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Bedside Ultrasound Assessment of Jugular Venous Compliance as a Potential Point-of-Care Method to Predict Acute Decompensated Heart Failure 30-Day Readmission

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Background—Heart failure is one of the most costly diagnosis-related groups, largely because of hospital readmissions. Objective assessment of volume status to ensure optimization before hospital discharge could significantly reduce readmissions. We previously demonstrated an ultrasound method of quantifying percentage of cross-sectional area (CSA) change of the right internal jugular vein with Valsalva that reliably estimates central venous pressure.

Methods and Results—Patients admitted with acute decompensated heart failure (ADHF) underwent ultrasound measurements of the right internal jugular vein at end-expiration and during the strain phase of Valsalva to determine a percentage of CSA change. An initial subgroup of patients with right heart catheterization and accompanying ultrasound measurements of the right internal jugular vein identified a percentage of CSA change predictive of right atrial pressure (RAP) ≥12 mm Hg. Images of admitted ADHF patients were obtained at admission and discharge for final analysis. Simultaneous right heart catheterization and right internal jugular vein ultrasound measurements demonstrated that a <66% CSA change predicted RAP ≥12 mm Hg (positive predictive value: 87%; $P<0.05$, receiver operating characteristic curve). Elevated admission RAP by percentage of CSA change normalized by discharge ($P<0.05$), indicating that this test is significantly responsive to therapeutic interventions. Using the cutoff value of 66% CSA change, normal RAP at discharge had 91% predictive value for patients avoiding 30-day readmission ($P<0.05$).

Conclusions—This bedside ultrasound technique strongly correlates to invasive RAP measurement in ADHF patients, identifies restoration of euvolemia, and is predictive of 30-day ADHF readmission. This tool could help guide inpatient ADHF treatment and may lead to reduced readmissions. (*J Am Heart Assoc*. 2018;7:e008184. DOI: 10.1161/JAHA.117.008184.)

Key Words: cost effectiveness • heart failure • ultrasound

C hronic heart failure (CHF) is a common and costly disease state. Unfortunately, the incidence and prevalence of this diagnosis are increasing at alarming rates, mirroring our aging population and improved survival of acute coronary syndromes and other cardiovascular pathologies. It is estimated that 5.1 million Americans have CHF, with an incidence of 10 per 1000 population after age 65 years, with projections of a 25% increase in prevalence and a 120% increase in healthcare costs by the year 2030.[1] Much of that cost comes from hospitalizations related to acute decompensated heart failure (ADHF) syndromes. ADHF is the onset of the signs or symptoms of heart failure requiring unplanned office visits, emergency room visits, or hospitalization.[2] It results from elevated ventricular filling pressures causing pulmonary and systemic congestion. Detection of ADHF is primarily accomplished when there is clinical or radiological evidence of congestion such as patient-reported dyspnea or orthopnea, weight gain, presence of lower extremity edema, visual estimation of jugular venous pressures, or plain film evidence of pulmonary vascular engorgement. Treatment progress with diuresis and discharge planning often revolves around improvement in the clinical signs of congestion and/or symptom improvement; however, these signs remain imperfect surrogates for true intravascular hemodynamics, as shown by ADHF 30-day readmission rates as high as 25% with a significant proportion (37–48%) attributable to CHF.[3–6]

Accurate assessment of filling pressure during physical examination is critical for CHF-related decision-making. The

