Anemia at Hospital Admission and Its Relation to Outcomes in Patients With Heart Failure (from the Polish Cohort of 2 European Society of Cardiology Heart Failure Registries)

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Anemia is a commonly observed co-morbidity in heart failure (HF). The aim of the study was to assess prevalence, risk factors for, and effect of anemia on short- and long-term outcomes in HF. The study included 1,394 Caucasian patients hospitalized for HF, with known hemoglobin concentration on hospital admission, participating in 2 HF registries of the European Society of Cardiology (Pilot and Long-Term). Anemia was defined as hemoglobin concentration of <13 g/dl for men and <12 g/dl for women. Primary end points were (1) all-cause death at 1 year and (2) a composite of all-cause death and rehospitalization for HF at 1 year. Secondary end points included inter alia death during index hospitalization. In addition, we investigated the effect of changes in hemoglobin concentration during hospitalization on prognosis. Anemia occurred in 33% of patients. Predictors of anemia included older age, diabetes, greater New York Heart Association class at hospital admission and kidney disease. During 1-year follow-up, 21% of anemic and 13% of nonanemic patients died (p <0.0001). Combined primary end point occurred in 45% of anemic and in 33% of nonanemic patients (p <0.0001). Anemia was strongly predictive of all the prespecified clinical end points in univariate analyses but not in multivariate analyses. Changes in hemoglobin concentration during hospitalization had no effect on 1-year outcomes. In conclusion, anemia was present in 1/3 of patients with HF. Mild-to-moderate anemia seems more a marker of older age, worse clinical condition, and a higher co-morbidity burden, rather than an independent risk factor in HF. © 2017 Elsevier Inc. All rights reserved. (Am J Cardiol 2017;119:2021−2029)

Identification and prevention of risk factors for heart failure (HF) decompensation constitute the fundamentals of comprehensive care in HF.[1−3] Although anemia is a commonly observed co-morbidity in HF, associated with significantly worse prognosis, there is no certain explanation on how it affects mortality, provokes HF exacerbations, and influences the course of hospitalization.[4−9] There are encouraging reports on the effectiveness of iron therapy in reducing HF symptoms; however, there are no favorable results in terms of mortality in HF.[10−13] Thus, clinical implications of anemia in HF remain to be established. The aim of this study was to evaluate the prevalence of anemia in patients hospitalized for HF, compare baseline characteristics and course of index hospitalization of anemic and nonanemic HF patients, and determine the impact of anemia on short- and long-term outcomes in HF. Additional objectives of the analysis were to assess risk factors for anemia in HF patients and to evaluate changes in hemoglobin concentration during hospitalization and their prognostic significance in HF.

Methods

The study is based on 2 prospective, multicenter, observational surveys of patients with HF, conducted by the European Society of Cardiology (ESC). The first, ESC-HF Pilot Survey, which has already been completed, was conducted from October 2009 to May 2010 in 136 European cardiology centers, including 29 centers from Poland.[14] The second, ESC-HF Long-Term Registry, is a 3-phase study, conducted in 211 European cardiology centers, including 35 centers from Poland.[15] In the ESC-HF Pilot Survey and during phase I of the ESC-HF Long-Term Registry (lasting from May 2011 to April 2013), patients were enrolled on 1 specific day of the week for 12 consecutive months in each of the participating centers. In phase II and phase III (still on-going) of the ESC-HF Long-Term Registry, patients are enrolled during 5 days per trimester. The current analysis included Polish participants of the ESC-HF Pilot Survey and of phase I of the ESC-HF Long-Term Registry.
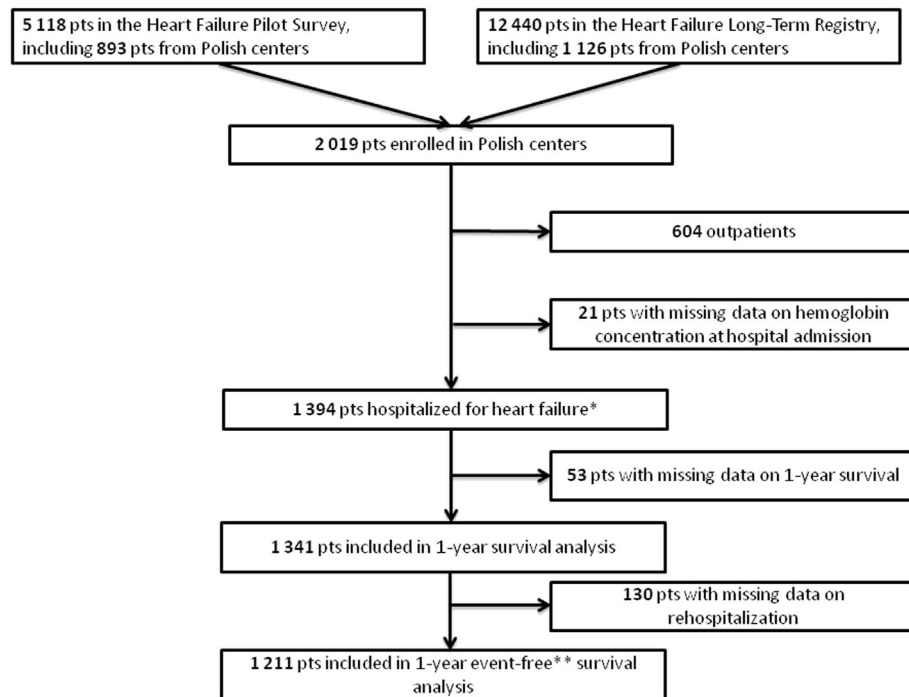
Figure 1. Flow chart of patient enrollment in the current analysis. *included in the comparative analysis of anemic and nonanemic patients and in the analyses of in-hospital outcomes. **death or rehospitalization for heart failure. pts = patients.

