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Equivalence of the Bioimpedance and Thermodilution Methods in Measuring Cardiac Output in Hospitalized Patients With Advanced, Decompensated Chronic Heart Failure

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• BACKGROUND *An accurate and reliable noninvasive method for determining cardiac output/cardiac index would be valuable for patients with acutely decompensated advanced systolic heart failure.*
• OBJECTIVES *To determine whether a correlation exists for cardiac output and index determined by using bioimpedance and thermodilution in patients with acutely decompensated complex heart failure and if differences between results with the 2 methods could be explained by the patients' advanced condition.*
• METHODS *Cardiac output and index were determined by using bioimpedance and thermodilution in 33 patients. Echocardiographic and electrocardiographic data were assessed to determine if differences between results with the 2 methods could be explained by the patients' advanced condition. Concordance correlation coefficients and Bland-Altman agreement between methods were calculated.*
• RESULTS *Four patients were excluded from analysis because reliable measurements could not be obtained; the remaining 29 patients constituted the study population. Mean cardiac outputs determined by thermodilution and bioimpedance were 5.48 and 5.40 L/min, respectively (ρ_c =0.89, P < .001), and mean cardiac indexes were 2.67 and 2.65 (ρ_c = 0.82, P < .001). Mean bias (limits of agreement) between data pairs was 0.08 (-0.18 to 0.35) L/min (P = .52) for cardiac output and 0.03 (-0.097 to 0.16; P = .61) for cardiac index. Six data pairs (21%) had an absolute percent difference greater than 15%. Of these, 50% had a higher thermodilution value.*
• CONCLUSION *Determinations of cardiac output and index by both methods were significantly correlated. Mean bias between the 2 methods was small, suggesting clinical utility for bioimpedance in patients with complex decompensated heart failure. (American Journal of Critical Care. 2004;13:469-479)*

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Heart failure is a debilitating condition associated with frequent clinical decompensation and major morbidity that requires hospitalization. The Acute Decompensated Heart Failure National Registry recently reported data on 40 952 patients hospitalized for heart failure in the United States.[1] Nationally, 77% of patients entered the hospital system after arriving at the emergency department. The first inpatient site of care was the coronary or intensive care area for 14% and an intermediate care area for 7%. Thus, nearly one quarter of patients admitted to the hospital for decompensated heart fail-

ure required monitoring and an aggressive treatment approach to manage the condition.

Patients with advanced systolic heart failure often have comorbid conditions, and poor pump function may necessitate hemodynamic monitoring to guide therapy. Traditionally, pulmonary artery catheters have been used to monitor and adjust medications to optimize hemodynamic status. Sequential (snapshot) or continuous measurements of hemodynamic parameters can be used to predict clinical responses to pharmacological and nonpharmacological therapies. In addition, timing of therapeutic adjustments in the plan of care may be affected by the presence of hemodynamic data. In a study[2] of patients with low cardiac output states in a coronary care unit in which cardiac output determined by using a continuous method was compared with output determined by using an intermittent method (every 4 hours), the method used affected delivery of care. Continuous measurement of cardiac output increased the number of treatment decisions and actions by healthcare providers and decreased the length of hospital stay by a median of 2 days.[2] Although no randomized, blinded, controlled studies have been done to evaluate the benefits of hemodynamically guided care or to determine if continuous data are more beneficial than brief snapshots, healthcare providers use hemodynamically guided care to monitor the course of treatments, especially in patients with advanced heart failure who are hospitalized with complex decompensation (severe hypervolemia, hypoperfusion, acidosis, and comorbid condition or other aggravating factors).

Several studies[3,4] have raised concerns regarding the appropriateness of the routine use of pulmonary artery catheters in critically ill patients because the catheters are associated with increased morbidity and mortality, and these concerns could be associated with an increase in the cost of acute care. In a recent study[5] to assess the severity of illness, use of a pulmonary artery catheter was associated with decreased mortality in the most severely critically ill patients and with increased mortality in patients with less severe illness. In 1997, the Society of Critical Care Medicine developed a consensus statement[6] about the use of pulmonary artery catheters in patients with a variety of diseases and disorders. For patients with heart failure, the society reported that use of pulmonary artery catheters was of uncertain value and recommended a randomized, controlled trial to assess whether or not the benefits outweigh the risks to patients. The Evaluation Study of Congestive Heart Failure and Pulmonary Artery Catheterization Effectiveness (ESCAPE) trial was designed to determine the safety and effectiveness of adding hemodynamic data obtained by using a pulmonary artery catheter to the clinical assessment of patients admitted to the hospital with acutely decompensated heart failure.[7] This multicenter, randomized trial is ongoing and will provide valuable information about the utility of pulmonary artery catheters in patients with advanced heart failure. In a substudy of the ESCAPE trial, Bioimpedance Group, the diagnostic and prognostic utility of impedance cardiography will be evaluated.

