Original Contribution

Monitoring the response to treatment of acute heart failure patients by ultrasonographic inferior vena cava collapsibility index

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Objective: Our aim was to determine if N-terminal pro-brain natriuretic peptide (NT-proBNP) or sonographic measurements of inferior vena caval (IVC) diameters and collapsibility index (IVC-CI) have a role in the monitoring of acute heart failure (AHF) therapy.

Methods: Inferior vena caval diameters of 50 healthy people (control group) were measured to determine the normal values of the IVC parameters. We then prospectively enrolled patients who were admitted to the emergency department (ED) with a primary diagnosis of AHF. At presentation, IVC diameters were measured during expiration and inspiration, and blood was drawn for NT-proBNP. We repeated the measurement of the IVC parameters and collected a second blood sample 12 hours after the therapy was administered. The data were analyzed in SPSS 15.0 (IBM, Armonk, NY) using the Student t test and Mann-Whitney U test.

Results: A total of 97 subjects were enrolled: 47 in the patient group and 50 in the control group. The mean IVC diameters during expiration were 2.10 ± 0.37 cm before and 1.57 ± 0.24 cm after the therapy (P < .001). The mean IVC diameters during inspiration were 1.63 ± 0.40 cm before and 0.90 ± 0.26 cm after the therapy (P < .001). The mean IVC-CI rose from 22.80% ± 10.97% to 43.09% ± 13.63% (P < .001). After the therapy, there was no difference between the IVC-CI of the patients and controls (P = .246). There was no significant change in the mean NT-proBNP levels after the therapy.

Conclusion: Inferior vena cava collapsibility index may be helpful in monitoring AHF patients’ responses to therapy in the ED.

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1. Introduction

Heart failure (HF) is a major public health problem and is among the most significant causes of morbidity and mortality for older adults in many countries. In the United States, for example, the HF had a prevalence of 5800000 and a yearly incidence of 550000. The incidence of HF increases with age, and it is the leading cause of hospitalization for those 65 years or older, in whom the incidence is 10 per 1000 [1]. In last few decades, there have been dramatic advances in the treatment of chronic HF, but acute HF (AHF) was initially ignored despite being associated with high in-hospital mortality and rehospitalization rates [2]. However, in the last decade, increased attention has been given to AHF, and the terms acute heart failure and acute heart failure syndromes (AHFS) have begun to be regularly used [3,4]. Heart failure consumes 1% to 2% of the total health expenditure in Europe, and hospital management of AHF represents 67% to 70% of this cost [5]. Thus, AHF is a substantial social and financial burden that will continue to grow as successful treatments for previously fatal cardiovascular diseases are implemented [2].

Acute heart failure syndromes are defined as gradual or rapid changes in the signs and symptoms of HF resulting in a need for urgent therapy that may result in unplanned hospitalizations or emergency department (ED) visits [3,4]. The ED is the principal portal of entry for hospitalized AHFS patients. The ED is, for most patients, their initial point of definitive health care contact; it is also the location where primary stabilization is achieved and the site where disposition decisions are generally made [6]. Because the definitive resolution of AHFS patients symptoms is rarely achieved in the ED and due to the challenges of identifying patients at risk for poor outcomes in the ED, including acute and 30-day adverse cardiac events, 80% of
patients who present to the ED with AHFS are hospitalized [7,8]. Evidence-based options for ED management are limited because most ED interventions are based on local practices derived from chronic HF studies or trials conducted on hospitalized patients [9].

Our aim was to compare N-terminal pro-brain natriuretic peptide (NT-proBNP) levels and sonographic measurements of inferior vena caval (IVC) diameters and collapsibility index (IVC-CI) in the monitoring of AHF therapy in the ED.

2. Methods

2.1. Study design

We conducted a prospective cohort study from January 2009 to January 2010. Our local ethics committee approved the study protocol, and written informed consent was obtained from the participants before ultrasonographic examination.

2.2. Study setting and population

This study was conducted at an academic, adult tertiary care center ED in Turkey. This ED serves more than 240,000 adult patients annually and has an overall admission rate of 20%. All patients older than 18 years who were admitted to the ED of Atatürk Research and Training Hospital, Izmir, Turkey, with the primary diagnosis of AHF were screened prospectively. Exclusion criteria included younger than 18 years, pregnancy, liver transplantation, mechanical ventilation, acute abdomen, renal failure, patients who were transferred from other hospitals after the administration of diuretics, bronchodilators, or vasoactive medicines, or an inability to consent for the study.