evaluation of the right internal jugular vein (RIJV) allows assessment of central venous pressure and is a direct measure of right atrial pressure (RAP). The majority of patients with ADHF have elevated RAP, which reflects elevated left ventricular filling pressures. Therefore, measurement of RAP is a fundamental part of the bedside heart failure evaluation. This is traditionally accomplished by assessment of the height of the RIJV meniscus, which provides a manometric measure of RAP. In clinical practice, however, estimation of central venous pressure by assessment of the RIJV is accurate in <50% of cases and frequently is unobtainable.[7,8] Thus, accurate assessment is difficult, and significant interobserver variability exists, even between highly trained clinicians. In fact, clinicians often underestimate RAP with this technique, which may lead to undertreatment, higher readmission rates, and, ultimately, increased overall cost of treatment for heart failure. Invasive measurement by right heart catheterization is increasingly utilized in the management for heart failure patients and carries both safety and financial burdens. We previously demonstrated in patients undergoing right heart catheterization (n=67), that portable bedside ultrasound could be used to detect elevated RAP with a negative predictive value of 94%.[9] This finding stems from the basic biomechanical properties of veins: At low pressure, venous compliance is high, and an increase in pressure, such as during Valsalva, would be expected to cause a large change in visualization of the vein's cross-sectional area (CSA). Conversely, at high venous pressure, compliance is low, and increases in pressure (Valsalva) would be expected to cause only small changes in CSA.[9] Intraobserver and interobserver testing showed negligible variability with this method (Spearman correlation coefficients of 0.904 [*P*<0.0001], with intraclass correlation of 0.8752

[κ=1], and 0.9662 [*P*<0.0001], with intraclass correlation of 0.8779 [κ=0.9], respectively).[9] In this study, we aimed to determine whether estimation of RAP using the ultrasound measurement of RIJV CSA change with Valsalva correlates with hypervolemia in patients admitted with ADHF and could predict 30-day rehospitalization.

Methods

The study design was approved by the University of Pittsburgh institutional review board. All participants provided informed consent. The data that support the findings of this study are available from the corresponding author on reasonable request.

Patients

Adult patients with ADHF admitted to the heart failure service at University of Pittsburgh Presbyterian Hospital were eligible for enrollment. Enrollment information is detailed in Figure 1. No imaging was performed while patients were on inotropic support with dobutamine or milrinone. Demographic data and baseline clinical characteristics such as age, sex, weight, body mass index, ejection fraction, BNP (B-type natriuretic peptide) levels, and comorbidities were collected.

Ultrasound Imaging

Two-dimensional imaging of the RIJV was performed using a portable ultrasound imaging system (iLook 25; Sonosite Corp) with a standard vascular probe (broadband 10–5 MHz linear array transducer designed for vascular access). The patients were supine with the head of the bed elevated to 45°. The ultrasound examination was performed at the bedside, where the vascular ultrasound probe was placed at the apex of the triangle formed by the 2 heads of the right sternocleidomastoid muscle with the head of the patient turned to the left. The imaging angle of the probe was adjusted to obtain a cross-sectional view of the RIJV in the center of the ultrasound screen, with depth adjusted to maximize the image. Once a clear cross-sectional view of the RIJV was visualized, still frame images of the RIJV were captured at end-expiration during a relaxed breathing pattern, and then a second set of images was obtained during the strain phase of Valsalva. The Valsalva maneuver was standardized with a simple manometer attached to a short disposable tube, and the patient was required to forcefully expire and generate pressure of at least 40 mm Hg. The still images were uploaded in bitmap (.bmp) format using software provided with the ultrasound system (Infraview; Sonosite Corp) and analyzed using ImageJ software (National Institutes of Health). Jugular vein cross-sectional measurements at end-expiration and during the stain phase of Valsalva were obtained by manually tracing the luminal edge
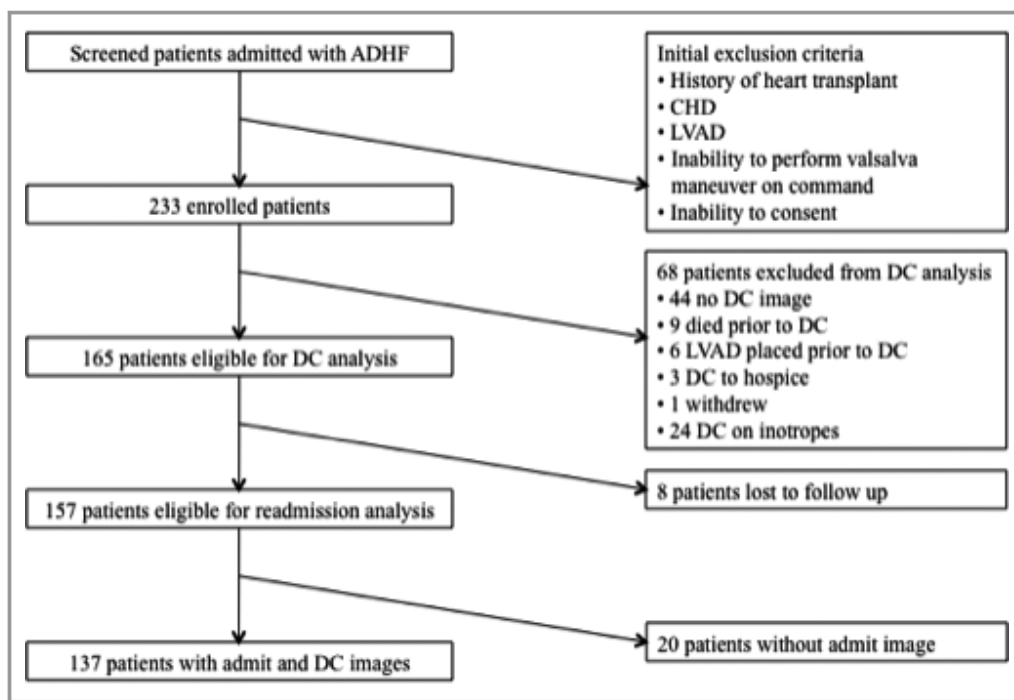
Figure 1. Study design flowchart. ADHF indicates acute decompensated heart failure; CHD, congenital heart disease; DC, discharge; LVAD, left ventricular assist device.