The risks of using a pulmonary artery catheter during heart failure may not outweigh the benefits.

An accurate and reliable noninvasive method for measuring cardiac output and cardiac index could be a valuable adjunct in the clinical management of patients with acutely decompensated heart failure. Hemodynamic information obtained noninvasively, if correlated with cardiac output/index determined by using the thermodilution method, could help avoid the potentially life-threatening complications of infection, artery perforation, and arrhythmia that can occur with placement of a pulmonary artery catheter. In addition, noninvasive hemodynamic monitoring most likely would decrease costs because of reduced expenditures for equipment and savings in physicians' and nurses' time. These factors could lead to more widespread use of noninvasive measurement of cardiac output and more timely and appropriate hemodynamically guided therapy in the management of patients with acute decompensation, especially patients with a complex decompensation that requires intravenous inotropic agents, vasodilators, diuretics, and other agents.

Bioimpedance cardiography uses a low-amplitude, high-frequency alternating signal to calculate impedance of the flow of electricity through the chest. With this method, the instantaneous changes in electrical impedance and various other parameters are measured, from which stroke volume, cardiac output, cardiac index, and other hemodynamic parameters, including systemic vascular resistance, can be calculated. Cardiac output/index determined by using bioimpedance with a commercially available device (BioZ ICG monitor, CardioDynamics, San Diego, Calif) correlated strongly with cardiac output/index determined by using the thermodilution method in patients with stable, mild to advanced heart failure.[8] It is unknown, however, if results of impedance cardiography correlate well or have a high level of agreement with thermodilution results in patients with acutely

decompensated, complex heart failure who require critical care management.

The purposes of this study were to determine the relationship between determinations of cardiac output/index obtained by using thermodilution and bioimpedance in patients with decompensated advanced systolic heart failure and to determine if differences, if any, between cardiac output/index determined by these 2 methods can be explained by structural and functional heart alterations associated with advanced heart failure.

Impedance cardiography calculates impedance to the flow of electricity through the chest to determine cardiac output.

Methods

Setting and Sample

This study was performed between August 2001 and May 2002 in the heart failure intensive care unit (HF-ICU) at the Cleveland Clinic Foundation, Cleveland, Ohio, a tertiary care medical center with more than 1000 beds. The appropriate institutional review board approved this retrospective review study. No written informed consent from patients was required because impedance cardiography data were collected as part of a systematic review and were not used in clinical management of the patients. Insertion of a pulmonary artery catheter was considered the standard of care in this unit, and determination of cardiac output/index by impedance cardiography coincided with routine injections used for measurement of cardiac output via the thermodilution method. Medical records (written and electronic data) were retrospectively reviewed to obtain patients' demographic data, medical history, and cardiac function parameters. All patients gave verbal consent to have the leads for the impedance cardiography system applied (for the purpose of assessing new equipment for possible purchase), to be monitored for 10 to 20 minutes, and to have their hemodynamic data recorded for the purpose of comparing cardiac output/index obtained by using these 2 methods.

Patients admitted to the HF-ICU with a primary diagnosis of left ventricular systolic dysfunction, defined as an ejection fraction of 0.35 or less, and in whom a pulmonary artery catheter was in place were considered an acceptable comparison group to determine the accuracy of bioimpedance data. Ejection fraction was based on recent (within 3 months) echocardiographic results available in the medical record. On the basis of the availability of study personnel, 33 consecutive patients who were in a stable clinical state were evaluated. A stable clinical state was defined as the absence of respiratory distress when placed in a 0° to 20° supine position and no recent (within 1 hour) increase in dosage of intravenous vasoactive medications because of worsening systolic or mean blood pressure, arterial or mixed venous oxygen saturation, or heart rate. Patients were not monitored if they had a high level of anxiety; had recently (within 1 hour) been physically active; excepted to be transferred from a chair to a bed; were undergoing hemodialysis, ultrafiltration, mechanical ventilation with continuous positive airway pressure, or life-saving treatments other than mechanical ventilation; or were using a left ventricular assist device (including intra-aortic balloon pump). No patients were excluded on the basis of the type of structural or functional heart disease.

After the leads for impedance cardiography were applied, we were unable to accurately collect and record bioimpedance data from 4 patients. In 3 of these patients, electrical interference and inability of the impedance cardiography system to provide a stable impedance signal and impedance waveform prevented accurate monitoring. In 1 patient, a new onset of atrial fibrillation developed with a rapid, irregular ventricular response. The strength of the impedance signal deteriorated before cardiac output measurements were obtained, and the impedance cardiography leads were removed.

