

Correlation of Limb Bioimpedance to Echocardiographic Indicators of Congestion in Patients with NYHA Class II/III Heart Failure

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ABSTRACT

Purpose: The treatment of heart failure (HF) in the United States is estimated to exceed \$30 billion each year and is anticipated to increase to a staggering \$70 billion by the year 2030. This makes the management of HF one of the leading challenges Medicare will face in the years to come. Traditional methods to detect impending congestion such as body weight and physical examination findings are often non-specific and lack sensitivity making them inadequate to recognize fluid overload and prevent decompensation. It has been suggested that bioimpedance spectroscopy (BIS) can be used as a surrogate marker for detecting fluid overload and therefore, serve as an adjunct to clinical exam findings.

Methods: This study examines the relationship between a BIS device and echocardiographic parameters associated with volume overload with same day measurements in the first 8 patients with NYHA Class II/III HF on an IRB approved protocol. Each patient was followed 3 times a week for 4 weeks within the hospital outpatient setting. At each visit BIS measures were recorded for whole body as well as arms and legs. Additionally, signs and symptoms, weight and echocardiograph findings were all recorded.

Results: Correlations of BIS measurements with echo parameters were performed. The leg impedance measurement correlated strongly with echo findings; inferior vena cava (IVC) size ($p=0.001$), right atrial pressure (RAP) ($p<0.001$), and pulmonary artery systolic pressure (PAS) measurements ($p<0.001$).

Conclusion: Preliminary findings demonstrated excellent correlations with BIS measurements and IVC size, right atrial pressure and pulmonary artery systolic pressure measurements which suggest a possible alternative method to detect fluid overload despite the small sample size. Trending a patient's impedance using the SOZO device at home or the practitioner's office may assist clinicians in providing more accurate, individualized HF care.

Keywords

Bioimpedance spectroscopy, Heart failure.

Introduction

The evaluation of congestion in heart failure (HF) patients has relied predominantly on physical examination findings [1]. Jugular venous distention (JVD) and rales have been proven to be beneficial as a marker for congestion, as has central venous pressure (CVP) [1]. JVD is often found late in the course of a HF exacerbation. Therefore, earlier markers to aid in the evaluation of congestion have been sought. Bedside ultrasound, correlating inferior vena cava (IVC) size to CVP, has been shown to be a useful marker for

new fluid overload in HF patients [2]. Unfortunately, this requires an operator skilled in its use. As with other technologies, this may be associated with increased cost, and may not be available for all HF patients.

Bioimpedance has been offered as an adjunct to traditional physical exam findings. However, challenges including variability in electrode placement, body positioning, and time constraints have been documented [3]. Both single and multi-frequency bioimpedance have previously been investigated as a means to detect early congestion, but early results did not show these to be reliable indicators [4]. Single-frequency bioimpedance analysis

(SF-BIA) relies on the information from a single frequency reading, typically 50 kHz. Population-specific algorithms (based on gender, ethnicity, height, weight, and age) are then used to estimate the various body composition compartments. Although multi-frequency bioimpedance (MF-BIA) analyzers use 2 or more frequencies, they are still limited in their ability to differentiate fluids in the body, particularly in patients with fluid imbalances, due to the use of calculations based on normalized fluid distributions. By using a wider spectrum of frequencies, bioimpedance spectroscopy (BIS), a graph can be constructed to estimate the impedance at frequencies of zero and infinity (Cole analysis) [5]. These end-spectrum frequencies have been shown to yield individualized information specific to extracellular and total-body fluid with increased accuracy and without the need for normalized population-specific algorithms [6]. Using trends in BIS, a clinician can more accurately monitor fluid balance [6]. Recent use of impedance as an indicator of rising CVP suggests that it may prove helpful as an adjunct to physical examination findings, thereby improving the management and care of the chronic HF patient. This study was designed to evaluate BIS with transthoracic echocardiographic (TTE) parameters of volume overload.