of the vessel on the ultrasound image. This was performed by an investigator blinded to the patients' clinical status.

Study Design and Data Collection

Patients were enrolled during ADHF admissions to our heart failure service. Ultrasound images were obtained at admission during the acutely decompensated state. Additional ultrasound images were obtained before any right heart catheterizations to provide data for a receiver operating characteristic (ROC) curve to determine the optimal test parameter to identify elevated left ventricular filling pressures, defined as RAP $\geq$12 mm Hg. Discharge ultrasound images were taken once the patients were determined to be euvolemic and transitioned to oral diuretics. Patient weight, creatinine level, and net fluid status at the time of each image collection were also recorded. Early readmission data were obtained through review of the medical system's electronic medical records as well as by a phone call to each patient to ascertain whether they required readmission for ADHF in the 30 days after discharge from the index hospitalization.

Statistical Analysis

The change in RIJV CSA measurements between end-expiration and the strain phase of Valsalva were tabulated and compared with the resting RAP for all patients enrolled in

the study. A ROC curve was generated from these data, and the area under the curve (AUC) was tested for a significant difference from 0.5 (null hypothesis) using RAP $\geq$12 mm Hg to indicate hypervolemia. The ROC curve determined the optimal ultrasound measurement threshold to indicate volume overload to provide an AUC of $>0.8\pm0.05$. To test for associations between RAP and change in RIJV CSA with Valsalva, the Fisher exact test was used, given the relatively small sample size. The diagnostic utility of this percentage change in RIJV CSA with Valsalva was assessed by calculating the sensitivity, specificity, and positive and negative predictive values. To test the association between change in RIJV CSA with Valsalva and early readmission, defined as 30 days, the Fisher exact test was again used. The diagnostic utility of the ultrasound measurement at discharge was assessed by calculating the sensitivity, specificity, and positive and negative predictive values. Statistical significance was defined as 2-sided $P<0.05$. Statistical analysis was performed with SPSS Statistics 20 (IBM Corp). Exploratory analyses were conducted to test whether key patient characteristics at baseline such as age, comorbidities, renal function, BNP, net fluid status, and weight were associated with the percentage change in RIJV CSA using Wilcoxon rank-sum tests for continuous data and χ^2 or Fisher exact tests for categorical data. Multivariable logistic regression was used to adjust for the effect of these factors on RAP and percentage change in RIJV CSA. The analyses were conducted according to the