Instrumentation and Procedure

Agreement between the 2 methods for determining cardiac output/index was determined on the basis of data collected from a single set of readings from each patient by using thermodilution bolus method and by using bioimpedance monitoring (software version 2.26, CardioDynamics, San Diego, Calif). Thermodilution data were obtained by using either the Abbott 7.0F (4 ports) pulmonary artery catheter (Abbott, North Chicago, Ill) or the Biosensors International 7.5F (5 ports with an extra right atrial infusion port) catheter (Newport Beach, Calif) and a Marquette Solar 9500 bedside monitor (General Electric Medical Systems Information Technology, Milwaukee, Wis).

The data collectors (NMA and MDH), both registered nurses with extensive experience with pulmonary artery catheters, conducted all thermodilution cardiac output measurements and hemodynamic monitoring operations. Before agreement between the 2 methods was assessed, patients were placed supine with the head of the bed elevated to 20°. The position of the pulmonary artery catheter was verified by waveform analysis, the computation constant was confirmed, and the transducer was leveled and zeroed.

One of us (NMA), who is highly experienced in using bioimpedance in emergency and critical care settings, performed or supervised all determinations made by using bioimpedance. Dual bioimpedance sensors were applied to the root of the neck and to the midaxillary line at the level of the xiphoid process, as recommended by the manufacturer. Because of the presence of the pulmonary artery catheter over the right internal jugular vein, the upper sensors were positioned with the right-sided sensor posterior to the right ear lobe and the left-sided sensor 180° opposite, just anterior to the left ear lobe. Impedance and electrocardiographic signal strengths were at least 3 of 4 on the light-emitting diode bar graphs before readings were monitored and recorded. The pacemaker on-off feature was used when patients were pacemaker dependent. Head and neck movement did not affect signal strength; therefore, patients could talk and turn their heads while being monitored. The actual right atrial and pulmonary artery wedge pressures as indicated by the bedside hemodynamic monitor were used for bioimpedance calculations of systemic vascular resistance/index and left cardiac work/index, respectively. Height and weight values, and thus body surface areas, were transferred from the bedside monitor to the bioimpedance system during setup and were used to calculate cardiac indexes for both methods (ie, bioimpedance and thermodilution).

For each patient, after ensuring that the patient was in a steady-state condition, one nurse measured cardiac output by using a room-temperature fluid bolus technique. Before each injection, the blood temperature curve on the cardiac output screen was assessed to ensure that the temperature was not fluctuating. We have found that slight fluctuation in blood temperature (both increases and decreases) is common among patients with advanced decompensated chronic heart failure, and although the fluctuation rarely alters blood temperature values, the cardiac output curve may be uneven or the injection time may be prolonged, invalidating the cardiac output reading. Exactly 10 mL of 5% dextrose in water was injected through a standard cardiac output injection kit connected to the right atrial port of the pulmonary artery catheter. Injection time was less than 4 seconds. The cardiac output curve was examined with each injection to ensure that the curve and the injection time were normal. Counterbalancing of techniques (alternating the order of recording bioimpedance data immediately before or immediately after thermodilution bolus measurements) was used. A total of 3 thermodilution measurements (3 boluses injected) were obtained for each patient. Cardiac output values were deemed invalid if the respective curves were abnormal or if the injection time was prolonged. The delay between each bolus injection was at least 2 minutes; injections were not timed to the respiratory cycle.

The second nurse recorded cardiac output, cardiac index, systemic vascular resistance, thoracic fluid content, and stroke volume as indicated by the bioimpedance monitor each time a bolus was injected for the thermodilution measurements. The bioimpedance system was programmed to provide updated hemodynamic values by using a 30-beat (heart rate) data averaging process and a 30-second screen update interval. Derived measurements were continuously displayed.

Mean cardiac output values were calculated on the basis of the 3 thermodilution measurements (3 boluses) and the 3 bioimpedance measurements. Mean cardiac index was calculated for the mean thermodilution and the mean bioimpedance values. Oxygen saturation and heart rate were monitored and recorded from the bedside monitor and were used to determine continued steady state. Neither of the nurses was blinded from observing what the other nurse was doing or from viewing the data on the impedance cardiography monitor.

Demographic, medical history, cause of heart failure, and echocardiographic data were collected retrospectively for all 33 patients by chart review. Electrocardiographic information was obtained as part of routine nursing care directly from the bedside monitor when pulmonary artery wedge pressure waveform data were obtained. These chart data were used to analyze and record heart rhythm and QRS interval.

Data Analysis

Before evaluating the equipment and on the basis of established bioimpedance data from other reports, we sought to determine the proper sample size for agreement in cardiac output measurements. For an α of .05 and a β of .20, a minimum of 16 patients was required to determine a clinically significant mean difference of 0.1 L/min in cardiac output. We found no published reports of the sample size required to determine if patients' comorbid conditions and functional and structural heart abnormalities were predictive of poor correlation, so our goal was to monitor 30 patients.