Methods

Patients with New York Heart Association (NYHA) Class II or III heart failure were eligible for this study. Based on the inclusion criteria, a total of 10 patients were recruited into the study, two of whom later withdrew. IRB approval was obtained for this study (Scripps IRB #IRB-16-6852). After informed consent was obtained, baseline measurements were recorded in the cardiology clinic. These included BIS measures, cardiac rhythm assessment, weight and TTE. BIS measures were made using the SOZO® device (ImpediMed, Australia). The SOZO device utilizes BIS to generate a spectrum of frequencies (>250) to provide impedance measurements at both zero (extracellular fluid) and infinity (total body water) frequencies. The SOZO system is a 4-channel device that takes tetrapolar measurements using stainless steel hand and foot plates. A single reading measures impedance over a sweep of frequencies, of multiple body segments (whole body, arms and legs).

Technical Information

Per protocol guidelines, eleven to thirteen subject visits occurred over a four-week period. Visits were scheduled at two-to-four-day intervals, within a five-hour window for time of day to standardize the fluid balance across the cohort. At each subject visit, weight, blood pressure, and impedance measurements of the whole body, left and right arms, and left and right legs were recorded. At each clinic visit, a limited TTE were performed by licensed echocardiographers and reviewed by Board-certified cardiologists to obtain echocardiographic measurements of IVC size, pulmonary artery pressure (PAS) and right atrial pressure (RAP).

The quality of the BIS measures was reviewed by one person for internal consistency. The subsequent calculation of RAPs, which are derived from the IVC size, was performed according to

recommendations by the American Society of Echocardiography (ASE) and were utilized as a measure of preload and volume. RAP values were categorized into three groups: group 1 included any RAP below 8 mmHg, group 2 included values of 8-14.99 mmHg, and group 3 included all values equal to 15 mmHg. The ASE has defined a normal RAP as 3 mmHg, intermediate as 8 mmHg, and high as 15 mmHg.

Statistical Analyses

Descriptive analyses were used to summarize subject characteristics. Analysis of Variance (ANOVA) with follow-up t-tests were used to compare right and left leg and arm BIS measurements between RAP change groups. Correlation of BIS measurements with established clinical markers of HF were used to determine if use of the SOZO® device is comparable to these markers. Pearson correlations were calculated between TTE measurements and the BIS measurements of body segments (arms and legs). Pearson correlation was then used to determine the association between BIS measures and PAS, because pulmonary hypertension has been recognized as a predictor of mortality in patients with dilated cardiomyopathy [7].

Results

Ten patients were accrued to the study with 2 patients withdrawing. Table 1 presents the eight patient characteristics including age, gender, baseline rhythm, ejection fraction, and NYHA Class.

	Age	Sex	Baseline Rhythm	EF%	NYHA CLASS
Patient 1	77	M	SB	60	II
Patient 2	71	F	AFib	63	III
Patient 3	79	M	AFib	62	II
Patient 4	78	M	SR	67	II
Patient 5	56	M	SR	35	II-III
Patient 6	withdrew				
Patient 7	56	F	AFl	<35	II
Patient 8	81	M	AFib	59	NR
Patient 9	withdrew				
Patient 10	78	F	SB	64	III

Table 1: Patient Characteristics.

NR: Not Reported. M: Male, F: Female, SB: Sinus Bradycardia, AFib: Atrial Fibrillation, SR: Sinus Rhythm, AFl: Atrial Flutter.

Of the patient visits, the majority had a RAP reading belonged in RAP group 1(<8 mmHg) (65.9%). Groups 2 (8-14.99 mmHg) and 3 (15+ mmHg) accounted for 14.0 and 10.8% of measurements, respectively. This measure was missing in 4.3% of visits. There was a significant difference between groups using the raw RAP data for both the right and left leg ($p < .0001$), suggesting that the difference in the established RAP levels is larger than the effects of height and weight, which can skew impedance data.

Strong correlation values were found between BIS measures and TTE measures. The highest correlation of impedance to IVC was with the legs, (left and right leg: -0.76, p – value:<.0001; Table 2,

Figures 1 and 2). Similarly, leg impedance measures were strongly and negatively correlated to RAP measures (right leg: -0.61, p - value = <.0001; left leg: -0.65, p - value = <.0001; Table 3, Figures 3 and 4).

