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Non-invasive measurement of cardiac output during coronary artery bypass grafting

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Abstract

Objective: A new device, using whole body bioresistance measurements and a new equation for calculating stroke volume has been developed. Using this equation, an attempt was made to correlate whole body bioresistance cardiac output with thermodilution cardiac output in patients undergoing coronary artery bypass grafting. **Methods**: Thirty-one adults undergoing elective coronary artery bypass grafting were studied prospectively. Simultaneous paired cardiac output measurements by whole body bioresistance and thermodilution were made at five time points during coronary artery bypass grafting: in anesthetized patients before incision (T_1), after sternotomy (T_2), after opening the pericardium (T_3), ten min post bypass (T_4), and in the intensive care unit (T_5). The patients had a mean of three thermodilution cardiac outputs compared with a mean of three bioimpedance measurements at each time point. The bias and precision between the methods were calculated. **Results**: There was good correlation between bioresistance cardiac output (*nCO*) and thermodilution cardiac output (*ThCO*) measurements in both groups for all recorded times. The patients' mean *ThCO* and *nCO*, as well as bias and precision between methods were calculated. Mean *ThCO* ranged between 4.14 and 5.06 l/min; mean *nCO* ranged between 4.12 and 4.97 l/min. Bias calculations ranged between –0.072 and 0.104 l/min. Precision (2 SD) calculations ranged between 0.873 and 1.228 l/min for 95% confidence intervals. Pearson's correlation ranged from 0.919 to 0.938. **Conclusions**: Cardiac output measured with the new device correlates well with the thermodilution measurements of cardiac output during and immediately following coronary artery bypass grafting. The overall agreement between the two methods was good. The new device is an accurate non-invasive method of measuring cardiac output during coronary artery bypass grafting.

Keywords: Cardiac output; Cardiac surgery; Thermodilution; Electrical bioimpedance; Bioresistance; Hemodynamics

1. Introduction

Hemodynamic monitoring continues to be an integral part of peri- and postoperative care for patients undergoing cardiac surgery. Cardiac output (*CO*) is an important parameter in these measurements. To date, the clinical tool used to measure *CO* is the Swan–Ganz catheter using a thermodilution technique. However, the procedure is invasive, expensive, and may lead to complications [1,2].

A number of attempts have been made to determine *CO* in a non-invasive manner [3–6]. Using thoracic electrical bioimpedance techniques (TEB), moderate success has been achieved in some clinical settings [3,4,6–8]. The technique has been unsuccessful when applied to patients undergoing cardiac surgery [9–11]. A new non-invasive cardiac system device has been developed to utilize whole body bioresistance in a semi-empirical formula to determine the *CO*. Accuracy of the *CO* measurement using this device was established comparing thermodilution *CO* (*ThCO*) for patients undergoing right and left heart catheterization [12]. The purpose of this investigation was to compare the

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new technology for measuring cardiac output with thermodilution measured *CO* in patients undergoing coronary artery bypass grafting (CABG).

2. Patients and methods

2.1. Patients

Thirty-one patients undergoing elective, primary CABG were prospectively studied; 15 at Wolfson Medical Center and 16 at Johns Hopkins University School of Medicine. Patients with aortic valve insufficiency, mitral and tricuspid regurgitation or cardiac shunt were not included. The CABG was similar in both hospitals. All patients underwent a median sternotomy. Cardiopulmonary bypass was established using an aortic and single venous cannula. Diastolic arrest was achieved with cold sanguineous potassium cardioplegia in both antegrade and retrograde fashion. The internal mammary artery was used to graft the left anterior coronary artery (LAD) in all cases, and saphenous vein grafts were used to bypass the other obstructed vessels. Proximal anastomoses were performed using a partial cross clamp. During the study, no patient had atrial flutter nor atrial fibrillation.

2.2. Protocol

The study protocol was approved by Edith Wolfson and Johns Hopkins Institutional Review Boards. For each patient demographic and clinical data was tabulated. In each patient, *CO* measurements were taken at five different time intervals during the procedure; after induction of anesthesia but before incision (T_1), after sternotomy (T_2), after creation of a pericardial pocket (T_3), ten min after weaning from bypass (T_4), and immediately after arrival in the intensive care unit (T_5).

At each time interval, three adequate thermodilution measurements were made. All measurements were made at end expiration during the respiratory cycle. Thirty-one patients underwent 155 thermodilution *CO* measurements. Nineteen were excluded because of 10% variation between the measurements. Simultaneously, three bioresistance measurements were taken at each interval, and their average was considered the bioresistance *CO*.

Each bioresistance measurement took 20 s. Since these measurements were continuous, there was no time between measurements such that to achieve an average bioresistance *CO* measurement took 1 min.

