American Journal of Emergency Medicine (2012) **30**, 174–180

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The American Journal of Emergency Medicine

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Brief Report

Hemodynamic changes as a diagnostic tool in acute heart failure—a pilot study☆,☆☆

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Received 12 July 2010; revised 6 August 2010; accepted 19 August 2010

Abstract

Objectives: To examine whether posturally induced changes in cardiac output differentiate patients presenting with dyspnea to the emergency department (ED) with acute heart failure (AHF) from other causes.

Methods: This was an observational study of patients presenting to the ED with dyspnea. Exclusion criteria included ischemic chest pain, electrocardiographic changes diagnostic of acute myocardial infarction, pericardial effusion or chest wall deformities causing dyspnea, or heart transplant. Hemodynamic variables of cardiac index (CI), total peripheral resistance index, and thoracic fluid content (TFC) were determined in upright seated and supine positions 3 minutes apart using bioreactance technology (Cheetah Medical Inc, Portland, Ore). Acute heart failure was defined as either B-type natriuretic peptide 100 to 500 pg/mL and discharge diagnosis of AHF or a B-type natriuretic peptide greater than 500 pg/mL.

Results: Of 92 patients, 25 had AHF, 23 had asthma/chronic obstructive pulmonary disease (COPD), and 44 had dyspnea related to other conditions; 41 (44.1%) were male, 56 (60.2%) were African American, and the mean age was 58 ± 15.0 years. Mean baseline TFC was higher in AHF vs asthma/COPD (59.3 ± 26.0 vs 39.7 ± 14.8 1/kW, $P = .003$) and trended higher compared to other patients with dyspnea (49.2 ± 22.0, $P = .10$). Postural changes in mean CI were lower in AHF (−0.20 ± 0.84 L min^{-1} m^{-2}) vs asthma/COPD (1.20 ± 1.23 L min^{-1} m^{-2}; $P = .002$) and other dyspnea patients (0.82 ± 0.91 L min^{-1} m^{-2}; $P = .007$).

Conclusion: Patients with AHF have greater TFC but lower CI responses to postural changes compared to patients with asthma and COPD. Knowledge of these changes may help rapidly differentiate AHF from asthma and COPD in the ED.

1. Introduction

Acute heart failure (AHF) affects 5.8 million Americans, accounting for more than one million hospital admissions per year. Nearly 283 000 people die each year from complications of AHF. The cost of heart failure in the United States is

☆ Prior Presentations: Society of Academic Emergency Medicine Annual Meeting, New Orleans, May 14th, 2009 and Phoenix, AZ, June 5th, 2010. Society of Academic Emergency Medicine Western Regional, Sonoma, CA, March 21st, 2010.

☆☆ Funding Sources: Cheetah Medical, Inc (Portland, Ore).

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doi:10.1016/j.ajem.2010.08.016

significant, with $32.9 billion direct costs and indirect costs for 2010. [1] Despite advances in diagnostic techniques, AHF mortality is excessive, approaching nearly 2% within the first week after emergency department (ED) discharge. [2] Large, double-blinded clinical trials have demonstrated that emergency physicians are 75% to 80% accurate in differentiating AHF from other diseases based on clinical factors alone. [3-5] Data from the Acute Shortness of Breath Evaluation study have shown that early diagnostic testing strategies, such as obtaining B-type natriuretic peptide (BNP) levels, are helpful in reducing mean time to treatment by 27 minutes, need for hospitalization by 10%, hospital costs by $1844 per visit, and length of stay by 3 days. [6] Not all patients with a history of heart failure present to the ED for AHF. In one study, only 16.5% of admissions of patients with a history of heart failure were actually for this diagnosis; more than half were for noncardiovascular causes. Comorbidities such as asthma, chronic obstructive pulmonary disease (COPD), myocardial infarction, and pulmonary embolism are also common. [7] Even when BNP levels are combined with clinical judgment, diagnostic accuracy is only 82.5%. [4] The 17.5% error rate may be the result of the well-described limitations of BNP interpretation, which include obesity, renal failure, cor pulmonale, acute pulmonary embolism, and myocardial infarction. Additional investigative strategies are needed to improve the diagnostic accuracy in undifferentiated patients presenting with dyspnea.