2.3. Study protocol

Before the study began, 4 emergency medicine residents with minimum 3 years of experience underwent 2 hours of formal didactic ultrasound training and performed 30 measurements of the IVC from the subcostal approach under the supervision of an experienced sonographer. After the study was approved, IVC diameters of 50

healthy people without any chronic disease were measured to determine normal values for the IVC parameters. Once enrollment of AHF patients began, we recorded admission vital signs, AHF symptoms and signs, cardiac medications, serum chemistries, arterial blood gases, and NT-proBNP. N-terminal pro-brain natriuretic peptide levels were measured by the immune fluorescent method and expressed in picograms per millimeters. Within 30 minutes of hospital admission, all patients underwent a brief echocardiographic examination to confirm the AHF diagnosis performed by a cardiologist who was blinded to the study. One of the 4 emergency medicine residents, who was blinded to the echocardiographic results and was not responsible for the treatment of the patient, performed the ultrasonographic IVC measurements. Measurements were taken in the semisupine position using a Titan model ultrasound machine with a 3.5-MHz convex transducer (Sonosite Corp, Bothell, WA). Care was taken to record the maximal IVC diameter seen during an entire respiratory cycle. The maximum (IVC during expiration [IVCexp]) and minimum (IVC during inspiration [IVCins]) IVC diameters were measured distal to the confluence of hepatic veins in M mode (Fig. 1). Multiple measurements were performed on the same patient, and the widest and the narrowest measurements obtained in the same respiratory cycle were used in the statistical analysis. The images showing the obtained measurements were stored. The IVC-CI was calculated as (IVCexp − IVCins)/(IVCexp) × 100. Patients were treated according to the guidelines of the European Society of Cardiology [10].

A second ultrasonographic examination by the emergency medicine residents was performed once the treating cardiologist made the decision to discharge the patient from ED or to admit the patient to the cardiology ward. Disposition vital signs, symptoms and signs, serum chemistries, and NT-proBNP were recorded for all patients leaving the ED.

Acute HF patients were divided into 6 groups according to the guidelines of the European Society of Cardiology [10]; (1) worsening or decompensated chronic HF, (2) pulmonary edema, (3) hypertensive HF, (4) cardiogenic shock, (5) isolated right HF, or (6) acute coronary syndrome and HF. Readmission or repeat ED visits were ascertained by review of medical records and a telephone interview.

![Fig. 1. Sonographic view of inferior vena cava in M mode.](image-url)
30 days after discharge from hospital. Another resident, who was primarily responsible for the study, collected all the data.

2.4. Data analysis

All statistical analyses were performed using SPSS version 15.0 (IBM, Armonk, NY). Categorical data are presented as frequencies and percentages; normally distributed continuous data, as the mean ± SD with minimum and maximum values. The Student t test and the Mann-Whitney U test were used to compare the measured values before and after the therapy was administered. P < .05 was considered statistically significant.

3. Results

A total of 108 patients presented to the ED with the symptoms and signs of AHF during the study period. Sixty-one patients were excluded: 22 did not complete the study (3 died due to cardiogenic shock and 19 left the ED before a second ultrasound was performed), 21 presented from other centers after the initiation of a diuretic, 11 had renal insufficiency, 3 were intubated, and 4 were pregnant (Fig. 2, flow diagram). Forty-seven patients in the study group and 50 in the control group were enrolled in the study. Each of the 4 residents performed 10, 11, 13, and 13 IVC measurements, respectively. The mean age of the patient group was 70.89 ± 10.64 years (range, 49-90 years), and the mean age of control group was 62.92 ± 8.76 years (range, 49-79 years) (P < .001). Patient demographics are presented in Table 1. Of the 47 patients, 24 had acute decompensated HF, 9 had hypertensive HF, 8 had isolated right HF, 3 had pulmonary edema, and 3 had acute coronary syndrome and AHF. Comparisons of the IVC parameters of the patient and the control groups before and after the treatment are shown in Table 2. Blood chemistry and NT-proBNP results are shown in Table 3. Twenty-two of the patients were hospitalized, and 25 were discharged from ED according to the decision of the treating cardiologist. Of the patients, 6 (4 who were discharged from ED and 2 who were hospitalized) were readmitted to the ED within 1 month with the signs and the symptoms of AHF. None of the patients developed a major cardiovascular event.

4. Discussion

Fifty percent of all patients admitted to the hospital for HF are readmitted during the 6-month period after their initial admission [11]. These repeat admissions and hospitalizations lead to a high economic burden due to the cost of HF treatment. A decrease in hospitalizations for AHF may improve patients’ survival rates, reduce readmission rates, and reduce hospital costs.
Advances in AHF treatment have lagged behind those for chronic HF treatment. Worsening in the signs and symptoms of congestion, rather than low cardiac output, is the main reason for hospitalization due to HF [12,13]. Although congestion is the main reason for hospitalization, upon discharge, many patients have not lost body weight and continue to show signs of congestion [14,15]. The presence of congestion is associated with a poor prognosis, and reducing congestion is an important goal for therapy [16]. However, there is no established algorithm to evaluate the level of congestion present. The criterion standard to evaluate hemodynamic congestion in HF patients is cardiac catheterization to measure right atrial pressure and pulmonary capillary wedge pressure [17]. Left-sided filling pressures correlate reliably with right-sided filling pressures in 80% of patients (when right atrial pressure is >10 or <10 mm Hg, left atrial pressure is >22 or <22 mm Hg, respectively [correlation coefficient, 0.64; P < .001]) [18,19].