2.3. Thermodilution method

At both hospitals seven French true size thermodilution catheters (Baxter Healthcare, Irvine, CA) were inserted in the operating room after induction of anesthesia. The proper location of the thermodilution catheter was confirmed by hemodynamic measurements and by postoperative chest roentgenograms. The pulmonary artery catheter was connected to a thermodilution cardiac output monitor ('Horizon 2000', Mennen Medical, Israel was used at Wolfson Medical Center, and 7010 Series Marquette, Madison, WI at Johns Hopkins Institutions). Ten milliliters of room temperature 5% dextrose solution was injected manually at end-expiration by an experienced anesthesiologist who was unaware of the bioresistance *CO* results.

2.4. Whole body resistance method

NICaS™ 2001, a non-invasive cardiac system device (NICaS™ 2001, Teledyne-NIM, LLC, North Andover, MA, 510K, certificate number K942227), was utilized for measuring bioresistance *CO*. Two proprietary designed, NICaS™ disposable electrodes (510K, certificate number K972002) were applied to each wrist, and were then connected to the non-invasive cardiac system device. The system passed an AC current 30 kHz and 1.4 mA through the whole body. It then measured the resistive portion of the bioimpedance. Since the electrodes were placed on the distal aspect of the extremities, the current passed through all major arteries and veins of the systemic circulation. As such, the system measured the bioresistance of the systemic circulation and allowed calculation of the stroke volume.

In 1992, Tsoglin and Frinerman and developed a new semi-empirical formula for calculating the stroke volume (*SV*) [13].

$$SV = \frac{Hct_{\text{corr}}}{K_{\text{sex, age}}} \times k_{\text{el}} \times K_{\text{weight}} \times IB \times \frac{H_{\text{corr}}^2 \Delta R}{R} \times \frac{\alpha + \beta}{\beta}$$

where K_{el} is a coefficient related to blood electrolytes, K_{weight} is a ratio of a patient's weight to ideal weight, *IB* is the index balance equal to the ratio of the measured extracellular fluid (as measured from the baseline impedance) to the expected extracellular fluid volume, HCT_{corr} is a hematocrit correction factor proportional to measured hematocrit, $K_{\text{sex,age}}$ is a coefficient depending upon a patient's sex and age, *H* is a patient's height, ΔR is the incremental change of the resistive portion of the bioimpedance, *R* is the baseline whole body bioresistance and $\alpha + \beta/\beta$ is the ratio of the sum of the systole time plus diastole time divided by the diastole time derived from the fine structure of the varying portion of the bioresistance.

Using whole body resistance measurements and the above formula, *SV* was calculated and converted to *CO*.

2.4.1. Statistical analysis

The correlation between methods at each time point was evaluated by Pearson's correlation coefficient and simple linear regression. The degree of agreement between methods at each time point was evaluated by calculation of the bias (mean between-method difference) and precision (mean bias ±2 SD) [14].

Table 1
Patient demographic and clinical data

	Wolfson Medical Center	Johns Hopkins Medical Center
Males (*N*)	11	13
Females (*N*)	4	3
Average age (years)	63.26 ± 9.94	64.2 ± 9.37
Minimum age (years)	46	51
Maximum age (years)	79	81
Average weight (kg)	73.13 ± 14.74	87.14 ± 13.29
Minimum weight (kg)	42	59
Maximum weight (kg)	102	108
Average height (cm)	166.3 ± 10.4	176.92 ± 8.96
Minimum height (cm)	140	160
Maximum height (cm)	183	185
Temperature (°C)[a]	26.8 ± 0.77	25.56 ± 0.403
Number of vessels bypassed	3.33 ± 0.96	2.55 ± 0.73
Diabetes (%)	46.67	18.75
Hypertension (%)	53.33	56.25

[a]Lowest temperature during the operation.

3. Results

Thirty-one patients were evaluated in the study. Demographic and clinical data are shown in Table 1. The agreement between the average *CO* measured by bioresistance versus thermodilution is shown in Table 2. The plot of the regression analysis and difference versus mean for all measurements at all times in the 31 patients is shown in Fig. 1a,b. There was good correlation between *ThCO* and *nCO* ranges of cardiac output during all phases of CABG and the immediate postoperative period.

4. Discussion

The initial attempt to obtain *CO* by measuring the stroke volume (*SV*) through thoracic electrical bioimpedance (TEB) was performed by Kubicek [15] at the National Aeronautics Space Agency (NASA) where he introduced the equation that became the basis for bioimpedance cardiography:

$$SV = \rho((\mathrm{d}Z/\mathrm{d}t)) \times ((L^2T))/(Z_0^2)$$

where *SV* is related to the resistivity of blood (ρ), d*Z*/d*t* is the first peak of the derivative of the bioimpedance curve, *L* is the distance between the electrodes, Z_0 is the mean time averaged thoracic bioimpedance and *T* is the ventricular ejection fraction.