Demographic and hemodynamic data are expressed as means and SDs or as proportions. To assess agreement between paired mean thermodilution and bioimpedance measurements of cardiac output, the concordance correlation coefficient (ρ_c) was calculated. When desirable reproducibility is measured, concordance correlation tests correlation on the 45° line through the origin on a plot of one measurement against another. This method is superior to the Pearson correlation because the Pearson correlation is not restricted to

Table 1 Data on demographics and cardiac structure and function (N = 29)

Variable	Value*
Age, mean (SD), years	57.6 (11.0)
Sex, male	83
Race, white	82
Body mass index, mean (SD), kg/m^2	28.7 (6.1)
Ischemic cardiomyopathy	76
Dilated cardiomyopathy	17
Hypertensive heart failure	0
Alcoholic cardiomyopathy	7
Diabetes	41
Chronic obstructive pulmonary disease	21
Asthma	21
Atrial fibrillation	10
Ventricular tachycardia/premature ventricular complexes	0
Hypercholesterolemia	62
Renal insufficiency (creatinine >177 μmol/L)	17
Pacemaker	41
Implantable cardioverter defibrillator	34
Hemoglobin, mean (SD), g/L	112 (19)
Current medications	
Angiotensin-converting enzyme inhibitor	62
Hydralazine	41
Oral nitrate	45
Angiotensin II receptor blocker	7
β-Blocker	21
Digoxin	69
Amiodarone	28
Spironolactone	24
Oral loop diuretic	17
Intravenous loop diuretic (bolus or continuous)	72
Intravenous nitrate infusion	31
Intravenous nesiritide infusion	7
Intravenous dobutamine infusion	28
Intravenous milrinone infusion	14
Intravenous dopamine infusion	3
Left ventricular ejection fraction, mean (SD), proportion of 1.0	0.169 (0.075)
Left ventricular end-systolic diameter, mean (SD), cm (n = 27)	5.8 (1.4)
Left ventricular end-diastolic diameter, mean (SD), cm (n = 27)	6.4 (1.2)
Left atrial diameter, mean (SD), cm (n = 21)	4.9 (0.9)
Mitral valve regurgitation, 3-4+	34
Mitral valve stenosis	11
Tricuspid valve regurgitation, 3-4+	24
Aortic valve regurgitation, 3-4+	7
Aortic valve stenosis	22

*Values are percentage of patients unless indicated otherwise.

the 45° line.[9] The agreement between cardiac output values measured by bioimpedance and by thermodilution was assessed by calculating the mean bias, the SD of the bias, and the 95% confidence limits of agreement as described by Bland and Altman.[10] Absolute percent differences of greater than 15% between thermodilution and bioimpedance measurements of cardiac output were considered clinically significant, and the occurrences of such differences were examined. Specifically, factors related to patients such as ventricular function and valve function were examined to determine if advanced heart failure and/or valve regurgitation affected the accuracy of impedance cardiography. Logistic regression analysis was used to compare the differences for each variable. The SAS software version 8.2 (SAS Institute Inc, Cary, NC) was used for data analysis.

Results

Data on variables related to the cohort's demographics, cardiac structure, and function are provided in Table 1. The study population was primarily male, obese, and had many comorbid conditions. For the 29 patients whose data were analyzed, the mean age was 57.6 (SD, 11.0) years, mean left ventricular ejection fraction was 0.169 (SD, 0.075), and the prevalence of use of angiotensin-converting enzyme inhibitor or an

Table 2 Hemodynamic data (N = 29)

Variable	Mean	
Respiratory rate, breaths per minute	19.8	2.4
Heart rate, beats per minute	84.9	17.0
Systolic blood pressure, mm Hg	101.6	17.0
Diastolic blood pressure, mm Hg	53.0	6.8
Core blood temperature, °C*	36.9	0.6
Pulmonary artery systolic pressure, mm Hg*	45.9	13.7
Pulmonary artery diastolic pressure, mm Hg*	20.7	7.2
Pulmonary artery wedge pressure, mm Hg*	18.2	7.1
Right atrial pressure, mm Hg*	11.8	7.4
Mixed venous oxygen saturation, %	60.2	8.1
Arterial oxygen saturation, %	95.3	2.7
Pulmonary vascular resistance, dynes · sec · cm^{-5}*	208.9	122.0
Systemic vascular resistance, dynes · sec · cm^{-5}		
Thermodilution	837.9	266.8
Impedance cardiography	859.2	281.7
Cardiac output, L/min		
Thermodilution	5.48	1.43
Impedance cardiography	5.40	1.48
Cardiac index†		
Thermodilution	2.69	0.57
Impedance cardiography	2.65	0.57
Thoracic fluid content, kOhm‡	42.91	9.32
Stroke volume‡	64.8	18.2
Right ventricular systolic pressure, mm Hg§	41.8	11.8

*Calculated by thermodilution cardiac output.
†Calculated as cardiac output in liters per minute divided by surface area in square meters.
‡Calculated by impedance cardiography.
§Obtained by echocardiography.

alternative vasodilator and nitrate combination, diuretic therapy, and digoxin therapy was high. A total of 34% of patients had 3 to 4+ mitral regurgitation, and 24% had 3 to 4+ tricuspid regurgitation. A total of 41% had pacemakers and 34% had cardioverter-defibrillators. No patients were receiving mechanical ventilation when data were collected. Intravenous infusions of vasoactive agents were common: inotropic agents in 45% of patients, vasodilators in 31%, and inovasodilators in 14%.

