ORIGINAL PAPER

Comparison of Impedance Cardiography to Direct Fick and Thermodilution Cardiac Output Determination in Pulmonary Arterial Hypertension

Cardiac output (CO) is an important diagnostic and prognostic tool for patients with ventricular dysfunction. Pulmonary hypertension patients undergo invasive right heart catheterization to determine pulmonary vascular and cardiac hemodynamics. Thermodilution (TD) and direct Fick method are the most common methods of CO determination but are costly and may be associated with complications. The latest generation of impedance cardiography (ICG) provides noninvasive estimation of CO and is now validated. The purpose of this study was to compare ICG measurement of CO to TD and direct Fick in pulmonary hypertension patients. Thirty-nine enrolled patients were analyzed: 44% were male and average age was 50.8±17.4 years. Results for bias and precision of cardiac index were as follows: ICG vs. Fick (–0.13 L/min/m^2 and 0.46 L/min/m^2), TD vs. Fick (0.10 L/min/m^2 and 0.41 L/min/m^2), ICG vs. TD (respectively, with a 95% level of agreement between –0.72 and 0.92 L/min/m^2; CO correlation of ICG vs. Fick, TD vs. Fick, and ICG vs. TD was 0.84, 0.89, and 0.80, respectively). ICG provides an accurate, useful, and cost-effective method for determining CO in pulmonary hypertension patients, and is a potential tool for following responses to therapeutic interventions. (CHF. 2004;10(2 suppl 2):7–10) ©2004 CHF, Inc.

Cardiac output (CO) measurement provides valuable diagnostic and prognostic information in the management of patients with left- and right-sided cardiac dysfunction.[1,2] Pulmonary arterial hypertension (PAH), a condition characterized by elevation in the blood pressure of the pulmonary arteries of the lung, may result in right-sided heart failure and low CO. Untreated, the condition can be fatal. Despite the importance of CO in PAH, few studies have looked at the accuracy of current methods of CO measurements in this group of patients.

The purpose of this study was to compare the accuracy of impedance cardiography (ICG) to thermodilution (TD) and direct Fick in the measurement of CO and cardiac index (CI) in PAH patients.

Methods

The study protocol was approved by the Human Subjects Committee of the University of California, San Diego. Written informed consent was obtained for all patients. Patients who had been referred to the Pulmonary Vascular Program at the University of California San Diego Medical Center for evaluation of pulmonary hypertension were included in the study. All patients were considered clinically stable and the study was performed in the cardiac catheterization laboratory. Right heart catheterization was performed as part of the routine workup for the patients. A pulmonary artery catheter was placed via internal jugular vein in the usual manner, under fluoroscopic guidance. Exclusion criteria included age (<18 years), height (<4 ft or >7 ft 6 in), and severe obesity (>65% above ideal body weight).

All ICG CO (CO_{ICG}) measurements were performed with the BioZ ICG monitor (CardioDynamics, San Diego, CA). CO_{ICG} measurements were performed according to the manufacturer's guidelines during the same period when CO by TD method (CO_{TD}) was obtained by an independent cardiologist. Each CO_{TD} was determined as a function of the area under the temperature–time curve, using a CO computer (Com II CO monitor, Baxter-Edwards, Deerfield, IL). As the cardiologist injected each fluid bolus (10 mL room temperature, 5% dextrose) to obtain a minimum of three CO_{TD} values with <10% variation, the corresponding CO_{ICG} values were recorded. Unlike the CO_{TD} values, which were obtained usually at various times during the respiratory cycle, the CO_{ICG} values were continually displayed and updated on the ICG monitor every 10 beats. In this manner, at least three pairs of CO measurements were obtained for each patient. The physician-determined acceptable CO_{TD} measurements were averaged to obtain the final CO_{TD} for each patient. The recorded CO_{ICG} measurements corresponding to the accepted CO_{TD} measurements were also averaged for each patient to obtain the final CO_{ICG} for each patient. All recorded CO_{ICG} measurements were used without any being either objectively or subjectively rejected.