The surveys included both ambulatory and hospitalized HF patients, who were aged over 18 years. There were no specific exclusion criteria. Local ethics committees approved the surveys in accordance with the regulations of each participating country. All patients were provided with detailed information on the registries and signed informed written consent.

The current analysis included only patients admitted to hospital for new-onset or worsening HF, in whom data on hemoglobin concentration on hospital admission were available.

Patients were divided into 2 groups (anemic and nonanemic) according to hemoglobin concentration on admission. Following the World Health Organization criteria, anemia was defined as hemoglobin concentration of <13 g/dl for men and <12 g/dl for women. Severe anemia was defined as hemoglobin level <9 g/dl. Anemic and nonanemic patients were compared with regard to baseline characteristics, course of index hospitalization, diagnostic tests results, implemented treatment, in-hospital outcomes (death during hospitalization, length of hospital stay, time in intensive cardiac care unit [ICCU]) and 1-year outcomes (all-cause death and death or rehospitalization for decompensated HF).

The primary end points were (1) all-cause death at 1 year and (2) a composite of all-cause death and hospital readmissions for decompensated HF at 1 year. Secondary end points included (1) death during index hospitalization, (2) hospital stay >7 days, (3) time in ICCU >3 days, and (4) a worse clinical status (New York Heart Association [NYHA] class III or IV) at hospital discharge.

The main goal of the study was to determine whether anemia at hospital admission was predictive of the primary and the secondary end points in patients with HF. In addition, we assessed, whether changes in hemoglobin concentration during index hospitalization were related to 1-year outcomes

(all-cause death and death or rehospitalization for decompensated HF). Increase and decrease in hemoglobin concentration were defined as changes of ≥1 g/dl during index hospitalization. Finally, we sought to identify risk factors for anemia at admission in hospitalized HF patients.

Statistical analyses were performed using SPSS 22 (SPSS Statistics, Inc., Chicago, Illinois) and SAS 9.2 (SAS Institute Inc., Cary, North Carolina) software. Normally distributed continuous variables were presented as mean value and SD, whereas for ordinal variables and nonnormally distributed continuous variables, median value and interquartile range were given. Significance of differences between the 2 groups was determined by Fisher's exact test for categorical variables and the Mann-Whitney U test for continuous and ordinal variables. Cox proportional hazards regression model was used to identify predictors of the primary end points, as well as to assess association of hemoglobin changes during index hospitalization and 1-year outcomes. To determine the predictors of the remaining secondary end points, univariate and multivariate logistic regressions were performed. Multivariate analyses included all variables found to be statistically significant in univariate analyses, maintaining adequate events per predictor variable values.[16] The list of all variables included in univariate analyses (both in Cox proportional hazards analyses and in logistic regression analyses) is provided in Supplementary Table S1. Kaplan-Meier curves were developed for both primary end points. For all tests, p value below 0.05 was considered significant. All tests were 2 tailed.

Results

Figure 1 shows the flow chart of patient selection for the present study. Finally, the study group included 1,394