Bioreactance is a rapid, noninvasive technique used to assess cardiac output and other hemodynamic parameters. To obtain data with bioreactance, 4 electrocardiogram (ECG)-type dual lead (1 transmitting and 1 receiving) adhesive electrodes are applied to the bilateral anterior apices and bases of the thorax (Fig. 1), and an alternating current of fixed amplitude and frequency is applied across the thorax. Changes in the amplitude and phase of the measured voltage field varies proportionally to thoracic volume. Bioimpedance approaches relate changes in the amplitude of the voltage measured across the chest during a cardiac cycle to estimate cardiac output. In contrast, bioreactance estimates cardiac output by analyzing changes in the phase shifts between the applied current signal and the measured voltage signal during a beat that occur proportional to blood flowing out of the heart and into the aorta (Fig. 2). [8-11] In addition to cardiac output, mean bioreactance measures are indicative of the total thoracic fluid content (TFC) and have been shown to be abnormally high in AHF. [12] When coupled with noninvasive measurements of blood pressure, the device also provides a measure of total peripheral resistance. Compared to bioimpedance, bioreactance provides more reproducible results because it is not significantly affected by electrical noise, patient movement, respirations, lead placement, or body habitus. In a study of postoperative cardiac patients, bioreactance compared favorably with thermodilution, having identical precision and a relative error of less than 30% in 94% of patients. Cardiac output changes were also detected an average of 6.9 minutes faster than thermodilution [13].

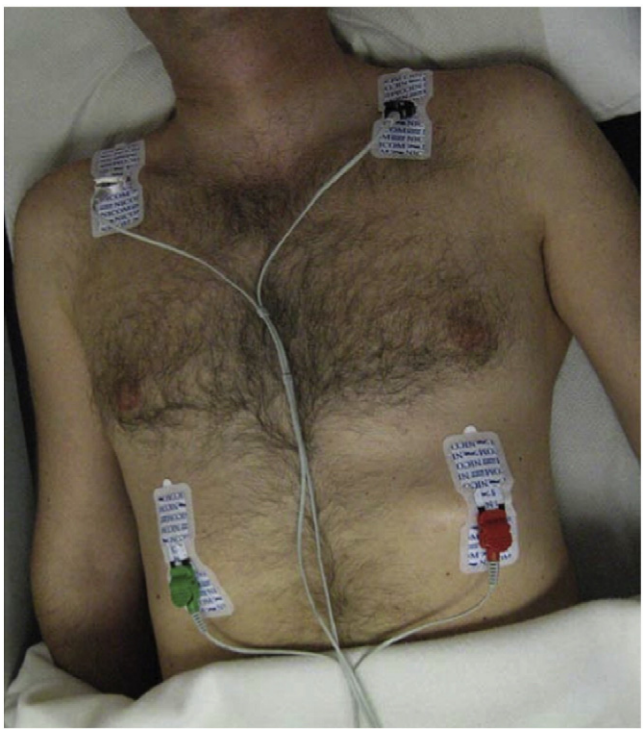

Fig. 1 Position of the bioreactance leads on the anterior chest wall.

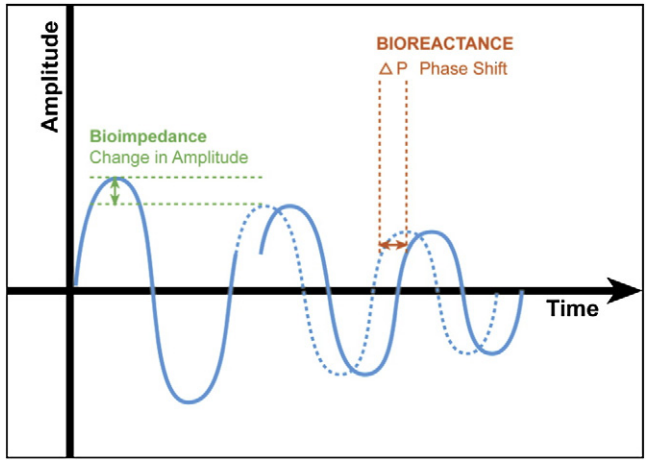

Fig. 2 NICOM measures a phase shift of an alternating electrical current, known as bioreactance, which is conceptually similar to a frequency modulation. Older technologies measure a change in amplitude, known as bioimpedance.