	IVC (correlation)	p
Right leg	-0.76	<0.001
Left leg	-0.76	<0.001
Total body left	-0.49	<0.001
Total body right	-0.48	<0.001

Table 2: Correlation of Leg Impedance with IVC size.

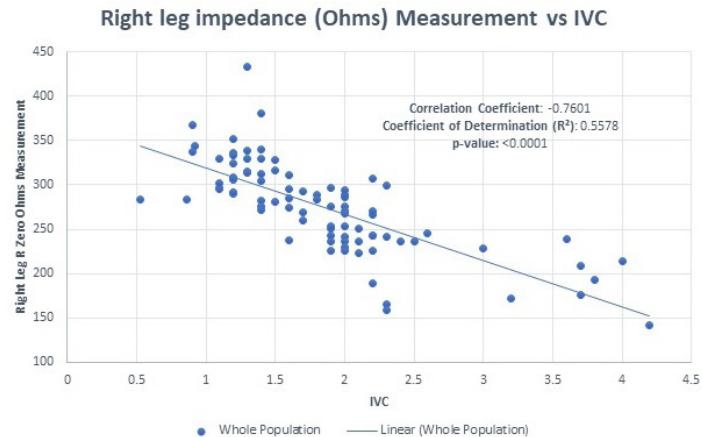


Figure 1: Correlation of Right Leg Impedance and IVC Size.

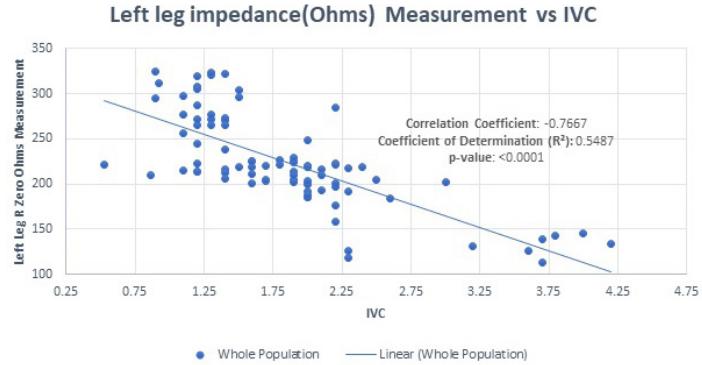


Figure 2: Correlation of Left Leg Impedance and IVC Size.

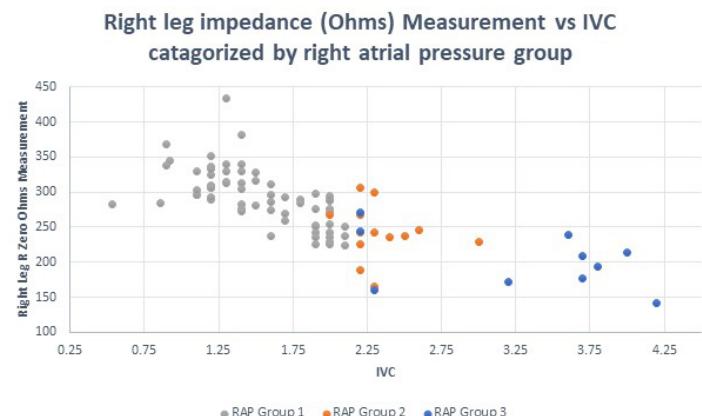


Figure 3: Correlation of Right Leg Impedance to Right Atrial Pressure.

	RAP (correlation)	p
Right leg	-0.61	<0.001
Left leg	-0.65	<0.001
Total body left	-0.39	<0.001
Total body right	-0.39	<0.001

Table 3: Correlation of Leg Impedance to Right Atrial Pressure.

