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Comparison of Hand-Carried Ultrasound Assessment of the Inferior Vena Cava and N-Terminal Pro-Brain Natriuretic Peptide for Predicting Readmission After Hospitalization for Acute Decompensated Heart Failure

Sascha N. Goonewardena, MD, Anthony Gemignani, MD, Adam Ronan, MD, Samip Vasaiwala, MD, John Blair, MD, J. Matthew Brennan, MD, Dipak P. Shah, MD, Kirk T. Spencer, MD, FACC

Chicago, Illinois

OBJECTIVES We sought to compare the value of serial assessment with hand-carried ultrasound (HCU) of the inferior vena cava (IVC) with brain natriuretic peptide (BNP) to identify patients with acute decompensated heart failure (ADHF) who will be readmitted or seek emergency department treatment after hospital discharge.

BACKGROUND Congestive heart failure (CHF) is a leading cause for hospitalization and, once hospitalized, patients with CHF frequently are readmitted. To date, no reliable index exists that can be used to predict whether patients with ADHF can be discharged with low readmission likelihood.

METHODS A total of 75 patients who were admitted with a primary diagnosis of ADHF were followed. All patients were assessed at admission and discharge with the use of routine clinical evaluation, BNP measurement, and HCU evaluation of the IVC by physicians with limited training in ultrasound.

RESULTS During the 30-day follow-up, 31 patients were rehospitalized or presented to the emergency department. Patients who were subsequently readmitted could not be differentiated from those who were not readmitted by their demographics, comorbidities, vital signs, presence of symptoms/signs suggestive of persistent congestion, hospital length of stay, or net volume removal. Routine laboratory tests, including assessment of renal function, also failed to predict readmission with the exception of serum sodium. Although admission BNP was similar in patients readmitted and not readmitted, pre-discharge log-transformed BNP was greater in patients who subsequently were readmitted. Patients who required repeat hospitalization had a larger IVC size on admission as well as at discharge. In addition, patients who were readmitted had persistently plethoric IVCs with lower IVC collapsibility indexes. At discharge, only serum sodium, log-transformed BNP, IVC size, and collapsibility were statistically significant predictors of readmission.

CONCLUSIONS This study confirms that, once hospitalized, patients with CHF frequently are readmitted. Bedside evaluation of the IVC with a HCU device at the time of admission and discharge, as well as pre-discharge BNP, identified patients admitted with ADHF who were more likely to be readmitted to the hospital. (J Am Coll Cardiol Img 2008;1:595–601) © 2008 by the American College of Cardiology Foundation

From the University of Chicago Hospitals, Chicago, Illinois.
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Congestive heart failure (CHF) is a major source of cardiovascular morbidity and a leading cause for hospitalization among patients older than the age of 65 years. Once hospitalized, patients with CHF frequently are readmitted with recurrent symptoms. To date, no reliable index exists that can be used to predict whether patients with acute decompensated heart failure (ADHF) are adequately treated and can be discharged with low readmission likelihood. Because many of these readmissions are due to congestion, the accurate determination of volume status could prove useful to establish the suitability for discharge.

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ABBREVIATIONS AND ACRONYMS

ADHF = acute decompensated heart failure
BNP = brain natriuretic peptide
CHF = congestive heart failure
EF = ejection fraction
HCU = hand-carried ultrasound
IVC = inferior vena cava
IVCCI = inferior vena cava collapsibility index
IVCmax = maximum diameter of the inferior vena cava
IVCsniff = minimum diameter of the inferior vena cava
logBNP = log-transformed values for brain natriuretic peptide
LV = left ventricle

Traditional bedside physical examination of a hospitalized CHF patient's volume status involves the assessment of several signs that have poor specificity and sensitivity or are difficult to perform accurately. Invasive measurements of right atrial pressure and pulmonary capillary wedge pressure are the gold standards for the determination of intravascular volume status but are impractical in most patients. Brain natriuretic peptide (BNP) has proven beneficial in the diagnosis of CHF. In addition to its diagnostic potential, BNP may have a role in the serial assessment and monitoring of patients with ADHF (1–4).