It has recently been suggested that hemodynamics can be objectively assessed by measuring CO changes occurring as a function of postural changes that shift blood from the legs to the central circulation. In euvolemia, postural fluid shifts results in increased CO due to the Frank-Starling mechanism. However, in volume overload, postural changes do not increase in cardiac output. A CO monitor provides a noninvasive means of making a hemodynamic assessment in undifferentiated dyspneic patients. [14] We chose to

evaluate cardiac index (CI), which corrects for differences in patient size (body surface area, or BSA). The formula is CI = CO/BSA.

The purpose of this study was to examine if postural CI changes and other noninvasive hemodynamic parameters can be used to diagnose AHF in patients with shortness of breath.

2. Methods

This was a prospective observational pilot study of patients presenting with acute dyspnea to the ED of an academic tertiary care center with an annual census of 64 000 patients per year. The study was approved by the institutional review board before study inception and registered at clinical trials.gov (NCT00707811). The study population was a convenience sample of patients presenting between April 1, 2008, and November 21, 2009, during the hours of 08:00 AM to 11:00 PM.

The inclusion criteria were presentation with nontraumatic dyspnea as a chief complaint in a patient able to provide informed consent and comply with study procedures. Patients were excluded if they had an ECG diagnostic for acute myocardial infarction or ischemic chest pain within the prior 24 hours, a history of a heart transplant, pericardial effusion, chest wall deformity suspected of causing dyspnea, or inability to obtain quality bioreactance signal.

After giving informed consent, patients had the bilateral electrode stickers placed on the midclavicular line over the clavicles and rib margins, and were connected to the monitor (NICOM, Cheetah Medical, Tel Aviv, Israel). Cardiac index, total peripheral resistance, and TFC were recorded after a patient had been in an upright, seated position with the hips flexed to 90° for 3 minutes. The patient was then placed supine (or as flat as tolerated) for 3 to 5 minutes and the measurements repeated.

Laboratory and other diagnostic testing was performed at the discretion of the treating physician. The final chest x-ray was interpreted by a board-certified radiologist. The ECG report was read by a board-eligible/certified emergency physician. Researchers were blinded to the results of laboratory testing, radiography studies, and admitting/discharge diagnoses, until after the bioreactance measurements were complete.

Table 1 Comparative demographic data

	Total	AHF	Asthma/COPD	Other
Mean age (±SEM)	57.4 (±1.6)	66.2 (±2.6)	52.1 (±3.0)	55.1 (±2.4)
Gender (male)	41 (44.1%)	14 (56.0%)	9 (39.1%)	18 (40.9%)
White	34 (36.6%)	11 (44.0%)	6 (26.1%)	17 (38.6%)
History of smoking	56 (60.2%)	15 (60.0%)	15 (65.2%)	26 (59.1%)
Medical history				
CAD	15 (16.1%)	10 (40.0%)	3 (13.0%)	2 (4.5%)
CHF	27 (29.0%)	19 (76.0%)	2 (8.7%)	6 (13.6%)
Asthma	39 (41.9%)	5 (20.0%)	18 (78.3%)	16 (36.4%)
COPD	25 (26.9%)	3 (12.0%)	13 (56.5%)	9 (20.5%)
Lung cancer	3 (3.2%)	0 (0.0%)	1 (4.3%)	2 (4.5%)
Lung transplant	3 (3.2%)	1 (4.0%)	0 (0.0%)	2 (4.5%)
Pneumonia	31 (33.3%)	7 (28.0%)	9 (39.1%)	15 (34.1%)
Pulmonary Hypertension	2 (2.2%)	1 (4.0%)	0 (0.0%)	1 (2.3%)
Sarcoidosis	5 (5.4%)	1 (4.0%)	3 (13.0%)	1 (2.3%)
Thromboembolism	9 (9.7%)	2 (8.0%)	0 (0.0%)	7 (15.9%)
Initial vital signs				
SBP, mean (±SEM)	133.9 (±2.0)	132.1 (±4.8)	135.6 (±3.7)	134.0 (±2.7)
DBP, mean (±SEM)	77.9 (±1.4)	77.4 (±3.5)	78.3 (±2.6)	77.9 (±1.7)
HR, mean (±SEM)	89.1 (±2.1)	85.4 (±4.0)	101.6 (±3.8)	84.6 (±2.7)
Resp rate, mean (±SEM)	20.9 (±0.8)	21.6 (±1.6)	21.4 (±1.1)	20.4 (1.2)
Temp, mean (± SEM)	36.7 (±0.1)	36.8 (±0.1)	36.6 (±0.2)	36.7 (±0.1)
Orthopnea	13 (14.0%)	7 (28.0%)	2 (8.7%)	4 (9.1%)
Rales	14 (15.1%)	7 (28.0%)	0 (0.0%)	7 (15.9%)
Wheeze	25 (26.9%)	6 (24.0%)	16 (69.6%)	3 (6.8%)
JVD	3 (3.2%)	2 (8.0%)	0 (0.0%)	1 (2.3%)
B-type natriuretic peptide (±SEM)	682 (137.5)	1370 (±229.7)	20.6 (±14.7)	110.7 (±26.2)
Pulmonary edema CXR	9 (9.7%)	9 (36.0%)	0 (0.0%)	0 (0.0%)
Ejection fraction (±SEM)	48.2 (±2.7)	38.6 (±4.2)	47.5 (±7.5)	58.4 (±1.3)