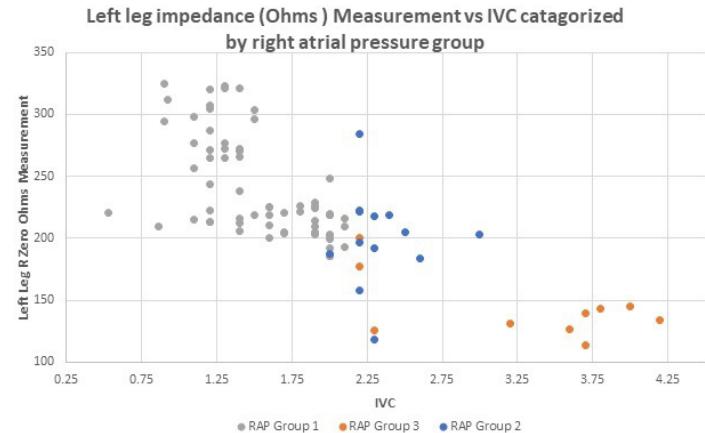


Figure 4: Correlation of Left Leg Impedance to Right Atrial Pressure.

No statistically significant correlation was found between left and right arm BIS measurements for both RAP and IVC measurements. Left and right arm BIS measurements were significantly associated with PAS measures (right arm = -0.58, p-value = < 0.0001; left arm: -0.53, p-value = < 0.0001) (Table 4, Figure 5). Among right arm BIS measurements, the correlation to PAS was markedly better in RAP group 3 (Figure 6). Total body BIS measurements were also all significantly associated with TTE measures, but in all cases the strength of the association was substantially less than that found for arms or legs.

	PAS	p
Right arm	-0.58	<0.001
Left arm	-0.53	<0.001
Total body left	-0.48	<0.001
Total body right	-0.56	<0.001

Table 4: Correlation of Limb Impedance to Pulmonary Artery Systolic Pressure.

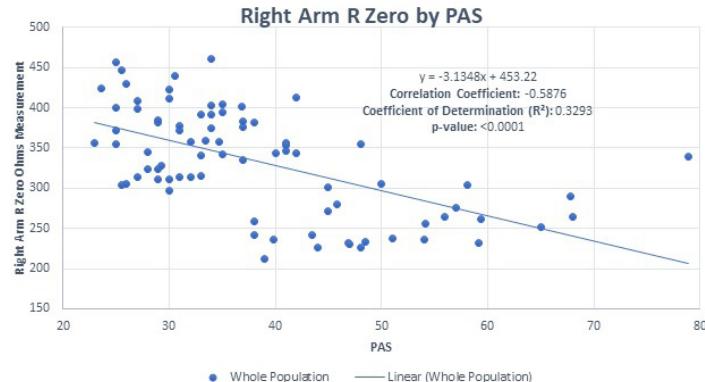


Figure 5: Correlation of Right Arm Impedance to Pulmonary Artery Systolic Pressure.

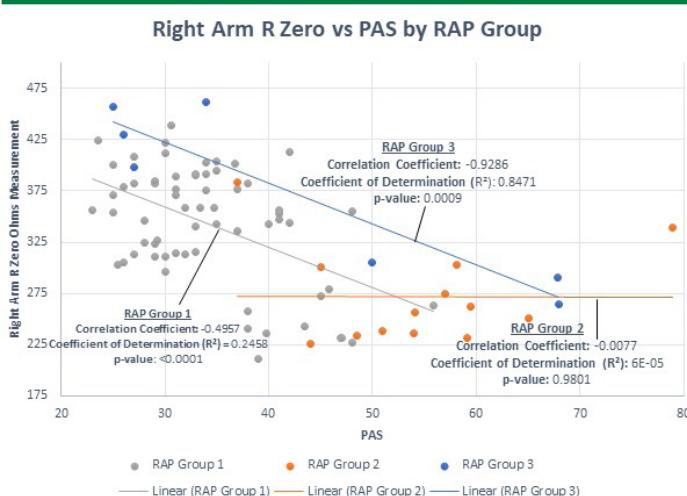


Figure 6: Correlation of Right Arm Impedance to Pulmonary Artery Systolic Pressure by Right Atrial Pressure Group.

Discussion

In the current analysis, whole-body and limb impedance measurements were monitored to help define their relationship to other important indicators of congestion and possible impending HF. Significant correlations were found between impedance and IVC size, with BIS measurements for both legs having the highest correlations observed. We believe that the legs represent a sizeable physiologic cylinder that has no air-filled structures. The lack of these air-filled structures limits the areas that might shield fluid from impedance changes over time [8]. Since the right leg has a more direct vascular route to the heart, we suspect that this gave it a higher correlation to CVP than the left, although more research is needed to confirm this observation.