Table 1. Baseline Patient Characteristics

Characteristic	Discharge RAP <12 mm Hg (n=85)	Discharge RAP ≥12 mm Hg (n=72) Baseline	P Value
Age, y	62±14	62±13	0.66
Male, %	73	63	0.08
CAD, %	49	58	0.26
HFpEF, %	33	19	0.06
HTN, %	58	64	0.43
COPD, %	21	33	0.09
OSA, %	29	25	0.54
DM, %	36	58	0.01
CKD stages 3–5, %	22	40	0.02
Total cholesterol, mg/dL	130±37 (n=71)	131±41 (n=60)	0.86
LDL, mg/dL	72±27 (n=69)	74±30 (n=59)	0.83
HDL, mg/dL	35±14 (n=71)	34±12 (n=60)	0.57
SBP admission, mm Hg	121±23 (n=84)	118±23	0.40
DBP admission, mm Hg	72±19 (n=84)	68±17	0.16
Temperature admission (C)	36.6±0.6 (n=84)	36.5±0.5	0.85
Heart rate admission, beats/min	86±15 (n=84)	84±18	0.52
Respiratory rate admission, breaths/min	19±3 (n=84)	19±3	0.38
BMI admission, kg/m^2	30.9±8.1 (n=83)	33.9±9.0 (n=71)	0.03
Cr admission, mg/dL	1.5±0.9 (n=84)	1.8±1.2	0.10
BNP admission, pg/mL	1014±1003 (n=71)	1032±962 (n=61)	0.91

Data are shown as mean±SD except as noted. BMI indicates body mass index; BNP, B-type natriuretic peptide; CAD, coronary artery disease; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; Cr, serum creatinine; DBP, diastolic blood pressure; DM, diabetes mellitus; HDL, high-density lipoprotein; HFpEF, heart failure with preserved ejection fraction; HTN, hypertension; LDL, low-density lipoprotein; OSA, obstructive sleep apnea; RAP, right atrial pressure; SBP, systolic blood pressure.

intention-to-treat principle with 2-sided hypothesis tests and α=0.05. Categorical data are presented as percentages, and normally distributed continuous data are presented as mean±SD. Log-transformed values for BNP (logBNP) were used to reduce the effect of the typical skewness of BNP values.

Results

A total of 157 patients were assessed (Table 1). An ROC curve was generated from those patients (n=76) with both right heart catheterization and RIJV imaging. The ROC curve was generated using percentage change in RIJV CSA during Valsalva and resting RAP (Figure 2). An increase in RIJV CSA of <66% with Valsalva predicted elevated RAP (≥12 mm Hg) with sensitivity of 77% and specificity of 75% (AUC: 0.79; 95% confidence interval [CI], 0.68–0.90; *P*<0.05, where the *P* value indicated the likelihood that the AUC is significantly different from the null hypothesis AUC value of 0.5). A positive test was defined as <66% increase in RIJV CSA during Valsalva. The