We hypothesized that because ultrasound evaluation of the inferior vena cava (IVC) size and collapsibility is an accurate predictor of right atrial pressure, this assessment might prove to be helpful in monitoring patients with ADHF (5,6). However, the cost and inconvenience of serial bedside evaluation of the IVC with large full-featured ultrasound platforms limits the applicability in clinical settings. Recent advances in hand-carried ultrasound (HCU) devices have made this technology ideal for point-of-care clinical assessments and their utility has been demonstrated in diverse clinical settings (7–14). In addition, multiple studies have demonstrated that noncardiologists with limited training and experience can perform focused HCU examinations with high reproducibility and accuracy (10,15–19). Therefore, in this work, we sought to compare the value of serial HCU assessment of IVC size and collapsibility with that of BNP to identify ADHF patients who will be readmitted or seek emergency department treatment after hospital discharge.

METHODS

Patients admitted to the University of Chicago Hospital with a primary diagnosis of ADHF were prospectively screened. Patients were excluded if they were transferred from an outside hospital, admitted to an intensive care unit, admitted with an acute coronary syndrome, required renal replacement therapy, or were unwilling or unable to provide informed consent. The treating cardiologist, who was blinded to the results of the HCU results, made management and discharge decisions. The Institutional Review Board of the University of Chicago approved the study.

Vital signs, CHF symptoms and signs, cardiac medications, and serum chemistries were noted on admission and at discharge. Dietary and medicine adherence were assessed with a subjective 4-point scale. N-terminal pro-BNP was measured on admission and discharge by electrochemiluminescence immunoassay in a standardized hospital laboratory. Readmission or emergency department visits were ascertained by review of medical records and phone interview 30 days after hospital discharge.

Internal medicine residents with minimal echocardiographic exposure and no previous formal training in ultrasonography performed the HCU studies. Before data acquisition, each of the residents underwent 4 h of formal didactic ultrasound training and performed 20 sonographer-supervised acquisitions and measurements of the IVC from the subcostal approach. Previous research has demonstrated a 90% success rate for obtaining IVC measurements for physicians with this amount of training (20).

Within 12 h of hospital admission, all patients underwent a brief echocardiographic examination with a HCU device (Optigo, Philips Medical Systems, Andover, Massachusetts). A second HCU examination was performed at the end of the hospitalization once the treating physicians made the decision to discharge the patient. Care was taken to obtain the maximal IVC diameter throughout the respiratory cycle. The maximum (IVCmax) and minimum (IVCsniff) diameter after having the patient sniff were measured 2.0 cm from the IVC right atrial junction with the use of electronic calipers. Images were not stored. The IVC collapsibility index (IVCCI) was calculated as (IVCmax − IVCsniff)/(IVCmax).

Table 1. Demographics and Past Medical History in All Patients

	All Patients
Age, yrs	61 ± 15
Male	53%
EF, %	29 ± 16
EF <40%	80%
ICM	42%
Previous CHF admission (6 months)	59%
Prior admission (6 months)	1 (2)
NYHA functional class I to II	30%
Hypertension	87%
Diabetes	41%
COPD	19%
CrCl <60 ml/min/1.73 m^2	61%
Atrial fibrillation	16%
Depression	15%
Good diet compliance	43%
Good drug compliance	71%
Doctor contact	51%

CHF = congestive heart failure; COPD = chronic obstructive pulmonary disease; CrCl = creatinine clearance; EF = ejection fraction; ICM = ischemic cardiomyopathy; NYHA = New York Heart Association.