The equation was modified by Bernstein [16] to:

$$SV = VEPT \times ((\mathrm{d}Z/\mathrm{d}t)/Z_0)T$$

where *VEPT* is a coefficient that represents the volume of electrically participating tissue. Using this equation, limited clinical success has been achieved in determining *CO* using bioimpedance techniques. Correlation to thermodilution techniques have been achieved in healthy volunteers, patients undergoing operations without cardiopulmonary bypass, patients undergoing procedures in the cardiac catheterization laboratory, and small numbers of intensive care unit patients [3,4,7,17–20].

This equation has been problematic due to difficulties in accurately computing *VEPT*, and its application becomes impractical in a patient undergoing rapid hemodynamic changes. Furthermore, determination of *VEPT* is dependent upon the accurate placement of electrodes, which is not always possible during open heart surgery. In addition, this equation still depends upon the first derivative of the bioimpedance curve, which is a rapidly fluctuating factor. As a result, attempts to correlate bioimpedance *CO* in the patient with thermodilution techniques during CABG have been unsuccessful [9,10].

In addition to practical problems, there is a conceptual problem in applying TEB to measure stroke volume. TEB measurements of the bioimpedance includes both systemic and pulmonary circulations. The two circulations cannot be separated by measurements and variation in proportion of these circulation will lead to inaccurate measurements of *SV* [21,22]. This will not happen in whole body bioresistance measurements where the systemic circulation dominates the measurement and reflects *LV SV*.

The physiological and physical basis of bioimpedance has been studied by many authors [23–25]. However, the variation between different tissues and their complex structures make it difficult to model their electrical behavior. In terms of bioresistance, the body may be divided into the 'blood compartment' and 'tissue compartment'. In the

Table 2
Agreement of *CO* by NICaS and thermodilution measurements ($n = 31$)

Time	Mean *ThCO*	Mean *nCO*	R/R^2	Regression slope[a]	SEE	*y* intercept	Bias (mean between-method difference) (l/min)	Precision mean ± 2 SD (l/min)
After anesthesia	4.19	4.19	0.93/0.86	1.128	0.328	–0.529	0.0086	–1.113–1.131
After sternotomy	4.14	4.12	0.92/0.85	0.898	0.185	0.404	–0.019	–0.863–0.823
After pericardiotomy	4.14	4.24	0.93/0.86	0.915	0.326	0.456	0.104	–1.015–1.223
Immediately after bypass	5.06	4.97	0.92/0.85	0.967	0.367	0.324	–0.0483	–1.234–1.138
ICU admission	4.71	4.62	0.94/0.88	0.891	0.306	0.424	–0.072	–1.156–1.012

SEE, standard error of the estimate; ICU, intensive care unit.
[a]*y*, cardiac output by NICaS 2001 bioimpedance; *x*, cardiac output by thermodilution.

'blood compartment', conductivity is high and therefore a current introduced into the body will travel primarily in this compartment. The resistance changes in this compartment as the blood volume varies in the great arteries due to pulsatile flow. In the 'tissue compartment', there is less significant current flow and constant resistance. In each individual, the resistance in the 'tissue compartment' is determined by the patient's height, lean body weight (muscle) to fat ratio, sex, age, body build, extracellular fluid volume, and electrolytes. In the 'blood compartment', the