CAD indicates coronary artery disease; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; Resp rate, respiratory rate; Temp, temperature; JVD, jugular venous distension.

Table 2 Other diagnoses

Diagnosis	n	%
AHF, BNP <100	1	2.3
Atrial fibrillation/flutter	6	13.6
Bronchospasm	3	6.8
Bronchiectasis	1	2.3
Bronchus obstruction	1	2.3
Chest pain, noncardiac	10	22.7
Facial edema	1	2.3
Hemoptysis	1	2.3
Hypertensive emergency	1	2.3
Interstitial lung disease	1	2.3
Nocturnal dyspnea	1	2.3
Pleural effusion	1	2.3
Pulmonary embolism	4	9.1
Pneumonia	4	9.1
Psychiatric	4	9.1
Unknown	4	9.1
Unstable angina	1	2.3
URI/viral	2	4.5

URI, upper respiratory illness. Some patients had multiple diagnoses. Numbers do not total 100%.

The presence of AHF was defined as either an ED discharge or hospital admission diagnosis of AHF combined with a BNP between 100 and 500 pg/mL or a BNP greater than 500 pg/mL. [6] Asthma and COPD were defined as an ED discharge or hospital admission diagnosis of either and a BNP less than 500 pg/mL. Patients who did not meet either diagnostic category were classified as "other." Physicians were blinded to bioreactance measurements throughout the hospital course. Researchers collecting outcomes data were blinded to results of bioreactance measurements until after they had recorded the final diagnosis.

Differences in hemodynamic measurements between groups were analyzed using a 2-tailed t test, with α defined as $P < .05$. Hemodynamic variables are reported with standard deviations. Multiple linear regression was performed using variables found to be significant per univariate analysis. A composite hemodynamic index, I_{hemo}, was derived from the parameters that differed significantly between groups using multiple linear regression analysis to arrive at the best fit to the respective values of BNP. The variables included in the composite index were TFC, dCI, and HR. Statistical analyses were performed using Microsoft Excel 2003 (Microsoft. Redmond, WA) and Sigmaplot 11.0 (Systat Software, Inc. Chicago, IL).

3. Results

A total of 92 patients were enrolled into the study. There were 41 (44.1%) males and 51 (55.4%) females; 34 (36.6%) patients were white, 56 (60.2%) were African American, and 2 (2.2%) were of other races. Mean age was 58.0 ± 15.0 years (range, 20-88 years). A complete list of demographic parameters is presented in Table 1. Acute heart failure was diagnosed in 25 (27.2%), asthma or COPD in 23 (25.0%), and dyspnea of other causes in 44 (47.8%) patients. The category of "other" consisted of atrial fibrillation (n = 6; 13.6%), noncardiac chest pain (n = 10; 22.7%), pulmonary embolus (n = 4; 9.1%), and dyspnea of unknown etiology (n = 4; 9.1%) (Table 2).

