods A total of 1,907 patients with HFrEF, defined by left ventricular ejection fraction <40% on echocardiography, were analysed in this multi-centre retrospective study. All patients were on medical therapy with a beta-blocker and an angiotensin-converting enzyme inhibitor. Patients were categorised into two groups based on platelet count measured within one month of the diagnosis of HFrEF: normal to mild thrombocytopaenia (platelet count 100,000-450,000 per uL); and moderate to severe thrombocytopaenia (platelet count <100,000 per uL). One-year all-cause mortality was compared between the two groups.

Results Mean age was 65±15 years and 62% of patients were male. Overall one-year mortality was 17.2% with higher mortality among patients with HFrEF and moderate/severe thrombocytopaenia compared to those with normal/mild thrombocytopaenia (33.0% vs. 15.4%, p <0.001). After adjusting for baseline characteristics, patients with HFrEF and moderate/severe thrombocytopaenia had a higher mortality compared to patients with normal/mild thrombocytopaenia (HR 1.84, 95% CI 1.33-2.56, p <0.001).

Conclusion In patients with HFrEF, higher degree of thrombocytopaenia is associated with higher all-cause mortality. These findings may support the use of platelet counts as a prognostic marker in the assessment of the patient with HFrEF.

Keywords Thrombocytopaenia • Heart failure with reduced ejection fraction

Abbreviations: HF, heart failure; HFrEF, heart failure with reduced ejection fraction; LVEF, left ventricular ejection fraction; EF, ejection fraction

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Introduction

Systolic heart failure (HF), with reduced left ventricular ejection fraction (HF*r*EF), is an increasingly prevalent clinical syndrome with high morbidity and mortality. More than half of patients with HF have reduced left ventricular ejection fraction (40% or less) [1]. The growing prevalence of HF is multi-factorial in nature, owing largely to an ageing population [2]. With an increase in clinical prevalence, there has been a similar rise in the number of hospitalisations and deaths attributed to HF. The economic and medical burdens imposed by HF warrant optimisation of prevention and management [2,3]. It is therefore imperative to identify predictive factors that facilitate evaluation of patients with HFrEF in order to best guide intervention and medical therapy. Established HFrEF prognostic markers include left ventricular ejection fraction (LVEF), left ventricle dilation, concomitant diastolic dysfunction, and reduced right ventricular function [4–7].

An association between thrombocytopaenia and adverse clinical outcomes has been identified in several diseases. More specifically, thrombocytopaenia has been found to serve as a marker of poor outcomes in acute coronary syndrome [8–10], chronic lymphocytic leukaemia [11], pulmonary hypertension [29], and intensive care unit patients [12]. While numerous studies have demonstrated increased platelet activation in HF [13], there are scarce data on the relationship between thrombocytopaenia and prognostic outcomes in patients with HFrEF. The purpose of this study was to examine the effect of thrombocytopaenia on the survival of patients with HFrEF.

Methods

Study Population

From January 2005 to January 2011, we identified 1,907 patients with HF*r*EF, aged ≥18 years old, with a platelet count ordered within one month of diagnosis. All patients had systolic congestive HF defined by ICD-9 coding for HF or systolic HF, and left ventricular ejection fraction (EF) <40% as determined by echocardiography. All included patients were started on optimal medical therapy for HF at the time of diagnosis; defined as combined treatment with a beta-blocker and an angiotensin-converting-enzyme inhibitor. Patients with ICD-9 code for diastolic HF alone were excluded. Patients were identified from the Montefiore Medical Center's Clinical Information System (Emerging Health Information Technology, Yonkers, New York) using the Clinical Looking Glass, a proprietary query tool and software application that allows clinicians and researchers to identify populations of interest from the Montefiore Medical Center's database, and to gather information about the demographics, clinical, and outcome data [30–34]. The database is combined monthly with the Social Security Death Registry, which allows extraction of mortality data. Hospitalisation data were obtained from Montefiore Medical Center's database. This multi-centre retrospective study was approved by the Institutional Review Board of Albert Einstein College of Medicine of Yeshiva University (Protocol Number: 13-01-025).

Study Design

Patients were classified into two groups stratified by the severity of thrombocytopaenia based on classifications used in prior studies [29]:

1) *Normal to mild (normal/mild) thrombocytopaenia*: Patients with HFrEF and platelet count between 100,000 and 450,000 per uL; *2) Moderate to severe (moderate/severe) thrombocytopaenia*: Patients with HFrEF and platelet count less than 100,000 per uL.

Measures and Outcomes

Follow-up began after an initial diagnosis of HFrEF and an established platelet count within one month after diagnosis. The primary endpoint of the study was one-year all-cause mortality.

Subjects were followed for one year after diagnosis by echocardiography and confirmed thrombocytopaenia. All data were extracted from the Montefiore Medical Center's clinical information system (Emerging Health Information Technology, Yonkers, New York). The database is combined monthly with the Social Security Death Registry, which allowed for extraction of one-year mortality rates.

Statistical Analysis

Continuous data are presented as mean and standard deviation, while categorical data are presented as numbers and percentages. Between-group comparisons were made using Student's *t* test, for continuous variables, and chi-square test for categorical data. A survival analysis was performed (Kaplan-Meier and Cox-regression model using one-year all-cause mortality as the endpoint). As our primary interest was to determine the independent relationship of thrombocytopaenia and mortality, our final multivariate Cox regression analysis was adjusted for baseline differences between groups and our final model included all significant predictors of mortality that were identified by univariate analyses. Statistical analyses were performed using STATA version 12.0 statistical software. A p value ≤0.05 was considered statistically significant.

Results

Baseline characteristics including demographics, clinical data, medications (including common medications associated with thrombocytopaenia), and echocardiographic data of 1,907 patients stratified by platelet count are presented in Table 1. A total of 194 patients (10.17%) had a value of less than 100,000 platelets and were classified as having moderate/severe thrombocytopaenia.