The hemodynamic data are shown in Table 2. The median length of time from HF-ICU admission to the start of impedance cardiography monitoring was 40 hours (2.5-185 hours). Mean cardiac output was 5.48 (SD, 1.43) L/min by thermodilution and 5.40 (SD, 1.48) L/min by bioimpedance. Mean cardiac index was 2.67 (SD, 0.57) by thermodilution and 2.65 (SD, 0.57) by bioimpedance.

In Figures 1 and 2, the mean values of cardiac output and cardiac index as determined by impedance cardiography are plotted against thermodilution values. The diagonal line indicates where the data points would be if the measurements obtained with the 2 techniques were identical. The concordance correlation coefficient (ρ_c) of all 29 paired measurements was 0.89 ($P < .001$) for cardiac output and 0.82 ($P < .001$) for cardiac index. A high Pearson correlation coefficient may not mean high agreement between methods of measuring cardiac output; however, in our study, the Pearson correlation coefficients were exactly the same as the concordance correlation for each method. The mean discrepancy (bias) between thermodilution and bioimpedance was very small: 0.08 L/min for cardiac output (range, -0.18 to 0.35) and 0.03 for cardiac index (range, -0.097 to 0.16), and the individual differences clustered around the mean (Figures 3 and 4). Mean precision (95% CI of the mean difference) was 1.38 L/min for cardiac output and 0.68 for cardiac index. For cardiac output, 1 data pair fell outside 2 SDs of the mean, and for cardiac index, only 2 data pairs fell slightly outside 2 SDs.

Six data pairs (21%) differed from each other by more than 15%. For 50% of these, the bolus thermodilution measurement was higher than the measurement made with impedance cardiography. In multivariate regression analysis, a low core body temperature and lower ejection fraction were associated with differences between cardiac output determined by thermodilution and by bioimpedance, and low core body temperature and presence of atrial fibrillation were associated with differences between cardiac index (Table 3). No other variables studied, including degree of mitral or tricuspid regurgitation, aortic insufficiency, degree of left atrial or

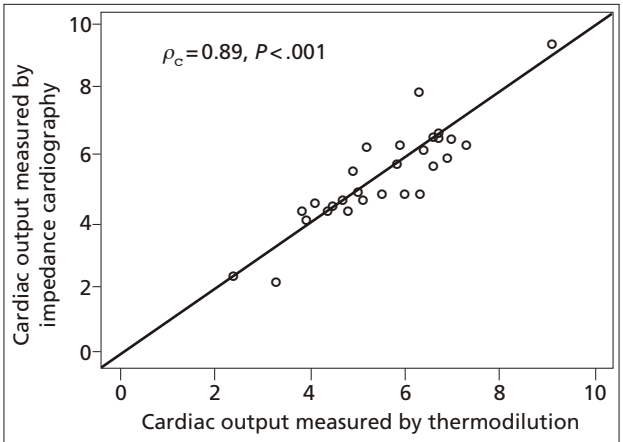

Figure 1 Concordance correlation plot for cardiac output. Diagonal line shows where data points would be if both techniques provided identical values.

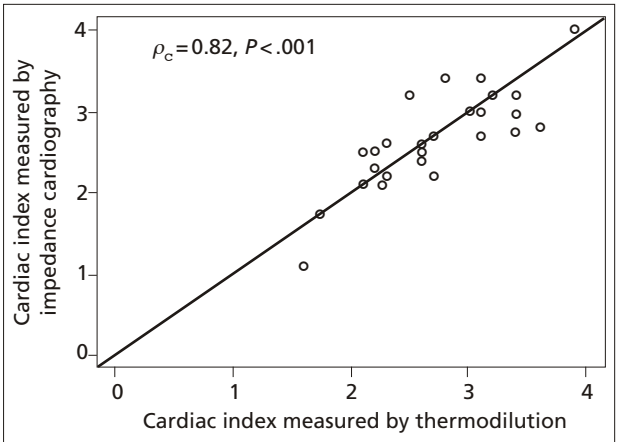

Figure 2 Concordance correlation plots for cardiac index. Diagonal line shows where data points would be if both techniques provided identical values.

ventricular remodeling, QRS width, body size, pacemaker use, other arrhythmias, or aggravating comorbid conditions were associated with significant differences between cardiac output or cardiac index determined with the 2 methods.

The overall difference between thermodilution and bioimpedance cardiac output was very small, but 21% of the pairs differed by more than 15%.