positive predictive value of the test was 87%, and the negative predictive value was 60%. As there can be a discrepancy in elevation of right- and left-sided filling pressures (R-L mismatch),[10,11] we reviewed the hemodynamic data and found 18 mismatches (24%), of which 6 patients had high pulmonary artery wedge pressure with low RAP and 12 had high RAP with low pulmonary artery wedge pressure. When removing the 18 R-L mismatches from analysis, similar results were found (increase in RIJV CSA of <73% with Valsalva predicted elevated RAP with sensitivity of 72% and specificity of 83%; AUC: 0.79; 95% CI, 0.66–0.92; *P*<0.05). Similarly, we separately analyzed patients with heart failure with reduced ejection fraction compared with preserved ejection fraction. In heart failure with reduced ejection fraction, an increase in RIJV CSA of <66% with Valsalva predicted elevated RAP (≥12 mm Hg) with sensitivity of 75% and specificity of 80% (AUC: 0.79; *P*=0.001), whereas in heart failure with preserved ejection fraction, an increase in RIJV CSA of <66% with Valsalva predicted elevated RAP (≥12 mm Hg) with sensitivity of 71% and specificity of 73% (AUC: 0.74; *P*=0.09).
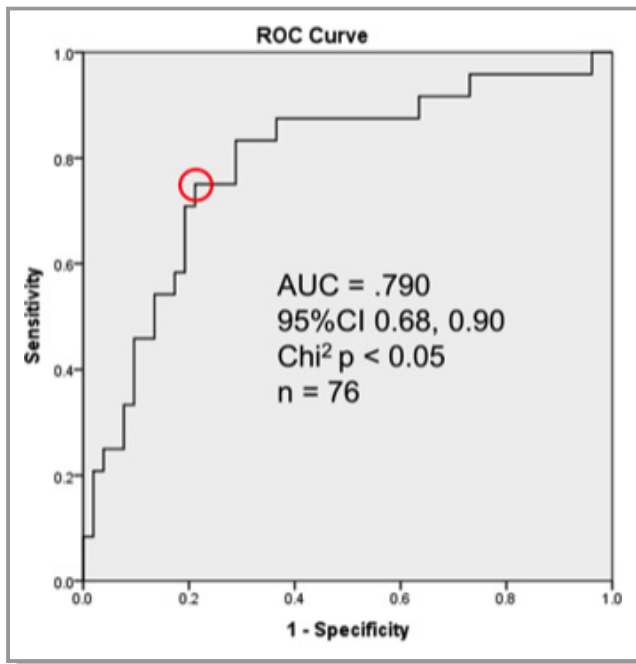
Figure 2. ROC curve of right internal jugular vein (RIJV) cross-sectional area (CSA) compared with right atrial pressure (RAP) representing optimal RIJV CSA (red circle). An increase in RIJV CSA of <66% with Valsalva predicted elevated RAP (≥12 mm Hg) with sensitivity of 77% and specificity of 75% (AUC: 0.79; 95% CI, 0.68–0.90; $P<0.05$). AUC indicates area under the curve; CI, confidence interval; ROC, receiver operating characteristic.

Table 2. Logistic Regression Analysis of Patient Characteristics and the Effect on 30-Day Readmission

Characteristic	Hazard Ratio	95% CI Lower	95% CI Upper	P Value
CSA <66% at discharge	5.2	1.4	19.4	0.02
Age	1.0	0.97	1.1	0.35
Sex	0.65	0.18	2.3	0.51
CAD	0.55	0.15	2.0	0.37
HFpEF	0.87	0.19	4.0	0.86
HTN	1.3	0.39	4.5	0.66
COPD	0.64	0.17	2.5	0.52
OSA	0.86	0.18	4.2	0.85
DM	0.75	0.21	2.7	0.66
CKD stages 3–5	0.61	0.17	2.1	0.44
BNP admission	1.0	0.99	1.01	0.80
BMI	0.99	1.0*	1.0†	0.79

An abnormal test (<66% increase in right internal jugular vein CSA) at discharge was independently associated with 30-day readmission (hazard ratio: 5.2; 95% CI, 1.4–19.4). BMI indicates body mass index; BNP, B-type natriuretic peptide; CAD, coronary artery disease; CI, confidence interval; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CSA, cross-sectional area; DM, diabetes mellitus; HFpEF, heart failure with preserved ejection fraction; HTN, hypertension; OSA, obstructive sleep apnea.
*Rounded from 0.999.
†Rounded from 1.001.