Statistical analysis. Categorical data are presented as percentages; normally distributed continuous data as mean ± SD; and non-normally distributed variables as median and interquartile range. Log-transformed values for BNP (logBNP) were used to reduce the effect of the typical skewness of BNP values. Patients were divided into 2 groups, no readmission and readmission, according to a composite outcome measure that included emergency department visit or hospital readmission at 30 days after the index hospitalization. Statistical differences between these groups were assessed with the use of unpaired *t* tests and chi-square analysis. Binary logistic regression was applied to test discharge variables' abilities to predict readmission. The 3 most significant variables on univariable analysis were added to the regression by the use of forward stepwise analysis. Receiver operator curves were calculated for continuous variables significant on univariable analysis. Optimal cutoff points were selected by maximizing accuracy. A p value <0.05 was considered statistically significant. Intraobserver variability is reported as the coefficient of variation.

RESULTS

A total of 75 patients were enrolled with a mean age of 61 years (53% men). Left ventricular (LV) systolic dysfunction was common (80%), and the mean ejection fraction (EF) was 29 ± 16%. Most patients had previous admissions for CHF in the last 6 months (59%), with the average number of CHF admissions numbering 1.6 ± 3.0 (range 0 to 20). Comorbidities were common (Table 1), as were typical CHF signs and symptoms (Table 2). Most patients were already on an outpatient CHF regimen with a high use of angiotensin-converting enzyme inhibitors, beta-blockers, and diuretics (Table 3). The mean admission BNP level was elevated at 12,163 ± 15,923 pg/ml (range 232 to 67,494 pg/ml). The IVC on admission was plethoric, with 67% of the patients having a diameter >2.0 cm (mean 2.3 ± 0.5 cm) and 90% of patients had a collapsibility index <50% (mean 27 ± 21%). Inferior vena cava size and logBNP were poorly correlated (r = 0.23), as were IVC collapsibility and logBNP (r = −0.12).

The average hospital length of stay was 4.1 ± 2.5 days (range 1 to 14 days). Net diuresis averaged 6.1 ± 6.6 liters, with significant improvement in CHF signs and symptoms (Table 2). There were significant reductions in systolic blood pressure, diastolic blood pressure, and heart rate and small-but-significant reductions in serum sodium and increases in bicarbonate with therapy (Table 4). During the hospitalization, there was a 40% decrease in BNP values. Although IVCmax decreased and IVCCI increased, 44% of the patients continued to have an IVC diameter >2.0 cm, and 66% had IVC collapsibility <50% at discharge. Ninety-six percent of patients were prescribed a diuretic at discharge, and the rates of angiotensin-converting enzyme inhibitor and beta-blocker use were increased compared with admission.

During the 30-day follow-up, 31 patients were rehospitalized or presented to the emergency department. A total of 84% of the patients in whom

Table 2. Vital Signs and CHF Symptoms/Signs in All Patients

	All Patients		
	Admission	Discharge	p Value
HR (beats/min)	87 ± 19	80 ± 14	0.001
SBP (mm Hg)	127 ± 28	117 ± 24	0.01
DBP (mm Hg)	72 ± 14	62 ± 13	<0.001
Net diuresis (liters)	—	4.4 (5.9)	—
LOS (days)	—	4.1 ± 2.5	—
PND	51%	16%	<0.001
Abd distention	40%	14%	0.01
Dyspnea	92%	16%	<0.001
Increased JVP	92%	79%	0.05
Edema	72%	12%	<0.001

Abd = abdominal; CHF = congestive heart failure; DBP = diastolic blood pressure; HR = heart rate; JVP = jugular venous pulse; LOS = length of stay; PND = paroxysmal nocturnal dyspnea; SBP = systolic blood pressure.

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Table 3. Medication Usage in All Patients

	All Patients		
	Admission	Discharge	p Value
ACEi or ARB	70%	85%	0.10
Beta blocker	74%	81%	0.32
Aldo blocker	21%	37%	0.03
Diuretic	85%	96%	0.02
H/I	10%	12%	0.60
Inotrope	—	17%	—
Nesiritide	—	1%	—

ACEi = angiotensin-converting enzyme inhibitor; Aldo = aldosterone; ARB = angiotensin receptor blocker; H/I = hydralazine-isosorbide.

the readmission diagnosis was known were admitted for CHF (63% CHF, 12% non-CHF, 24% unknown). On admission to the hospital, patients who were subsequently readmitted could not be distinguished from those who were not readmitted by age, EF, CHF class, comorbidities, vital signs, or symptoms. Although medication compliance and physician follow-up did not differ between groups, more patients in the group not readmitted had self-reported adherence to dietary sodium restriction (62% vs. 26%; $p = 0.04$). Patients who were already being treated with a beta-blocker or diuretic at admission were more likely to be readmitted.