The baseline CI of patients with AHF, asthma/COPD, and other causes were 2.86 ± 0.87, 3.29 ± 1.04, and 3.03 ± 0.92 L min^{-1} m^{-2}, respectively, which were not significantly different from each other (AHF vs asthma/COPD, $P = .12$; AHF vs "other," $P = .45$; asthma/COPD vs "other," $P = .30$) (Table 3). However, patients with AHF had a lower CI increase to preload augmentation when moved from sitting to supine positions (0.20 ± 0.84 L min^{-1} m^{-2}) compared to patients with asthma/COPD (1.20 ± 1.23 L min^{-1} m^{-2}; $P = .002$) as well as other causes of dyspnea (0.82 ± 0.91 L min^{-1} m^{-2}; $P = .007$) (Fig. 3A). In addition, baseline TFC was higher in AHF (59.3 ± 26.0 1/kW) compared to asthma/COPD (39.7 ± 14.8 1/kW; $P = .003$), but not compared AHF and other causes (49.2 ± 22.0 1/kW; $P = .10$) (Fig. 3B). Change in TFC in response to being placed in the supine position did not differ significantly between the 3 groups (dTFC = 0.87 ± 3.8, 0.85 ± 4.9, and 0.96 ± 4.8 1/kW for AHF, asthma/COPD, and "other," respectively; P = not significant for all; Fig. 3C). Postural changes in heart rate were less in response to supine positioning in AHF (−0.73 ± 2.76 beats per minute [bpm]) as compared to asthma/COPD (−3.22 ± 3.92 bpm; $P = .014$) and other causes of dyspnea (−3.75 ± 4.12 bpm; $P = .002$) (Fig. 3D).

B-type natriuretic peptide values were available for 54 (58.7%) of the patients, the cohort used to determine the composite index, which yielded the following regression:

Table 3 Hemodynamic changes with change in position

	CHF	Asthma/COPD	Other	P (AHF vs A/C)	P (AHF vs other)	P (A/C vs other)
CI (L min^{-1} m^{-2})	2.86 ± 0.87	3.29 ± 1.04	3.03 ± 0.92	.124	.446	.302
δCI (L min^{-1} m^{-2})	0.20 ± 0.84	1.20 ± 1.23	0.82 ± 0.91	.002	.007	.153
TFC (1/kW)	59.31 ± 26.04	39.70 ± 14.84	49.19 ± 22.02	.003	.098	.070
δTFC (1/kW)	0.87 ± 3.82	0.85 ± 4.92	0.96 ± 4.80	.989	.936	.932
δHR	−0.73 ± 2.76	−3.22 ± 3.92	−3.75 ± 4.12	.014	.002	.611
Index	750 ± 541	96 ± 509	243 ± 506	.000	.000	.266

A/C indicates asthma/COPD.