In total, 157 patients had ultrasound evaluations of the RIJV at the time of discharge (Table 1). Trends were noted in the group with a normal change in RIJV CSA during Valsalva, suggesting RAP <12 mm Hg, in that they were more commonly male ($P=0.08$), had preserved ejection fraction heart failure ($P=0.06$), and had less chronic obstructive pulmonary disorder ($P=0.09$). In patients with an abnormal change in RIJV CSA during Valsalva, there was statistically more diabetes mellitus ($P=0.01$), chronic kidney disease stage ≥3 ($P=0.02$), and higher body mass index ($P=0.03$). There was a significant difference in the ultrasound test outcome

Figure 3. Fisher exact test results comparing 30-day readmission with change in right internal jugular vein cross-sectional area. ΔCSA indicates change in cross-sectional area.

(normal or abnormal RIJV CSA change) between the admission and discharge images (n=137, $P<0.05$). Of the 137 patients with both admission and discharge imaging, 90 (66%) had an abnormal RIJV CSA change at hospital admission, with only 31 patients (34%) improving RIJV CSA change to ≥66% ($P<0.05$); importantly, these patients were less than half as likely to be readmitted compared with patients with a persistently abnormal internal jugular CSA change. There were 23 early (30-day) readmissions in the study population, representing an early readmission rate of 15%. Using Fisher exact testing (Figure 3), patients with ≥66% increase in RIJV CSA during Valsalva had a 91% predictive value for avoiding 30-day readmission ($P<0.05$). Patients with an abnormal test, <66% increase in RIJV CSA, were more than twice as likely to be readmitted compared with those with a normal test (21% versus 9%). After controlling for age, sex, BNP, and comorbidities, an abnormal test (<66% increase in RIJV CSA) at discharge was independently associated with 30-day readmission (hazard ratio: 5.2; 95% CI, 1.4–19.4; Table 2).

Typical ultrasound images from 2 patients admitted with ADHF in our study are shown in Figure 4. Patient A has little change in RIJV CSA during Valsalva at admission, reflecting elevated RAP (25 mm Hg). After diuresis, at discharge, the normal RIJV CSA has been restored, reflecting normal RAP (7 mm Hg). This patient avoided 30-day readmission. Patient
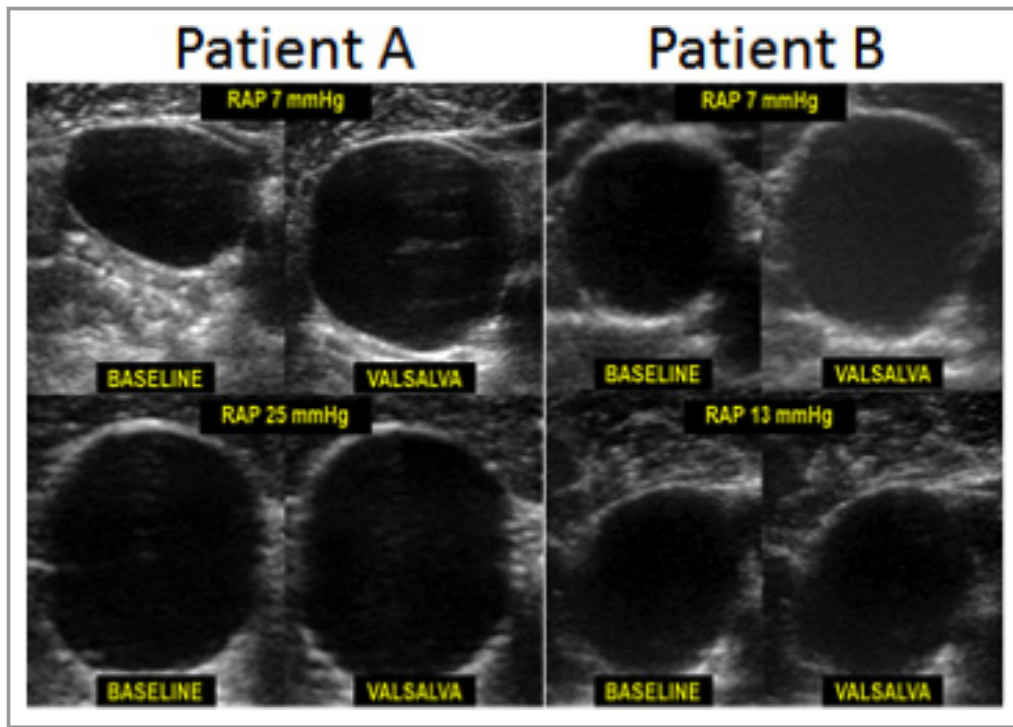
Figure 4. Typical ultrasound images from study patients. The upper row of images shows changes in right internal jugular vein (RIJV) cross-sectional area (CSA) with Valsalva at discharge, and the lower row of images shows changes in RIJV CSA with Valsalva at admission. Patients A and B had CSA change <66% admission (bottom row) and CSA change >66% at discharge (top row). RAP indicates right atrial pressure.

