Ratio of Systolic Blood Pressure to Right Atrial Pressure, a Novel Marker to Predict Morbidity and Mortality in Acute Systolic Heart Failure

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Congestion is the main contributor to heart failure (HF) morbidity and mortality. We assessed the combined role of congestion and decreased forward flow in predicting morbidity and mortality in acute systolic HF. The Evaluation Study of Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness trial data set was used to determine if the ratio of simultaneously measured systolic blood pressure (SBP)/right atrial pressure (RAP) on admission predicted HF rehospitalization and 6-month mortality. One hundred ninety-five patients (mean age 56.5 years, 75% men) who received pulmonary artery catheterization were studied. The RAP, SBP, and SBP/RAP had an area under the curve (AUC) of 0.593 ($p = 0.0205$), 0.585 ($p = 0.0359$), and 0.621 ($p = 0.0026$), respectively, in predicting HF rehospitalization. The SBP/RAP was a superior marker of HF rehospitalization compared with RAP alone (difference in AUC 0.0289, $p = 0.0385$). The optimal criterion of SBP/RAP <11 provided the highest combined sensitivity (77.1%) and specificity (50.9%) in predicting HF rehospitalization. The SBP/RAP had an AUC 0.622, $p = 0.0108$, and a cut-off value of SBP/RAP <8 had a sensitivity of 61.9% and specificity 64.1% in predicting mortality. Multivariate analysis showed that an SBP/RAP <11 independently predicted rehospitalization for HF (estimated odds ratio 3.318, 95% confidence interval 1.692 to 6.506, $p = 0.0005$) and an SBP/RAP <8 independently predicted mortality (estimated hazard ratio 2.025, 95% confidence interval 1.069 to 3.833, $p = 0.030$). In conclusion, SBP/RAP ratio is a marker that identifies a spectrum of complications after hospitalization of patients with decompensated systolic HF, starting with increased incidence of HF rehospitalization at SBP/RAP <11 to increased mortality with SBP/RAP <8. **(Am J Cardiol 2017;119:1061−1068)**

Heart failure (HF) is the most common cause of hospitalization in patients over the age of 65 years[1] causing approximately 1 million admissions annually in the United States and accounting for $37.2 billion in health care expenditure.[2] Despite the progress achieved in reducing morbidity in patients hospitalized with HF, rates of rehospitalization remain high exceeding 50% within 6 months after discharge.[3] Also, survival after the diagnosis of HF—although improved substantially over time—remains quite poor. In a recent analysis from the Efficacy of Vasopressin Antagonism in Heart Failure Outcome Study with Tolvaptan (EVEREST) trial, after median follow-up of 9.9 months, 971 patients died (24.2%).[4] Awareness of predictors of HF rehospitalization and mortality is crucial to identify which patients may need more intense monitoring and therapy. Herein, we evaluated the combined role of right atrial pressure (RAP)—a marker of congestion—and systolic blood pressure (SBP)—a rough marker of forward flow—in predicting rehospitalization for HF and 6-month mortality. It is well established that congestion is a main predictor of HF morbidity and mortality in HF.[5] Low SBP is a common finding in advanced HF and has been an important marker of postdischarge mortality,[6−10] but there is only limited evidence to show that it predicts rehospitalization due to HF.[11]

The aim of this study is to evaluate whether a simple marker defined as the ratio of SBP to RAP, hereafter denoted SBP/RAP, predicts mortality and rehospitalization for HF; in particular, we address whether forward flow (as measured by SBP) contributes added prognostic value for HF rehospitalization beyond congestion (RAP) alone.

Methods

The Evaluation Study of Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness (ESCAPE) trial was a National Heart, Lung, and Blood Institute−sponsored randomized, multicenter study that enrolled 433 patients with acute decompensated systolic HF at 26 sites and compared the outcomes of patients who were managed with clinical assessment plus pulmonary artery catheterization (PAC) versus clinical assessment alone. Inclusion criteria included an ejection fraction (EF) of $\leq$30%, SBP of $\leq$125 mm Hg, hospitalization for HF within the preceding year, treatment during the preceding month with >160 mg of furosemide equivalents daily and angiotensin-converting enzyme inhibitor therapy, and at least 1 sign and 1 symptom