Although diuresis is the mainstay of AHF therapy, there are no physical examination findings or imaging modalities that can objectively determine total body water and its distribution between body compartments. In some AHF patients (eg, AHF secondary to hypertensive crisis), the main problem is the shift of body water to the pulmonary compartment, due to increase in afterload, rather than volume overload. Most of these patients are euvolumeic, and thus, rapid diuresis may worsen the actual hemodynamic problem by increasing the systemic vascular resistance. In patients with volume overload, intravascular and extravascular fluid, rate of diuresis, and oncotic pressure all play an important role in determining the hemodynamic parameters. There are no guidelines on when to discharge AHF patients; thus, the decision to discharge a patient is subjective and based on the relief of patients’ signs and symptoms.

Ultrasonographic examination of IVC diameter and collapsibility have been used in diagnosis and therapy of chronic HF [20-22] because they are a reliable measure of right atrial pressure, which is a measure of volume status [23,24]. Even handheld ultrasonographic machines can measure IVC parameters reliably [23,25,26]. The objective of this study was to demonstrate that IVC parameters could assist in monitoring treatment of AHF or AHFS. Our study is the first study of this technique based solely in the ED.

In a study on 23 patients with right HF and 33 healthy volunteers, IVC diameters and collapsibility during inspiration and expiration were compared at the beginning of the therapy, and a significant difference between the 2 groups was found [21]. The IVC diameter started to decrease by the third day, and by the tenth day, there was no difference between the IVC diameters and collapsibility of the patients and the healthy volunteers. At the beginning of this study, the mean collapsibility indices for patients and volunteers were 19% and 33%, respectively. At the end of the follow-up period, a 37% variation in the collapsibility indices of the patients was found. In our study, the mean collapsibility indices of the patients and volunteers were 43.1% and 22%, respectively. We attribute the higher mean collapsibility index in our patient group to the inclusion of patients’ with both right and left HF. As IVC diameters decreased, the collapsibility index increased, proportionately. Although IVC diameters of the patient group were higher at the end of the therapy compared with those of the control group, there was no significant difference in the mean collapsibility indices between the 2 groups. The higher diameters were thought to be the result of relatively short follow-up period of 12 hours.

In a study on healthy subjects, the mean collapsibility index was found to be 46% [27]. In another study, HF patients were hospitalized for 4 days, and the mean volume of urine produced during this time was 6.1 L. Then, the IVC parameters were measured, and it was found that 66% of the patients still had mean collapsibility index less than 50% [22]. As absolute IVC diameters differ between patients, decreased IVC collapsibility measured during a single respiratory cycle may be a better measure of a patient’s volume status [27]. Inferior vena caval collapsibility index values of between 15% and 50% are diagnostic for HF [20,21,27]. A variation of 15% or less in IVC diameters during a single respiratory cycle is highly sensitive and specific for diagnosing congestive HF [27]. In healthy volunteers, IVC diameters also decrease after donating blood [28]. However, because a baseline value is unknown, measuring IVC diameters is a poor diagnostic test. As the absolute values of IVC diameters differ between patients, a single measurement of the diameter cannot determine a patient’s volume status [29].

Inferior vena caval diameters were used to guide HF therapy in 2 prior studies: in the first, patients had a mean weight loss of 4.7 kg by the tenth day, and in the second, patients had a mean diuresis of 6.1 L over 4 days [21,22]. In our study, patients had a mean diuresis of 3.9 L of urine during the 12-hour period, and there was no significant change in the blood urea nitrogen and the creatinine values. Although there is no cut-off value to define a poor response to treatment, we found that all patients with diuresis of less than 2.2 L of urine were readmitted to the ED within 1 month of their initial presentation.