B was also admitted with ADHF but with less extremely elevated RAP (13 mm Hg), and initial imaging again revealed a blunted increase in RIJV CSA during Valsalva. With successful treatment and diuresis, RAP returned to normal, as did the response of the RIJV CSA during Valsalva.

Discussion

In the United States, patients aged >65 years account for 6.5 million hospital days for CHF.[11] CHF is the most common and costly diagnosis-related group for Medicare patients. The cost, which is mainly related to hospitalizations in the United States alone, is >$34 billion per year.[12] Treatment developments have decreased morbidity and mortality for CHF, but ADHF still carries a high 30-day readmission rate.

Many studies have been conducted to evaluate the predictive values for readmissions and have used both novel and readily available methods. In general, these studies are heterogeneous with respect to end points. End points vary from composite cardiac measures to both heart failure–specific and all-cause readmissions within 30 days to durations of ≥6 months, with inconsistent study designs (ie, ambulatory or ADHF). Studies include evaluations of clinical parameters such as angina, low systolic blood pressure, edema levels, elevated jugular venous pressure, age, depressive symptoms, and the

presence of coronary heart disease and pacemakers.[13] Serum biomarkers have received the most attention, as simple objective measurements that can be and are routinely performed at admission, such as BNP,[14–16] blood urea nitrogen,[17,18] hemoglobin and hematocrit,[19] cystatin,[15] and cardiac troponin.[15] Hemodynamic predictors have also been evaluated to more specifically determine volume status to prevent premature hospital discharges and to reduce readmissions. Two-dimensional echo-Doppler techniques have been used to measure early diastolic velocity and tissue-Doppler techniques have been used to measure early diastolic mitral annular velocity as a measure of left ventricular filling pressure to estimate hemodynamic profiles and to predict outcomes[14]; however, the evidence for this technique, even under exercise or pharmacologic stress, remains limited, and further validation of its efficacy is required.[20–23] Recently the concept of impedance, which correlates to pulmonary artery wedge pressures, as measured by cardiac resynchronization therapy defibrillator devices, has shown promise but requires an implanted device.[24] Simpler bedside ultrasound devices have been used to measure hepatic venous flow[25] and inferior vena cava collapsibility index[16,26,27] as measures of RAP and central venous pressure, respectively. Ultimately, no technique has emerged as a validated and reproducible predictor of early 30-day readmission following treatment for ADHF.

In this study, we confirmed the ability of simple bedside ultrasound measurement of the internal jugular vein to detect elevated RAP in ADHF patients. In our ADHF patient group, the cutoff value for CSA change was different than in our validation cohort based on the ROC curve data (Figure 2).[9] In the previous group, the majority of the patients studied were euvolemic, whereas the current patient group hospitalized was acutely decompensated. Consequently, the prevalence of disease (elevated central venous pressure) was different, and thus a different cut point on the ROC curve was obtained. Nonetheless, even with this different cut point, our test had similar sensitivity and specificity for predicting elevated RAP (≥12 mm Hg), as reported earlier. The positive versus negative predictive values were reversed from those observed previously, largely because of a higher prevalence of elevated RAP in the current study group; therefore, our measurement predicted elevated RAP (≥12 mm Hg) with a positive predictive value of 87%. Discrepancy between elevation of right- and left-sided filling pressures in heart failure (R-L mismatch) could induce error in our results; however, we found such mismatch occurring only in a minority of patients (24%), similar to prior reports, and exclusion of these patients did not alter the test characteristics.[10]