Prior studies using bedside ultrasound have documented a correlation of IVC size to CVP. Clinicians use the CVP measurement as an indication of fluid status. We theorized that as fluid accumulates, the elevation of RAP or (CVP) might be identified earlier with a decrease in impedance. We took the measurements for IVC size and broke them up into 3 categories of high, medium, and low for RAP. We based these categorical values on the measures derived from the TTE established by the American Society of Echocardiography (ASE). We postulated that knowing a patient's IVC and CVP trends would enable the clinician to combine established measures of fluid assessment to help manage a patient more successfully.

The correlations of impedance to PAS as shown in Table 4 are of strong interest. Extracellular fluid (ECF) has been shown in previous studies using deuterium to be the predominant compartment during congestion [9,10]. The improved correlation at higher PAS suggests that as congestion progresses, the ECF is the principal fluid and BIS measures will be more accurate.

At lower PAS, some of the retained fluid may be in other compartments, thereby reducing the correlation. Because PAS measurements are not readily available, BIS may be a surrogate

noninvasive marker to detect elevations in filling pressures. This measure reflects pulmonary hypertension and may have broader use than just fluid management. Our findings showed that the arms had stronger correlations than the legs. We hypothesize that these results occurred because the arms are a non-air-filled structure in closer proximity to the heart than the legs [8].

The SOZO device for BIS has been shown to give improved discrimination of volume overload from HF as a cause of dyspnea in patients presenting to the emergent setting, and is sensitive to changes in both pulmonary and peripheral edema [3]. Unfortunately, the variability in lead placement, patient positioning, and a mix of BIS, BIA, and MF-BIA data has given varied results for HF. We believe this variability has prevented widespread adoption of BIS in this context. We believe that the SOZO device overcomes the lead placement barrier by using fixed stainless-steel electrodes, which allows for easy operator use with low interoperator variability.

The ability to obtain this information with an easy-to-use, non-invasive method would be valuable to any healthcare provider as part of caring for a patient with HF, or any condition in which a patient's fluid status fluctuates. If further studies confirm its utility, BIS could become part of the optimized management in the standard of care for HF patients. Another application of the SOZO device is that HF patients can use the device at home, which may assist in telemonitoring of HF patients and preventing re-admissions, improving quality of life, and limiting unnecessary visits. We believe home use of the SOZO device would provide valuable data when used in a Bayesian framework with weight and symptoms to develop overall management for HF treatment.

Limitations

Limitations to this study were in large part due to its purpose, which was exploratory in nature. The largest limitation was the small sample size. That even this small cohort enabled us to detect signals from the SOZO device indicates that further study in a larger group is important. Additionally, this study focused only on the BIS measurements and did not collect data for patient outcomes outside of information regularly collected as part of a HF patient's standard of care.

We were impressed by the significant correlations seen between the BIS measurements obtained with the SOZO system and traditional TTE measures of congestion. Previous impedance studies using conventional measurement methods have failed to demonstrate effectiveness in detecting decompensation due to study limitations [4]. However, the new design of SOZO has eliminated some of the issues previously resulting in conflicting data.

The preliminary data from the SOZO system is promising. Further research using a larger sample size and studying the potential effects of the SOZO system impedance monitoring on 30-day readmissions, medical decision making, patient-reported HF symptoms, and quality of life would be of great benefit.

Conclusion

The management of the chronic HF patient continues to challenge the primary care provider. Most HF patients are managed by body weight, physical examination findings, and intermittent diagnostics like echocardiography. These traditional methods of evaluation often fail to aid the practitioner in detecting fluid overload and impending decompensation. Staggering healthcare costs and financial penalties associated with 30-day readmission served as the impetus for this study. The use of SOZO is predicated on a correlation between impedance measurements and established measures of fluid. Despite the small study size, correlations of the SOZO device impedance measurements with IVC, RAP, and PAS suggest a possible alternative method to detect fluid overload. The results suggest that there is a relationship that could be used at low cost, is noninvasive, and easy to use. However, due to limitations to the study design, further research is needed to determine the utility of the SOZO device.

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