Natriuretic peptides (NPs) (eg, brain natriuretic peptide [BNP] and NT-proBNP) are neurohormones specifically secreted by the cardiac chambers in response to increased wall tension secondary to volume and pressure overload. Both BNP and NT-proBNP increase in AHF, and the degree of increase is correlated with the severity of disease [30,31]. Brain natriuretic peptide and NT-proBNP may be chronically elevated in patients with HF. High levels of NPs before discharge are strong, independent predictors of death and readmission after a hospitalization for AHF and superior to other clinical and laboratory variables [32,33]. Thus, measurement of the levels of NPs before discharge can be useful in identifying patients at high risk for developing adverse events. A decrease in the levels of NPs before discharge in patients with high levels on admission (as observed in patients with congestion) may be a useful indicator of a reduction in filling pressure [34]. Serial measurements of BNP or NT-proBNP levels combined with the patient’s clinical status may be helpful in monitoring the response to HF treatment [35]. Wu et al [36] found that the best time to repeat the BNP level was on the seventh day, and they do not advise daily BNP measurement. In our study, most of the patients had acute decompensated chronic HF, and they had highly elevated levels of NT-proBNP. Although patients experienced relief of their symptoms during 12-hour treatment period in the ED, we could

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**Table 2**

The IVC parameters of the control and patient groups before and after treatment

<table>
<thead>
<tr>
<th></th>
<th>IVCexp</th>
<th>IVCins</th>
<th>IVC-CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before treatment</td>
<td>2.10 ± 0.37</td>
<td>1.63 ± 0.40</td>
<td>22.80 ± 10.97</td>
</tr>
<tr>
<td>Control group</td>
<td>1.57 ± 0.24</td>
<td>0.90 ± 0.26</td>
<td>43.09 ± 13.63</td>
</tr>
<tr>
<td>P</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>After treatment</td>
<td>1.85 ± 0.41</td>
<td>1.14 ± 0.42</td>
<td>39.75 ± 14.48</td>
</tr>
<tr>
<td>Control group</td>
<td>1.57 ± 0.24</td>
<td>0.90 ± 0.26</td>
<td>43.09 ± 13.63</td>
</tr>
<tr>
<td>P</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
<td>.246</td>
</tr>
</tbody>
</table>

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**Table 3**

The laboratory test results of patients before and after treatment

<table>
<thead>
<tr>
<th>Test</th>
<th>Before treatment</th>
<th>After treatment</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>BUN</td>
<td>25.78</td>
<td>25.19</td>
<td>.201</td>
</tr>
<tr>
<td>Creatinine</td>
<td>1.01</td>
<td>1.01</td>
<td>.904</td>
</tr>
<tr>
<td>Sodium</td>
<td>136.82</td>
<td>139.61</td>
<td>.287</td>
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<tr>
<td>Potassium</td>
<td>4.22</td>
<td>3.74</td>
<td>.001</td>
</tr>
<tr>
<td>Troponin</td>
<td>0.27</td>
<td>0.53</td>
<td>.024</td>
</tr>
<tr>
<td>CK-MB mass</td>
<td>3.00</td>
<td>3.20</td>
<td>.362</td>
</tr>
<tr>
<td>NT-proBNP</td>
<td>12058.49</td>
<td>12587.00</td>
<td>.560</td>
</tr>
</tbody>
</table>

Abbreviations: BUN, blood urea nitrogen; CK-MB, creatine kinase-MB.
not detect a decrease in the levels of NT-proBNP, most likely due to the chronic elevation of NT-proBNP. There was no difference in prognosis at 30 days after admission between the discharged and hospitalized patients, and none of the patients developed a major cardiovascular event. Only 6 patients returned to the ED with the symptoms of AHF within 1 month of enrolling in the study.

5. Limitations

Our study has some limitations. First, it was performed at a single center, and the number of patients enrolled was limited due to limited period. Second, we did not measure the patients’ symptoms on an objective scale, and we did not determine the long-term prognosis of the patients. Third, some IVC diameter measurements may have been affected by the presence of valvular heart diseases (eg, tricuspid regurgitation) in some of our patients. Fourth, we only used M mode for measuring IVC diameters and, thus, could not compare our results with those from 2-dimensional B mode. As the inferior vena cava does not have a uniform diameter along its course through the abdomen, the level where the ultrasound beam or M mode line intersects it may affect the IVC measurements obtained. The cranio-caudal displacement of the inferior vena cava with the movement of the diaphragm during the respiratory cycle, abnormalities in the sequence of atrial-ventricular contraction during the cardiac cycle, the amount of sonographer compensation for abdominal and chest wall movements, and the axis of collapse may all influence the measurements. Although M mode has some inaccuracies, we used a simple and standardized method for evaluating IVC parameters. Further studies of this method, addressing the limitations that we identified, are required.

6. Conclusion

We showed that IVC-CI might help in monitoring the response of AHF patients to therapy in the ED. We propose that ultrasonographic measurement of IVC parameters to guide AHF therapy should be standardized and incorporated in the routine echocardiography performed on AHF patients by cardiologists. We do not recommend a second NT-proBNP measurement in the ED.

References


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