In total, 157 patients had an ultrasound measurement at the time of discharge, and an observed early readmission rate of 15% resulted in 23 total early readmissions. With a negative predictive value of 91%, the test was able to identify those patients who did not require hospital readmission with recurrent ADHF within the next 30 days. Although the bedside ultrasound measurement had low sensitivity and specificity, its negative predictive strength has the potential to identify patients earlier in their hospital course who are sufficiently compensated in their disease and who would be ready to continue management as outpatients. In terms of a marker of decompensation, this ultrasound technique can be used to determine the effectiveness of diuretic therapy. Approximately 50% of patients had an abnormal test at discharge, and they were twice as likely to be readmitted within 30 days versus the normal test group. Discharge BNP was not the standard of care at our institution, so it was not collected routinely, but the similar percentages of patients with persistently low RIJV compliance seen at discharge in this study and elevated BNP at discharge in prior studies (≈50%) raise the possibility that these phenomena may be concurrent and represent a high-risk population.[28] This tool could assist clinical decision-making and potentially alter discharge planning to reduce readmissions.

The translational outlook for the proposed methodology is promising. Our current standard assessment of ADHF patient volume status is inaccurate and may contribute to unnecessary readmission, which is profoundly costly. In this work, we demonstrate the utility of this noninvasive, objective, rapid, and portable technique for predicting freedom from hospital readmission at 30 days. This approach leverages our understanding of vascular physiology and growing availability of portable ultrasound. We envision that all heart failure patients admitted with ADHF will undergo a daily objective assessment of volume status, using our technique, that will be recorded in the medical record and used to guide diuretic therapy and discharge planning. Our current approach requires off-line image analysis and calculation of change in internal jugular CSA, which is currently not performed in real time. The main impediment to this vision is the integration of automatic vein edge detection to allow for real-time calculation of change in internal jugular CSA. By incorporating an automatic edge detection algorithm into the ultrasound system software, change in internal jugular CSA could be performed as a point-of-care test for real-time translation into patient management.

This study includes several limitations. It was performed at a single institution and ideally should be validated in a larger multicenter study. Although discrepancy between elevation of right and left-sided filling pressures (R-L mismatch) can occur in heart failure which might impact these findings, this occurred in too small a number of patients to separately analyze; however, excluding them from analysis did not substantially alter the CSA cut point and test characteristics. R-L mismatch may result from pulmonary arterial hypertension, but few patients of in the present cohort had pulmonary arterial hypertension driving an R-L mismatch (3 of 12 patients with elevated RAP and a normal pulmonary artery wedge pressure); this prevented more detailed analysis of this cohort but suggests that this test may be applicable to the majority of ADHF patients. Another confounder of variability in ultrasound measurements of left ventricular filling can be in the setting of heart failure with preserved ejection fraction[20]; however, test characteristics were similar between heart failure with preserved ejection fraction (n=18; AUC: 0.740 [P=0.09]; CSA of <66% with Valsalva predicted elevated RAP with sensitivity of 71% and specificity of 73%) and heart failure with reduced ejection fraction (n=55; AUC: 0.785 [P=0.001]; CSA of <66% with Valsalva predicted elevated RAP with sensitivity of 75% and specificity of 80%). We did not have data on atrial fibrillation and so cannot comment on whether this affects RIJV CSA change with Valsalva; although atrial fibrillation may be associated with reduced atrial compliance, we are not aware of any data to suggest that venous compliance is also affected. For readmissions not occurring within our health system, we acknowledge the potential inaccuracy of patient recall.

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Disclosures

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