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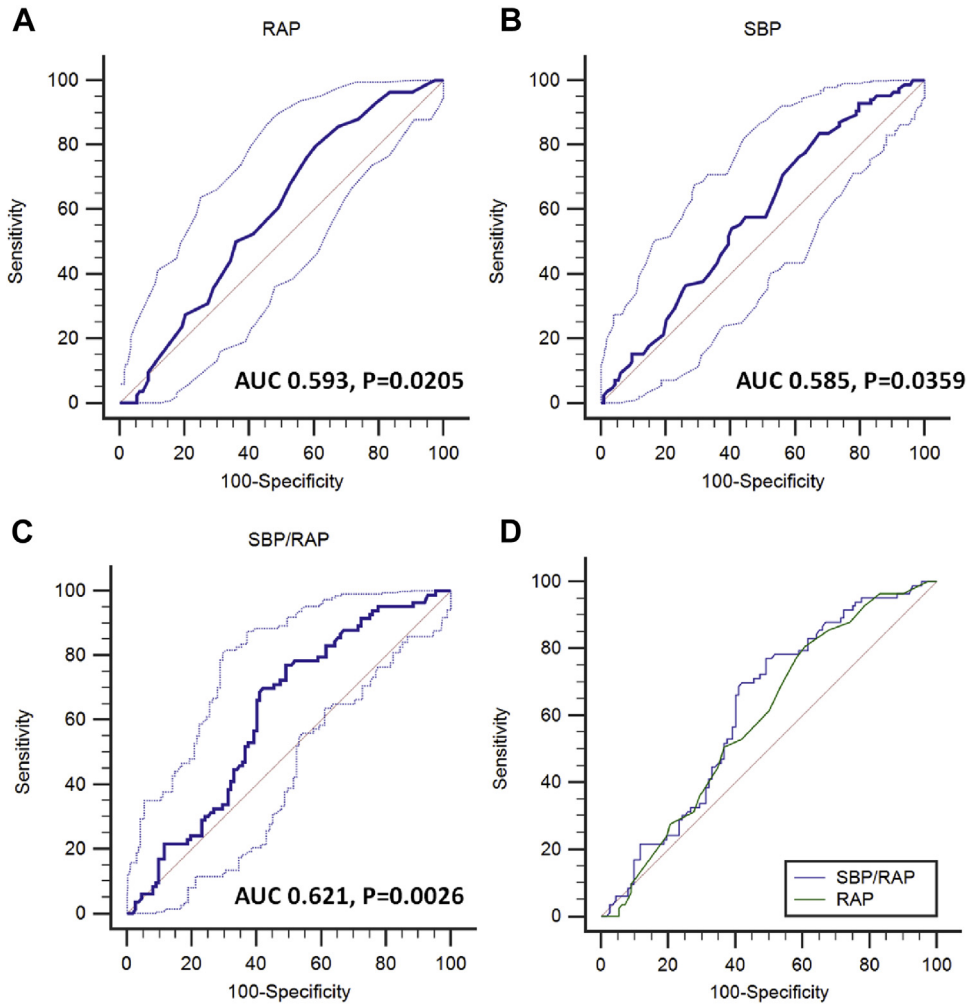

Figure 1. Receiver operating characteristic curve to detect the AUC and corresponding confidence bands of RAP *(A)*, SBP *(B)*, and SBP/RAP *(C)* in predicting rehospitalization for heart failure. Each panel shows the corresponding AUC and p value. *(D)* Receiver operating characteristic curves comparing AUC of RAP versus SBP/RAP in predicting rehospitalization for heart failure (difference in AUC 0.0289, p = 0.0385).

of congestion. Exclusion criteria included creatinine >3.5 mg/dl. The study showed that the PAC did not significantly improve or worsen outcomes as assessed by the primary end point. Design, rationale, and results of the ESCAPE trial have been previously published.[12,13] Our objective was to examine the validity of SBP/RAP as a novel marker in predicting rehospitalization and mortality for HF. The study end points were HF rehospitalization and all-cause mortality up to 6 months after hospital discharge. Only patients who received PAC and had available hemodynamic measurements of both RAP and SBP were included in our analysis (n = 195). Although jugular venous pressure is a simpler bedside test to grade congestion in HF, it was measured in the ESCAPE trial as a categorical and not a continuous variable, and therefore, we have used RAP instead. We have used SBP measured concomitantly with RAP, not the manually checked SBP at the time of presentation, to ensure contemporaneous measurements.

We sought optimal cutoffs of SBP/RAP, in the sense of obtaining the highest combined sensitivity and specificity for predicting rehospitalization for HF and 6-month mortality. This defined high- and low-risk groups of patients for each of those 2 end points. We have used the Shapiro−Wilk test to examine the normality of distribution of continuous variables which were then expressed as mean ± standard deviation (or median and interquartile range) and compared between groups using independent samples *t* test for normally distributed variables or Mann−Whitney *U* test for non-normally distributed variables. Categorical variables were expressed as counts and percentages and were compared between groups using the chi-square test.

The ability of RAP, SBP, and SBP/RAP to predict rehospitalization for HF and mortality was assessed by calculating the area under the curve (AUC) of the receiver operating characteristic curve. Comparison of the AUC of the RAP and SBP/RAP was performed, using the Hanley and McNeil method as implemented in the MedCalc software.[14] Multivariate logistic regression analysis was performed to see if SBP/RAP predicts rehospitalization for HF after adjusting for known or presumed risk factors. A Hosmer-Lemeshow test was performed for this model, and both raw and optimism-corrected versions of the AUC statistic were obtained; the optimism-corrected version was acquired using the validate function in the rms package for