Cardiac output measurements via the Fick method (CO_{FICK}) were determined within 10 minutes of the paired CO_{TD} and CO_{ICG} measurements. A face mask was placed over the patient with a tight head strapping to ensure complete collection of expired gas. The system was

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checked periodically during the study for air leaks. Inhaled oxygen concentration was titrated at the beginning of the study with an oxygen blender to avoid hypoxia. Oxygen delivery was kept constant throughout, and stabilization of respiratory pattern was achieved by allowing a 5-minute rest period. Steady state was defined by a respiratory quotient between 0.65 and 0.9. Average steady state oxygen consumption was obtained using a portable indirect calorimetry monitor (Deltatrac, Datex Instrumentation, Helsinki, Finland). Briefly, it is an open system that analyzes the differential partial oxygen pressures (PO_2) of inhaled and exhaled gas using a paramagnetic oxygen sensor, and the gas flow is measured via a gas dilution system. To ensure accuracy, the system was calibrated before each study and the values were time-averaged over at least 5 minutes. Simultaneous arterial and mixed venous blood samples were then drawn for measurement of arterial oxygen saturation (SaO_2) and hemoglobin (Hgb) concentration. Arterial blood samples were obtained through either a radial or femoral arterial puncture, and the mixed venous blood samples were obtained from the distal port of the pulmonary artery catheter. Oxygen content was calculated using the equation:

$$\text{Oxygen content} = 1.34 \times \text{Hgb} \times SaO_2 + 0.003 \times PO_2$$

The CO_{FICK} was then calculated by dividing the average oxygen consumption (VO_2) value with the difference between the concentration of aterial oxygen (CaO_2) and concentration of mixed venous oxygen content (CvO_2):

$$CO_{FICK} = VO_2/CaO_2 - CvO_2$$

All CO measurements were indexed by the patient's body surface area and the following statistical analyses for comparing the average CO and CI for the three methods (CO/CI_{ICG}, CO/CI_{TD}, and CO/CI_{FICK}) were performed: Pearson's correlation, regression analysis, and Bland-Altman analysis[3] for bias and precision. Bias is defined as the mean of all CO errors, and precision is defined as the standard deviation of CO errors. Age variables are expressed as mean ± standard deviation. Student paired *t* test was used to determine statistical significance.

Results

Forty-two patients were enrolled in the study. Three were omitted from analysis, two due to the inability to obtain CO_{ICG} and one due to the inability to obtain CO_{FICK}. No serious complication occurred during the study. Final analysis included 22 women and 17 men. Age was 50.8±17.4 years, range 18 to 80 years. All patients survived.

Etiology of pulmonary hypertension was due to primary pulmonary hypertension (nine patients, seven women and two men), chronic pulmonary thromboembolic disease (28 patients, 13 women and 15 men), idiopathic pulmonary hypertension (one female patient), and mixed connective tissue disease (one female patient). Tricuspid valve regurgitation was evident in all patients (nine mild, 19 mild-moderate to moderate, and 11 moderate-severe to severe). Patent foramen ovale was present in 14 patients.

The results for Pearson's correlation, and Bland-Altman analysis for bias and precision (first standard deviation) for CO/CI_{ICG} as compared with CO/CI_{FICK} and CO/CI_{TD} are listed in the Table. The results for Pearson's correlation of CO ICG vs. Fick, TD vs. Fick, and ICG vs. TD were 0.84, 0.89, and 0.80, respectively.

CO/CI_{ICG} vs. CO/CI_{FICK} Comparison. See Figure 1 for a scatterplot of the paired CO_{ICG} and CO_{FICK} measurements. When the 39 paired average CI_{ICG} vs. CI_{FICK} measurements were tested with the Bland-Altman analysis, the bias and precision were –0.13 L/min/m^2 and 0.46 L/min/m^2 respectively, with a 95% level of agreement between –1.05 and 0.79 L/min/m^2 (Figure 2).

The results for Pearson's correlation and the Bland-Altman analysis for bias and precision (first standard deviation) for CO/CI_{ICG} compared with CO/CI_{FICK} and CO/CI_{TD} are listed in the Table. The results for Pearson's correlation of CO ICG vs. Fick, TD vs. Fick, and ICG vs. TD were 0.84, 0.89, and 0.80, respectively.

CO/CI_{TD} vs. CO/CI_{FICK} Comparison. See Figure 3 for a scatterplot of the paired CO_{TD} and CO_{FICK} measurements. The results for Pearson's correlation, and Bland-Altman analysis for bias and precision ± standard deviation for CO/CI_{TD} compared with CO/CI_{FICK} are listed in the Table. Bias and precision were 0.10 L/min/m^2 and 0.41 L/min/m^2, respectively, with a 95% level of agreement between –0.72 and 0.92 L/min/m^2 (Figure 4).

CO/CI_{ICG} vs. CO/CI_{TD} Comparison. Bias and precision were –0.43 L/min/m^2 and 0.53 L/min/m^2 respectively, with a 95% level of agreement between –0.1.49 and 0.63 L/min/m^2.

