Clinical Investigation

Discordance Between Hemoconcentration and Clinical Assessment of Decongestion in Acute Heart Failure

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ABSTRACT

Introduction: Hemoconcentration has been proposed as a surrogate for successful decongestion in acute heart failure (AHF). The aim of the present study was to evaluate the relationship between hemoconcentration and clinical measures of congestion.

Methods and Results: We studied 704 patients with AHF and volume overload. A composite congestion score was calculated at admission and discharge, with a score >1 denoting persistent congestion. Hemoconcentration was defined as any increase in hematocrit and hemoglobin levels between baseline and discharge. Of 276 patient with hemoconcentration, 66 (23.9%) had persistent congestion. Conversely, of 428 patients without hemoconcentration, 304 (71.0%) had no clinical evidence of congestion. Mean hematocrit changes were similar with and without persistent congestion (0.18 ± 3.4% and −0.19 ± 3.6%, respectively; $P = .17$). There was no correlation between the decline in congestion score and the change in hematocrit ($P = .93$). Hemoconcentration predicted lower mortality (hazard ratio 0.70, 95% confidence interval 0.54–0.90; $P = .006$). Persistent congestion was associated with increased mortality independent of hemoconcentration ($P_{trend} = .0003$ for increasing levels of congestion score).

Conclusions: Hemoconcentration is weakly related to congestion as assessed clinically. Persistent congestion at discharge is associated with increased mortality regardless of hemoconcentration. Hemoconcentration is associated with better outcome but cannot substitute for clinically derived estimates of congestion to determine whether decongestion has been achieved. (*J Cardiac Fail 2016;22:680–688*)

Key Words: Congestion, heart failure, hemoconcentration, hematocrit, outcomes.

The principal cause for hospitalization due to acute heart failure (AHF) is related to symptoms of congestion.[1–3] However, many patients have only partial relief of dyspnea and congestion, even when guideline-recommended therapies are implemented.[2,4–6] Persistent congestion at hospital discharge is associated with increased risk for rehospitalizations for heart failure (HF) and mortality.[4,6] Therefore, the primary therapeutic objective in the majority of patients admitted for AHF is to optimize volume status.[1]

Given the inherent inaccuracies of the clinical assessment of congestion,[1] reliable markers of inpatient decongestion are needed to guide therapy and discharge decision making. Effective fluid removal may lead to intravascular volume contraction, resulting in hemoconcentration. Recently, hemoconcentration has been suggested as a surrogate for successful decongestion during aggressive fluid removal in AHF.[7–9]

However, hemoconcentration as a marker of effective decongestion is not without potential limitations. Failure to hemoconcentrate during hospitalization may be explained by confounding factors such as subclinical bleeding.[10] In addition, hemoconcentration, as evidenced by an increasing hematocrit (Hct), may indicate that fluid removal has temporarily exceeded the plasma refill rate[11] while the patient remains congested.

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Although there is a strong relationship between the clinical assessment of congestion and mortality,[1,4,12,13] earlier studies have not established the additive value of hemoconcentration to the systematic clinical evaluation of congestion. The aim of the present study was to evaluate the relationship between hemoconcentration and clinical measures of congestion and the incremental value of hemoconcentration for the prediction of post-discharge clinical outcomes in patients with AHF.

Methods

AHF Cohort

From January 2008 to April 2014, patients admitted to the Rambam Medical Center, Haifa, Israel with the primary diagnosis of AHF entered a prospective registry.[14] Eligible patients were those hospitalized with new-onset or worsening preexisting HF as the primary cause of admission or those with significant HF symptoms that developed during a hospitalization for which HF was the primary discharge diagnosis.[15] In addition, patients were required to have a B-type natriuretic peptide (BNP) level >400 pg/mL at admission (AxSYM BNP microparticle enzyme immunoassay; Abbott Laboratories, Abbott Park, Illinois). Cardiac troponin I assay was performed with the use of the Architect system (Abbott Diagnostics), with a 99th-percentile cutoff point of 0.028 ng/mL. Medical records were extracted periodically with the use of computerized search and reviewed by trained abstractors who verified that the diagnosis of HF was appropriate.

For the present analysis, we excluded patients without signs of congestion at admission, with baseline hemoglobin (Hgb) level <9 g/dL, receiving transfusion during hospitalization, missing discharge Hct data, with chronic kidney disease stage V (estimated glomerular filtration rate [eGFR] <15 mL • min^{-1} • 1.73 m^{-2}), and who died during the index admission. The study was approved by the Institutional Review Committee on Human Research.

Hemoconcentration

Hemoconcentration was defined as an increase in both Hgb and Hct levels between baseline and discharge.[8,9] eGFR was derived from the abbreviated Modification of Diet in Renal Disease study equation.[16]

Congestion Score

Assessment of congestion at hospital admission and discharge was done by the treating physician. The degree of congestion at admission was evaluated based on a combination of several signs and symptoms.[17] We constructed a score that shared components common to earlier studies, which used different congestion scores.[1,4,12,13,18,19]

A 9-point scale ranging from 0 to 8 was constructed as follows: raised jugular venous pressure ≥8 cm H_2O (1 point), hepatomegaly (1 point), presence of peripheral edema (absent/trace, 0 points; slight, 1 point; moderate, 2 points; marked, 3 points; and anasarca, 4 points), pulmonary rales (1 point), and 3rd heart sound (1 point). A composite congestion score was calculated by summing the individual scores at the time of admission and at discharge. Persistent congestion was defined as a congestion score >1 at discharge.

Clinical End Points

After hospital discharge, mortality and HF rehospitalization data were acquired by means of reviewing the national death registry and independently reviewing the hospital course for major clinical events if the patient had been rehospitalized. In the event of multiple hospitalizations for a single patient, only the first admission meeting the aforementioned inclusion criteria was used for the analysis. The primary end point was all-cause mortality and the secondary end point was the composite of death or HF rehospitalization.

Statistical Analysis

The baseline characteristics of the groups were compared with the use of unpaired *t* tests for continuous variables and the χ^2 statistic for categoric variables. Changes in Hct by categories of congestion score were assessed by means of nonparametric 1-way analysis of variance (Kruskal-Wallis test).

The association of clinical variables and hemoconcentration were assessed with the use of a logistic regression model. Event-free survival was estimated with the use of the Kaplan-Meier method, and curves were compared by means of the log-rank test. Stepwise Cox proportional hazards models with backward selection were used to determine which variables were significantly related to the primary or secondary end points. Variables associated with mortality or time to readmissions or due to HF in the univariate Cox regression analysis (Wald test; $P < .10$) were used in the multivariable Cox model. The following baseline clinical characteristics were considered in the multivariate procedure: age, sex, baseline systolic blood pressure, baseline eGFR, baseline blood urea nitrogen (BUN), BNP levels, history of diabetes mellitus and hypertension, atrial fibrillation, elevated troponin level at admission, and ejection fraction (dichotomized at 45%), hemoconcentration and congestion score (0, 1, 2, and ≥3). The following medications were adjusted for as dichotomous variables, indicating the use or nonuse of the medication at hospital discharge: β-blockers, angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, digoxin, and spironolactone.

Differences were considered to be statistically significant at the 2-sided $P < .05$ level. Statistical analyses were performed with the use of Stata version 13.1 (College Station, Texas).