Discussion

Impedance cardiography provides noninvasive, readily available, and continuous measurements of cardiac output and other hemodynamic parameters such as systemic vascular resistance. Bioimpedance measurements of cardiac output must be compared with measurements obtained with the current standard technique to ensure the reliability of the new method. Reliability of data is critical because treatment decisions to optimize hemodynamic status are based on such data. Patients with advanced, decompensated heart failure may be admitted to the critical care unit for the primary purpose of using hemodynamically guided therapy to stabilize their condition. In this study, bioimpedance data showed excellent correlation with data obtained by a standard thermodilution technique, and bias and limits of agreement between the 2 methods for both cardiac output and cardiac index were acceptable.

A review of the literature suggests that many factors can cause discrepancies between cardiac output measurements obtained by using 2 different methods. When thermodilution and metabolic (estimated and standard Fick methods) measurements of cardiac output were compared in critically ill patients, the mean coefficient of variation between measurements was only 3.5%; however, CIs for comparisons of thermodilution and metabolic measurements were wide.[11] That result led the researchers to conclude that use of estimated oxygen consumption for measurements of cardiac output determined by using the Fick method were a poor substitute for use of measured oxygen consumption.[11]

In current practice, most patients do not have oxygen consumption measured and therefore thermodilution has replaced the Fick method as the most commonly used method (and de facto reference standard) for measurement of cardiac output. However, evidence indicates that factors related to clinicians and equipment and intrinsic to patients may affect the accuracy and reproducibility of thermodilution measurements.[12-14] Likewise, the accuracy of impedance cardiography may be influenced by factors related to clinicians such as sensor placement, the digital signal processing system, and the algorithm and equations used to calculate cardiac output. Therefore, many human and technological factors could affect the correlation of cardiac output measurements made with the clinical standard (thermodilution) and measurements made with impedance cardiography.

Newer generation devices for impedance cardiography use more accurate equations to calculate cardiac output. In a recent review of impedance cardiography algorithms used to calculate cardiac output, Van De Water et al[15] found that cardiac output calculated by using the ZMARC equation showed the closest agreement to thermodilution cardiac output measurements. The ZMARC algorithm is the equation developed and

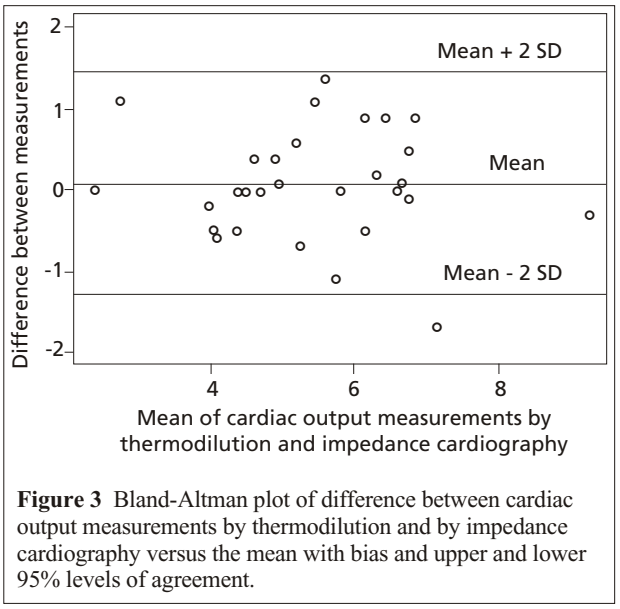

Figure 3 Bland-Altman plot of difference between cardiac output measurements by thermodilution and by impedance cardiography versus the mean with bias and upper and lower 95% levels of agreement.

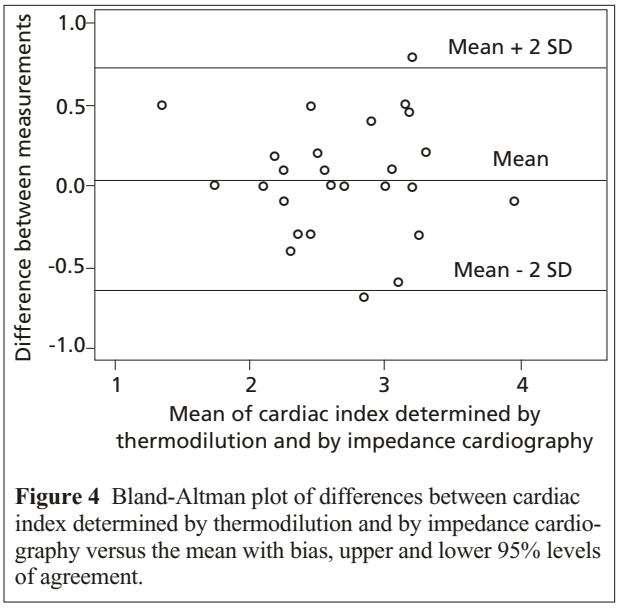

Figure 4 Bland-Altman plot of differences between cardiac index determined by thermodilution and by impedance cardiography versus the mean with bias, upper and lower 95% levels of agreement.

used by the CardioDynamics BioZ ICG monitor that was used in this study. Clinical studies in which this equation was used in patients with cardiac disease (surgical and medical patients) indicated close linear agreement and acceptable bias and precision between impedance cardiography and thermodilution for measurement of cardiac output.[16,17]

Accuracy of bioimpedance cardiac output may be affected by sensor placement, the digital signal processing system, and the algorithm used.