Discussion

The diagnosis and treatment of pulmonary hypertension often requires right heart catheterization procedures to assess pulmonary artery pressures, pulmonary vascular resistance, and CO. A truly continuous measurement of CO would be desirable to clinicians treating a variety of chronic and acute diseases, including pulmonary hypertension and heart failure. Through right heart catheterization, the TD method and Steward-Hamilton equation that utilizes temperature change over time has become the most common method of CO estimation in critically ill patients.[4–6] However, no method of CO estimation is perfect, and multiple clinical limitations of the TD method exist.[7–10] Technical issues can also affect the validity of TD, including computer calibration, catheter placement, rate of injection, temperature and volume of the injectate, timing of the injection during the respiratory cycle, and the position of the subject.[11]

The direct Fick method of CO estimation utilizes oxygen uptake and the arteriovenous difference in oxygen content to estimate CO and is often considered the most accurate method. However, direct Fick can be time intensive and operator dependent due to the need to draw both

Table. Intermethod Comparison					
	Pearson's Correlation (*R*)	CO Bias (L/min)	CI Bias (L/min/m²)	CO Precision (L/min)	CI Precision (L/min/m²)
ICG vs. Fick	0.84	–0.24	–0.13	0.87	0.46
TD vs. Fick	0.89	0.19	0.10	0.76	0.41
ICG vs. TD	0.80	–0.43	–0.23	1.01	0.53

CO=cardiac output; CI=cardiac index; ICG=impedance cardiography method; Fick=direct Fick method; TD=thermodilution method

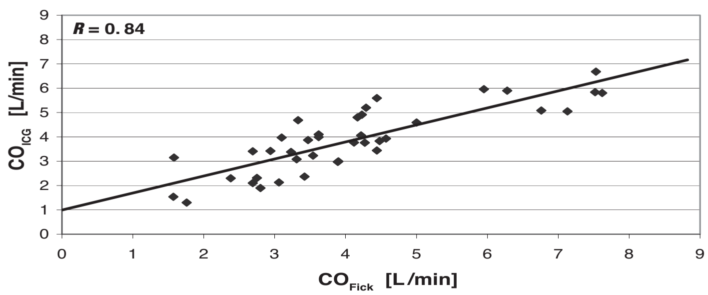

Figure 1. Scatterplot showing impedance cardiography (ICG) vs. direct Fick method (Fick). CO=cardiac output

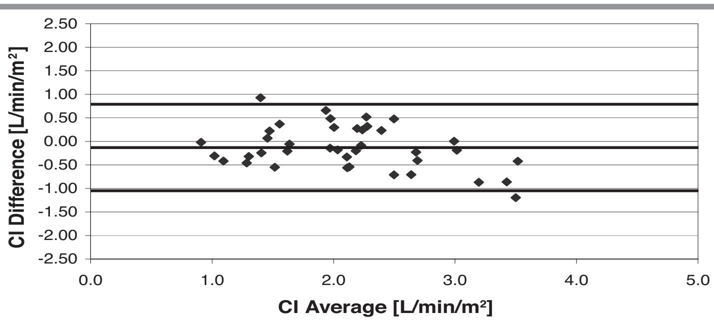

Figure 2. Bland-Altman analysis showing impedance cardiography vs. direct Fick method. CI=cardiac index

arterial and venous blood oxygen samples. TD has been compared with direct Fick in a variety of patient populations with generally good agreement.[12] Of course, TD from the right heart catheterization allows only intermittent measures of CO. Changes in hemodynamics that occur in minutes or even hours in response to therapeutic interventions or disease progression cannot be monitored.

Noninvasive ICG uses eight sites on four adhesive sensors on the neck and chest to monitor impedance changes based on the introduction of a low amplitude alternating current to measure hemodynamic parameters such as CO and systemic vascular resistance. ICG was introduced as a concept to monitor hemodynamics in the 1940s[13] and first commercialized in the 1960s.[14] In the 1980s, Sramek[15] and Bernstein[16] put forward an improved ICG method, but signal processing limitations and invalid assumptions in CO algorithms produced inconsistent performance that did not compare well to TD or direct Fick methods.[17] However, recent advancements with the latest generation of ICG devices have offered significant hope toward a new, noninvasive standard for hemodynamic monitoring. Recent trials with ICG have demonstrated acceptable intramethod reproducibility and intermethod comparison of accuracy with invasive methods.[18–21]