Admission serum laboratory values, including BNP, were indistinguishable between groups, with the exception of the admission sodium level, which was slightly lower in patients who were readmitted (137 vs. 140 mEq/l; $p = 0.001$). Although initial IVCmax was slightly larger in readmitted patients, the IVCCI was similar between groups. Before inpatient treatment, most patients had either an IVCmax >2.0 cm or IVCCI <50% in both the not-readmitted (91%) and readmitted group (96%).

Patients who were subsequently readmitted could not be differentiated from those who were not readmitted by their discharge vital signs or the presence of symptoms/signs suggestive of persistent congestion. Admission weight, discharge weight, and weight changes were statistically equal in the 2 groups. Patients who successfully remained out of the hospital did not have a longer length of stay or greater net volume removal. Discharge medications did not differ between groups, although inotropic drug usage was more common in patients readmitted.

Patients who remained out of the hospital in follow-up were more likely to have had a beta-blocker, aldosterone blocker, or diuretic started during their admission, which primarily reflects the relatively lower use of these agents in these patients on admission rather than the failure to start them in the readmission group. Pre-discharge routine laboratory values, including those reflecting renal function, were not useful in distinguishing between groups with the exception of serum sodium, which was lower in readmitted patients (134 vs. 137 mEq/l; $p = 0.004$). Serum BNP had extensive overlap between groups and was not statistically different; however, pre-discharge logBNP was greater in patients subsequently readmitted.

As a group, the HCU IVC measurements taken pre-discharge were statistically different between the patients who were readmitted and not readmitted. Patients who required repeat hospitalization had larger IVC maximal diameters and lower collapsibility indexes (Table 5). Using traditional cutoffs for increased right atrial pressure (IVC >2.0 cm or IVCCI <50%), we found that patients requiring rehospitalization had abnormal pre-discharge values of IVC size nearly 3 times as often (21% vs. 61%; $p < 0.001$) and abnormal IVC collapsibility 1.5 times more frequently (47% vs. 71%; $p = 0.01$) compared with the group of patients who were not rehospitalized.

Of all variables at discharge, only serum sodium ($p = 0.002$), logBNP ($p = 0.005$), IVCmax ($p < 0.001$), and IVC collapsibility ($p = 0.002$) were statistically significant predictors of readmission. In multivariate analysis with the 3 most significant variables, IVCmax and logBNP were the most powerful predictors (odds ratios 10.3 and 6.1, respectively, regression model $z = 23.4 + 2.3$ [IVCmax] $+ 1.8$ [logBNP] $- 0.25$ [serum sodium]). Receiver operator curves for these variables demonstrated area under the curves of 0.69, 0.78, and 0.74 for BNP, IVCmax, and IVC collapsibility, respectively (Fig. 1). Optimal cutoff points for predicting readmission were 2,327 for BNP (sensitivity 82%, specificity 56%), 2.0 cm for IVCmax (sensitivity 81%, specificity 72%), and 38% for IVC collapsibility (sensitivity 67%, specificity 75%). Intraobserver

Table 4. Serum Chemistries in All Patients

	All Patients		
	Admission	Discharge	p Value
Sodium (mEq/l)	138 ± 4	136 ± 4	<0.001
Bicarbonate (mEq/l)	24 ± 4	28 ± 4	<0.001
BUN (mg/dl)	35 ± 24	36 ± 23	0.43
Creatinine (mg/dl)	1.6 ± 0.7	1.5 ± 0.6	0.07
Creatinine clearance (ml/min/1.73 m^2)	50 ± 22	51 ± 20	0.55
Hemoglobin (g/dl)	12.2 ± 1.9	12.0 ± 1.9	0.79

BUN = blood urea nitrogen.