In a study of patients with advanced heart failure who underwent pulmonary artery catheterization, Drazner et al[16] compared impedance cardiography with invasive hemodynamic measurements. In that study, correlation and Bland-Altman agreement between cardiac output determined by bioimpedance and by the direct Fick method were equivalent to those between cardiac output determined by thermodilution and by the direct Fick method. Drazner et al found that Pearson correlations between impedance cardiography and thermodilution were 0.76 for cardiac output and 0.64 for cardiac index, much less than we found in our study (0.89 and 0.82, respectively). Demographic and hemodynamic data were similar among patients in our study and in the study of Drazner et al. However, Drazner et al performed their measurements in the cardiac catheterization laboratory. In addition, our patients were in acute distress from decompensated heart failure shortly before impedance cardiography monitoring. Our clinicians were not blinded to the readings on the bioimpedance monitor during measurement of cardiac output by the thermodilution method, as were the clinicians in the study by Drazner et al. Despite differences in methods, these 2 studies both indicate that impedance cardiography provides results that are comparable to results of accepted invasive techniques.

Low body temperature was a significant factor leading to a mean difference of greater than 15% between thermodilution and bioimpedance measurements of cardiac output and cardiac index. On the basis of prior research on acceptable differences between other determinations of cardiac output and thermodilution measurements of cardiac output,[18] we used 15% as the cutoff for a clinically acceptable allowable difference between methods. Our results could have been influenced by the smaller absolute difference between patients' body temperatures and injectate temperatures in these patients with very slight hypothermia; however, in studies in hypothermic patients, correlation was good between measurements obtained by using iced and room-temperature injectate.[12,13,19] Of note, most published studies of thermodilution measurements of cardiac output did not include a large number of patients with heart failure. A large ventricular cavity and intermittent low-flow state due to inconsistent contractility (pulsus alternans) and ventricular ectopy might influence temperature differences over time and flow of room-temperature injectate through the thermodilution catheter in patients with heart failure. Possibly, a lower body temperature and use of an impedance monitor that uses a 30-beat data averaging process result in a

Table 3 Variables related to the 6 data pairs that had a difference of greater than 15% between methods

Cardiac output

Variable	Estimate	SE	Wald χ^2	*p*
Low temperature	-5.71	2.82	4.1053	.04
Ejection fraction	-2.08	1.17	3.1401	.08

Summary: Patients with lower body temperature and lower ejection fraction were likely to be different.

Cardiac index

Variable	Estimate	SE	Wald χ^2	*p*
Atrial fibrillation	4.19	1.85	5.1368	.02
Low temperature	-3.62	1.78	4.1303	.04

Summary: Patients with atrial fibrillation and lower body temperature were likely to be different.

more accurate measurement of cardiac output in this subgroup. In reports of previous studies on agreement between thermodilution and bioimpedance measurements of cardiac output, the investigators did not discuss variables that reflect an absolute percent difference of greater than 15%. Further research is necessary to determine if low body temperature influences the accuracy of measurements of cardiac output and whether the thermodilution method with room-temperature injectate or the bioimpedance method is superior.

Patients with a lower ejection fraction and atrial fibrillation were also more likely to have an absolute percent difference of greater than 15% between pairs of cardiac output and cardiac index data, respectively. Because both a low ejection fraction and atrial fibrillation with an irregular ventricular response can affect the flow state, and these same patients were more likely to also have a lower body temperature, these factors may be related and may act as mediator variables. Again, further research on the affect of variables that influence flow states in patients with heart failure might provide an explanation for these findings and aid in determining if impedance cardiography is superior to thermodilution for measuring cardiac output when specific clinical variables exist.

Differences in bioimpedance and thermodilution cardiac output were found in subjects with low body temperature or low ejection fraction and atrial fibrillation.

Of note, similar to other investigators who assessed accuracy of measurements of cardiac output in patients with atrioventricular valve dysfunction, we did not find differences between methods of measuring cardiac output associated with the presence or severity of valve regurgitation or stenosis. Left ventricular end-systolic, left ventricular end-diastolic, and left atrial diameter did not influence agreement between the 2 methods. In addition, use of intravenous vasoactive medications did not influence agreement between the 2 methods.