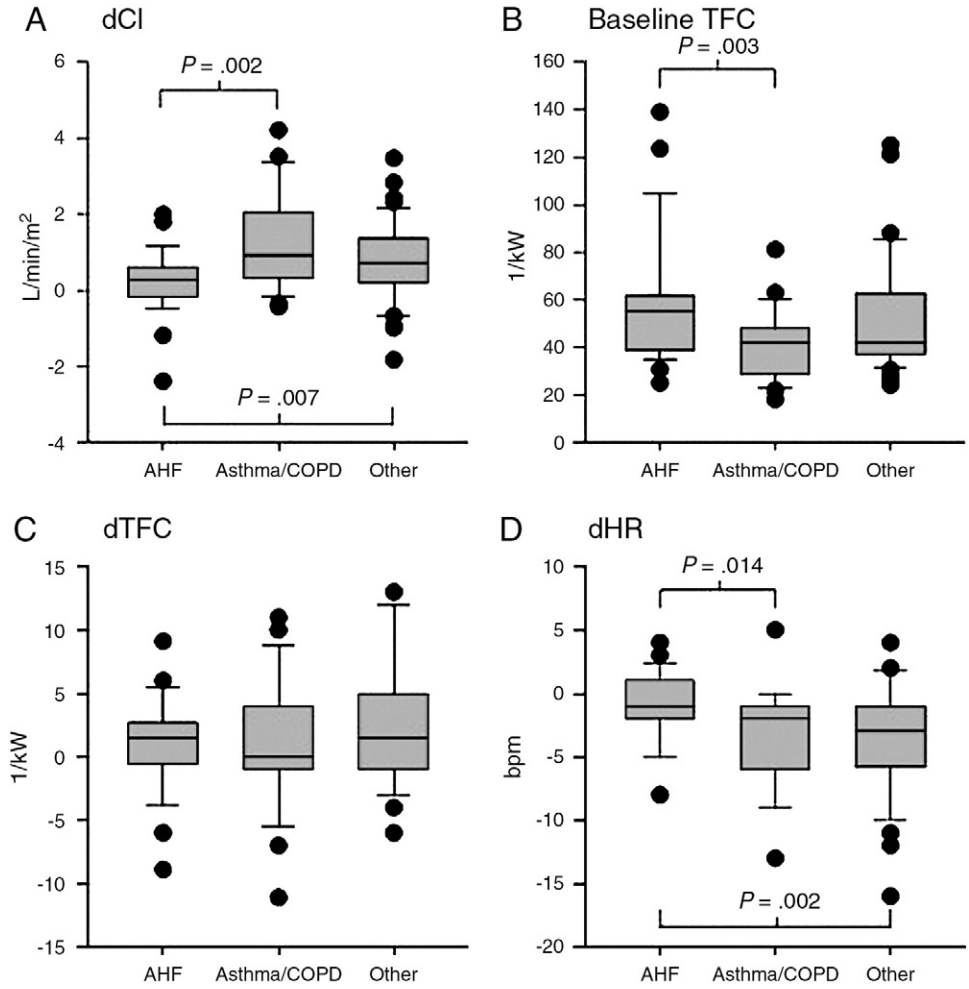

Fig. 3 Patient responses to preload augmentation by diagnostic classification. Patients with AHF had a blunted CI increase to preload augmentation (dCI; panel A) when moved from sitting to supine positions compared to patients with asthma/COPD ($P = .002$) as well as other causes of dyspnea ($P = .007$). In addition, baseline TFC (panel B) was significantly different comparing AHF and asthma/COPD ($P = .003$), but not comparing AHF and other causes ($P = .10$). Change in TFC (dTFC; panel C) in response to preload augmentation did not differ significantly between the 3 groups (P = not significant for all; panel C). Postural changes in heart rate (dHR, panel D) were reduced in response to preload in patients with AHF as compared to asthma/COPD ($P = .014$) and other causes ($P = .002$).

$I_{hemo} = 14.3 \times TFC - 234 \times dCI + 61 \times dHR$ ($P < .001$). Based on the coefficients and values, the most significant component of the index was the postural change in CI. I_{hemo} was significantly different between ADHF (750 ± 541), asthma/COPD (96 ± 509; $P = .00001$), and other causes of dyspnea (243 ± 506; $P = .0002$) in this derivation set.

4. Discussion

Patients presenting to the ED with AHF did not have significantly different baseline CIs compared to patients with asthma/COPD or other causes of dyspnea. However, when a postural change from sitting to lying was performed, patients with AHF exhibited a lower increase in CI and heart rate. The decreased responses to postural changes may be a reflection of the patient being in a fluid overload state and unable to increase their CI in response to an increase in preload that may occur with the supine position. As a result, they are working at or near the plateau of the heart's Starling curve and volume recruitment cannot increase cardiac output. In contrast, patients in a euvolemic state that are working on the ascending limb of the Startling curve can effectively increase cardiac output in response to volume recruitment. A second explanation of our findings may be that the supine position results in less diaphragmatic excursion secondary to increased abdominal pressure in the supine position. While plausible, decreased diaphragmatic excursion is unlikely to explain our results as cohorts without known myocardial dysfunction experienced significantly greater improvements in their CI. This further supports the expected pathophysiology, that patients with impaired myocardial function have little reserve and manifest less detectable change in CI. Whether a continuum of change across the spectrum of myocardial dysfunction (minimal impairment to cardiogenic shock) exists will require further study.