Table 5. BNP, IVC Size, and Collapsibility in All Patients and 2 Subgroups

	All Patients			Admission			Discharge		
	Admission	Discharge	p Value	No Readmit	Readmit	p Value	No Readmit	Readmit	p Value
BNP (pg/ml)	6,139 (9,714)	3,497 (4,824)	—	6,177 (10,091)	5,982 (9,208)	—	2,106 (3,298)	4,888 (5,112)	—
logBNP	3.8 ± 0.5	3.5 ± 0.6	<0.001	3.7 ± 0.6	3.8 ± 0.5	0.28	3.3 ± 0.7	3.6 ± 0.4	0.04
IVCmax (cm)	2.3 ± 0.5	2.0 ± 0.6	<0.001	2.2 ± 0.5	2.4 ± 0.4	0.02	1.7 ± 0.6	2.3 ± 0.5	0.001
IVCsniff (cm)	1.7 ± 0.7	1.2 ± 0.8	<0.001	1.5 ± 0.7	1.9 ± 0.6	0.03	0.9 ± 0.7	1.5 ± 0.7	<0.001
IVCCI (%)	27 ± 21	45 ± 27	<0.001	31 ± 23	23 ± 16	0.10	57 ± 27	36 ± 22	0.002

Admission and discharge values in all patients compared with paired *t* test. No readmit and readmit subgroups compared with unpaired *t* test.
BNP = brain natriuretic peptide; IVC= inferior vena cava; IVCCI = inferior vena cava collapsibility index; IVCmax = maximum diameter of the inferior vena cava; IVCsniff = minimum diameter of the inferior vena cava; logBNP = log-transformed values for brain natriuretic peptide.

variability was 7.5% for IVCmax and 9.7 % for IVC collapsibility.

DISCUSSION

This study confirms that, once hospitalized, patients with CHF frequently are readmitted because of recurrent symptoms. The readmission rate at 30 days in this study was 41%, which is similar to previously reported values of 30% to 44% within 1 to 6 months post-discharge (1–4,21). None of the clinical predictors were useful for distinguishing patients who would be readmitted from those not requiring rehospitalization, with the exception of inotrope use during the acute treatment, which has been noted previously (4). Although some studies suggest patients with lower LVEFs are more likely to be readmitted (2,3), others similar to our study did not find differences in LVEF between groups (1,4).

Most readmissions in CHF patients reflect that some patients with CHF, because of either dietary or medical noncompliance, reaccumulate excessive fluid. This observation is supported by the fact that self-reported adherence to a low-sodium diet was less common in patients readmitted. However, it is also likely that a large proportion of patients with CHF are undertreated and, although symptomatically improved, not euvolemic at the time of discharge despite the clinician's impression to the contrary. This hypothesis is consistent with our study, which shows that after a mean of 4 days of therapy and 6-liter net diuresis, there was a marked reduction in symptoms despite persistent elevations in BNP and nearly two-thirds of patients having persistently reduced IVC collapsibility.

Traditional bedside evaluation of a hospitalized CHF patient's volume status involves the assessment of lower-extremity edema, lung fields, and jugular venous pulse, which have poor accuracy for volume status. Consistent with these limitations, physical examination parameters, including vital signs, were no different between patients who were readmitted and those were not. Although deviation from dry weight can be a powerful clinical tool, an established dry weight was not known in the majority of these patients. Routine clinical chemistries also were unable to predict patient readmission other than serum sodium levels, likely reflecting a subgroup of patients with more severe CHF. Consistent with previous ADHF studies, pre-discharge BNP differed between patients readmitted and those not readmitted, whereas admission BNP did not (1–4).