Limitations of this study included our use of a convenience sample, although the demographics reflected patients with advanced heart failure, which was our intended population of patients. Because data were originally collected to evaluate whether to purchase an impedance cardiography system, data not associated with agreement of cardiac output measurements were collected retrospectively. Researchers were not blinded to the results of the other method when they were collecting data to determine the accuracy of cardiac output measurements, a situation that created the potential for bias in the recorded measurements of impedance cardiography and thermodilution. However, great care was taken to ensure that the data were collected and recorded in a consistent and methodical fashion. In addition, the cohort included a significant number of patients with 3 to 4+ tricuspid regurgitation, which can affect the reliability of thermodilution measurements of (right-sided) cardiac output.

All patients had undergone initial treatment and stabilization in the critical care unit. Therefore, none were in such unstable condition as to require mechanical ventilation or mechanical blood pressure support. Consequently, our results cannot be applied to patients who are receiving mechanical ventilation or who require mechanical support with either an intra-aortic balloon pump or a ventricular assist device. However, other researchers have reported positive clinical results with impedance cardiography in patients receiving mechanical ventilation[20] and in patients requiring left ventricular assist devices.[21] Last, we did not evaluate patients with conditions in which impedance cardiography has shown limitations in previous studies, such as end-stage septic shock.

Impedance cardiography does not provide intravenous volume data equivalent to data obtained with a pulmonary artery catheter (right atrial and pulmonary artery wedge pressures). In one study[16] no correlation was found between thoracic fluid content values obtained from impedance cardiography and pulmonary artery wedge pressure ($r=0.05$. $P=.71$). In our study, thoracic fluid content values and pulmonary artery wedge pressures were converted into quartiles to reflect hypo-

volemia, normal volume, moderate hypervolemia, and severe hypervolemia and quartile values for thoracic fluid content were specified for males and females. We found moderate positive correlation between thoracic fluid content and left ventricular diastolic pressures ($r = 0.39$; $P = .02$). Although significant, this correlation cannot be used as a guide in making clinical decisions without further study.

In our study, 4 (12%) of 33 patients had an unstable impedance or electrocardiographic signal that prevented accurate monitoring. The impedance cardiography monitor provided warning of poor electrocardiographic or bioimpedance signal strength via a light meter and on-screen warning messages. Thus, nurses were easily able to monitor the occurrence of an unstable signal and ensure that data obtained met minimum technical standards set up in the system. When the monitor displays a poor electrocardiographic signal in one lead position, the operator can choose another lead (4 options are available) to see if QRS amplitude and signal strength improves. An unstable impedance signal usually improves as the electrocardiographic signal improves; however, wide QRS tachycardia and consistently occurring ventricular ectopic beats may be an electrocardiographic limitation. If repositioning patients and other measures do not strengthen the impedance signal, the available options are to monitor the patient invasively after placement of a pulmonary artery catheter or to manage the patient without the benefits of hemodynamic data. Further study of the frequency of impedance waveform issues not related to QRS configuration and the position or skin adherence of impedance cardiography leads might provide valuable information about specific body habitus or other characteristics of patients that suppress bioimpedance and electrocardiographic signals.

Nonetheless, impedance cardiography is a useful monitoring technique in a critical care unit[22] and could decrease hospital costs associated with invasive hemodynamic monitoring.[23] In a small study[24] in which the investigators evaluated whether the availability of impedance cardiography could reduce the need for pulmonary artery catheterization, patients who were first determined to need invasive hemodynamic monitoring were subsequently monitored with impedance cardiography. In 71% of patients, use of impedance cardiography eliminated the need for a pulmonary artery catheter.[24]

Conclusions

Impedance cardiography is a noninvasive, beat-to-beat, operator-independent technology used to measure cardiac output and provide other hemodynamic measurements. Our results indicate that impedance cardiography provides accurate measurements of cardiac output and cardiac index with a small bias and narrow limits of agreement when compared with the bolus thermodilution method. Cardiac output is easier to measure by impedance cardiography than by thermodilution with a pulmonary artery catheter, can be applied quickly, and does not pose a risk of infection, blood loss, or other complications associated with arterial catheters. In addition, impedance cardiography allows continuous monitoring of cardiac output, unlike intermittent measurements with thermodilution, which involve injections of fluid boluses with the attendant risk of volume overload.

Once the impedance cardiography sensors are properly applied and information is entered into the system, the risk of clinician-induced error is minimal. Although not all studies reported in the literature are positive, cumulative correlation coefficients of impedance cardiography with a criterion standard in a variety of clinical conditions and populations of patients have validated this technique.[25] Our findings provide further validation of use of impedance cardiography in patients with acutely decompensated chronic heart failure in stable condition. In addition, the increased frequency of cardiac output data available with impedance cardiography might lead to more timely interventions, resulting in clinical improvement and a shorter stay in the intensive care unit.

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Commentary by Mary Jo Grap (see shaded boxes).

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