Baseline TFC was also a useful parameter in differentiating AHF from the asthma and COPD population but was not significant when comparing AHF to other causes of dyspnea. The lack of significance in the latter comparison is likely due to the small sample size of our pilot study, although it may also have been related to the heterogeneous nature of this population that may include patients in a relatively fluid overloaded state (eg, ascites/cirrhosis, acute myocardial infarction, atrial fibrillation, pleural effusions). Each of the 3 groups had similar increases in TFC when placed supine, suggesting that each was subjected to similar preload challenges in this position.

We also found that a composite hemodynamic index that incorporated information about TFC, dCI, and dHR provided a strong separation between AHF and patients in the other 2 groups. This index was derived from a subgroup of 54 patients with BNP levels obtained as a part of routine practice. Although the index was able to differentiate each population of dyspnea diagnosed in this study, it will need validation because our ED discharge/hospital admitting diagnosis may have been based on the BNP result.

Many clinicians have been suspect of noninvasive technologies for the measurement of hemodynamics because of prior experience with bioimpedance, citing problems with poor accuracy and precision. Bioreactance technology was developed to overcome these limitations, while retaining the simple and noninvasive nature of the measurement. Bioreactance has undergone extensive validation vs thermodilution in a variety of clinical settings including medical and surgical intensive care units, cardiac catheterization laboratories, in septic patients, and during exercise testing in healthy patients and in patients with heart failure over a range of New York Heart Association classes. [8-11,13,15,16]

Noninvasive cardiac monitoring takes only a few minutes to perform. This represents a significant advantage over serum biomarker strategies for AHF diagnosis. Using bioreactance, the probable etiology of dyspnea may be determined earlier in the patient's course, potentially leading to earlier treatment, shorter times to diagnosis, and decreased length of ED stay. Furthermore, unlike BNP, the use and interpretation of the present bioreactance-based strategy is not problematic in patients who are obese, have renal dysfunction, or are difficult to phlebotomize. Finally, although not evaluated in this study, serial measurements may be repeated after initial management to evaluate therapeutic response. Whether these advantages result in improved outcomes and reduced costs need to be examined further.

5. Limitations

There are several limitations of the present study. First, the group of patients in the "other" category (ie, those not clearly diagnosed with either heart failure or asthma/COPD) was composed of a heterogeneous group of patients. Many of the patients in the "other" category may have had fluid overload, which would behave similarly to CHF with regard to TFC and postural CI changes. For this reason, we believe that the most meaningful comparisons within the context of this pilot study were between those patients with a clear diagnosis of CHF or asthma/COPD, 2 relatively homogenous groups of patients. However, we did not exclude patients in the "other" category, as the purpose of the study was to evaluate hemodynamic changes in undifferentiated dyspnea.

A second limitation relates to spectrum bias and the necessity of recruiting dyspneic patients into a protocol that requires 3 minutes in the supine position. Ultimately, those with the greatest severity of illness were excluded from enrollment. However, because the less ill are generally more diagnostically challenging, and would be expected to have less hemodynamic perturbations, this bias lends support to our conclusion that bioreactance is a robust technology able to differentiate AHF from other causes of dyspnea. Consistent with this strategy, we did not control for β-blocker usage, which could potentially explain the lower heart rate change seen in AHF patients.

Another limitation to the study is that not all patients received a BNP measurement because this was obtained at the discretion of the treating physician. The outcome of AHF was determined based on ED discharge or hospital admission diagnosis, with BNP used to detect false positives (diagnosis of AHF with a BNP <100) and false negatives (diagnosis of no AHF with a BNP >500). All patients diagnosed with AHF had a BNP obtained. Some patients diagnosed with asthma, COPD, or other causes of dyspnea where BNP was not obtained may have been misdiagnosed.

Finally, our composite hemodynamic index was determined using multiple linear regression only from patients who had BNP testing performed. Different weighting of the hemodynamic variables may have occurred had we had BNP measurements on all of the patients in the population. In addition, the ED discharge/hospital admit diagnosis may have been based in part on the BNP. Application to a future validation set will be necessary.

6. Conclusion

Patients presenting to the ED with AHF can be differentiated from those with asthma/COPD and other causes of dyspnea by using bioreactance-measured hemodynamic parameters. Compared to other patients, those with AHF had greater baseline TFC and blunted increases in CI in response to postural changes. A composite index of these variables may be useful in differentiating these patients.

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