A method to monitor CO less intermittently with invasive catheters was introduced by Yelderman.[22] Often called continuous CO determination catheters, Haller et al.[23] and Zollner et al.[24] demonstrated that they do not really provide real-time monitoring of CO, with hemodynamic changes taking at least three and as long as 10 minutes to register fully. Although the accuracy of continuous CO catheters has been accepted clinically, differing opinions exist on the accuracy of the method compared with TD and direct Fick.[25,26]

Some have suggested that the ability to monitor hemodynamics continuously would reduce workload of medical personnel, and that the increased surveillance may result in more frequent medical interventions of critically ill patients, possibly improving outcomes.[27,28] A truly continuous method of hemodynamic monitoring would theoretically provide real-time determination of the effects of parenteral therapeutic agents, allowing titration of treatments based on patient-specific response. The ideal real-time monitor would also be noninvasive, and therefore reduce many of the clinical drawbacks surrounding the use of invasive hemodynamics monitoring, and provide a cost-effective method at the same time. Unfortunately, a validated tool to accomplish real-time monitoring of hemodynamics has been elusive.

In this study of spontaneously breathing, nonintubated pulmonary hypertension patients, ICG compared favorably in direct comparisons with the invasive methods (TD and direct Fick) and almost as well as the invasive methods compared with each other. ICG had greater bias and less precision and correlation when compared with TD than when compared with Fick, but there were no clinically significant differences between the accuracy of ICG and TD when compared with Fick, a result duplicated in another three-way comparison in heart failure patients.[29] With the known limitations of TD, clinicians and researchers evaluating the accuracy of ICG may be advised to question whether differences between ICG and TD are due to the limitations of ICG, TD, or both methods.

ICG does not provide intracardiac pressures such as pulmonary artery or pulmonary artery wedge pressure, or the derivative pulmonary vascular resistance measure, but does provide measurement of fluid trending and myocardial contractility.[29] Known limitations of ICG include severe aortic

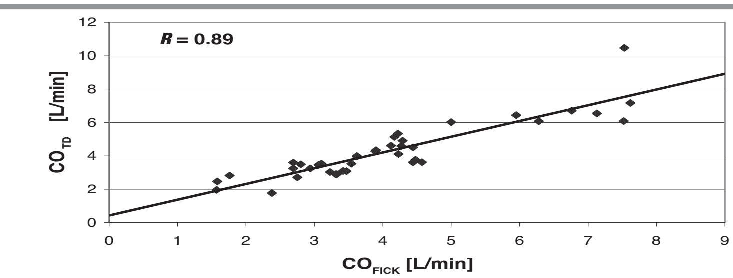

Figure 3. Scatterplot showing thermodilution (TD) vs. direct Fick method (Fick). CO=cardiac output

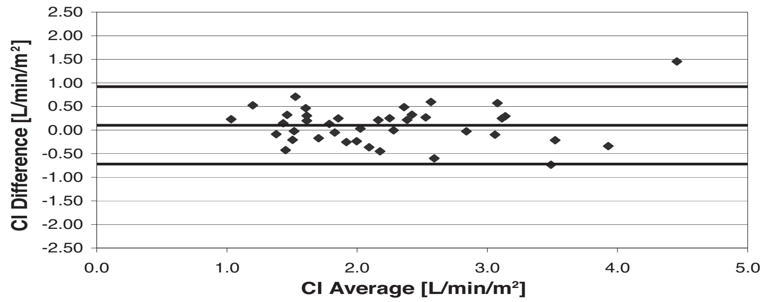

Figure 4. Bland-Altman analysis showing thermodilution vs. direct Fick method. CI=cardiac index

valve regurgitation, and end-stage septic shock.[31] ICG is a convenient, less costly alternative that is not associated with the complications and discomfort of right heart catheterization. It is also more rapidly performed and less invasive than direct Fick method, which is labor intensive and requires multiple blood samplings. Because ICG only requires minimal technical skill, it is also one of the easiest methods of CO determination available. In theory, ICG has the potential to selectively replace the other, more invasive procedures[32] of determination of CO, and extends hemodynamic monitoring to less acute settings outside the intensive care environment, including outpatient clinics.

Our study suggests that ICG may provide an accurate, useful, and cost-effective method for determining CO in pulmonary hypertension patients and is a potential tool for following responses to therapeutic interventions.

Acknowledgment: *The authors thank **Kirk U. Knowlton, MD,** for his help in performing all the cardiac catheterizations, and **Chantal C. Fletcher, MS,** for her help in ensuring the accuracy of the equipment used in the study.*

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