Several echocardiographic parameters have been shown to correlate with LV filling pressures and therefore might prove useful for assessing whether patients with ADHF have been adequately diuresed (22). The mitral inflow pattern has proved to be

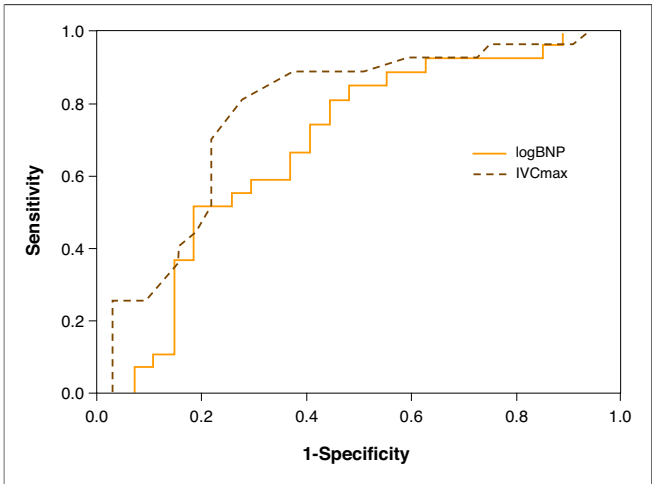

Figure 1. Receiver-Operator Curves

Receiver-operator curves for logBNP **(solid line)** and IVCmax **(dashed line)** to predict hospital readmission. The area under the curve is greater for IVCmax, indicating a greater likelihood of correctly predicting the need for repeat hospitalization after inpatient therapy for acutely decompensated congestive heart failure. logBNP = log-transformed values for brain natriuretic peptide; IVCmax = maximum diameter of the inferior vena cava.

inferior to BNP for predicting readmission in ADHF (3,4) and performs poorly in CHF patients with preserved LVEF. Tissue Doppler-derived E/E′ has shown promise in predicting post-discharge events in patients with ADHF (2). However, this technique requires sophisticated ultrasound devices as well as substantial expertise to perform and interpret. Ultrasound examination of IVC size and collapsibility has proven to be a robust marker of right atrial pressure, a surrogate of volume status (5,6,20). A major advantage of this approach is that IVC evaluation can be performed with a HCU ultrasound device that has limited 2-dimensional imaging capabilities (14,20). The substantially lower cost of HCU devices as well as their increased portability greatly increases the utility for bedside assessment. Their diagnostic utility when operated by personnel with limited training has been proven in multiple clinical settings (10,15–20).

In our study, HCU evaluation of IVC demonstrated that patients discharged after treatment for ADHF who were subsequently readmitted had significantly greater IVCs and lower IVC collapsibility that are consistent with persistent elevation in right atrial pressure. These readmitted patients had significant net diuresis (7.2 liters) and marked improvement in symptoms. However, we hypothesize that, despite this significant diuresis, these patients were likely discharged as persistently hypervolemic. Patients who are discharged with residual congestion are less likely to accommodate fluctuations in sodium intake without precipitating overt CHF symptoms requiring readmission.

Study limitations. There are several limitations to this study, including the relatively small sample size. In addition, these data do not confirm that, if a clinician acted on an abnormal pre-discharge log-BNP or IVCmax by keeping a patient in the hospital longer for further diuresis, that outcome would be altered. Finally, no analysis of the cost-effectiveness of these strategies is available.

CONCLUSIONS

Bedside evaluation of the IVC with a HCU device at the time of admission and discharge as well as pre-discharge BNP identified patients admitted with ADHF who were more likely to be readmitted to the hospital. Because the rate of hospital readmission for CHF patients within 6 months is as high as 50%, any disease-management strategy that could be used to reduce readmissions would prove valuable. It is possible that measurement of the IVC could be used to accurately identify patients who require earlier intensive therapy, more prolonged inpatient diuresis or closer outpatient follow-up to prevent their subsequent unanticipated hospital readmission.

Reprint requests and correspondence: Dr. Kirk T. Spencer, University of Chicago, 5841 S. Maryland MC 5084, Chicago, Illinois 60637. *E-mail: kspencer@uchicago.edu.*

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Key Words: echocardiography ■ congestive heart failure ■ hand-carried ultrasound ■ brain natriuretic peptide.