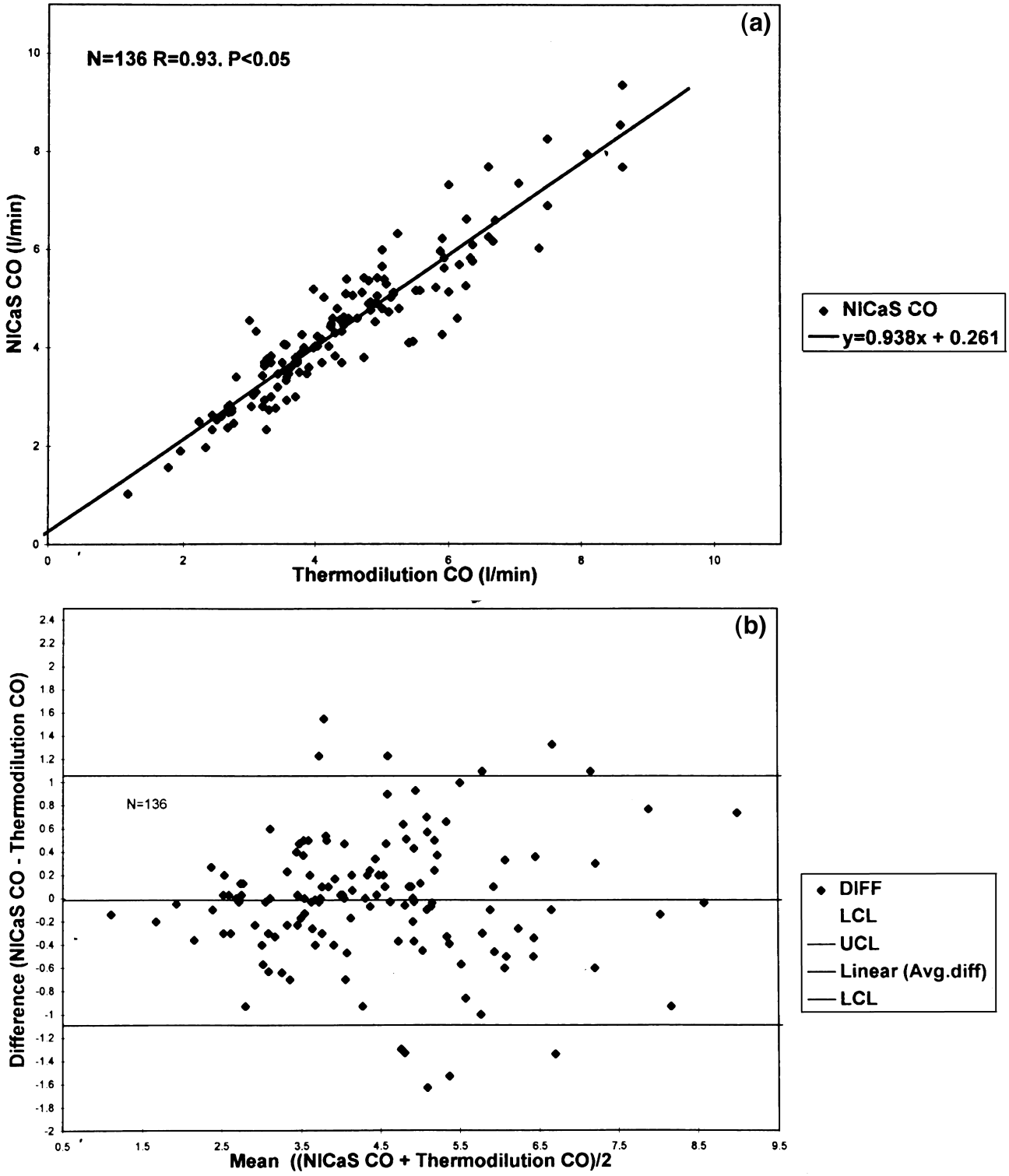

Fig. 1. (a) Linear regression analysis comparing bioresistance measured cardiac output with thermodilution cardiac output for all averaged measurements in the study. (b) Mean difference between bioresistance measured cardiac output and thermodilution cardiac output for all averaged measurements in the study.

resistance is determined by hematocrit, electrolytes and the pulsatile blood volume changes within the system. To measure *SV*, the pulsatile changes within the blood compartment and baseline bioresistance must be measured accurately and all other factors must be accounted for with appropriate correction factors. The measurement of whole body bioresistance allows for the accurate measurement of pulsatile changes and baseline resistance, and the proposed correction factors allow for the accurate calculation of the systemic bioresistance with which accurate *LV SV* can be calculated.

The method utilized in this study has been proven accurate in patients undergoing catheterization [12]. It was also shown to be accurate in a pilot study in patients undergoing CABG [26]. Compared with previous attempts to correlate bioresistance with SV, the equation has major advantages.

1. The equation does not depend on rapidly fluctuating time derivatives of bioimpedance.
2. The equation uses empirically derived coefficients that are obtained from laboratory values and simultaneously measured bioimpedance values instead of the artificial and difficult to approximate *VEPT*.
3. The precise placement of the electrodes is not a critical factor.
4. The NICaS™ electrode arrangement is optimal to measure the left ventricular *SV*.
5. The respiration has almost no effect on the NICaS™ *CO* measurements in real time.

The new methodology showed good correlation between thermodilution and bioresistance *CO* during all phases of CABG and the immediate postoperative period in two independent hospital populations. Correlation was good in all ranges, including low cardiac output. This fact is important since patients undergoing CABG frequently have low cardiac output. This was even true in the immediate post cardiopulmonary bypass period where changes in the patients' volume status, temperature, blood electrolytes and hemodynamics are changing rapidly. Such a correlation would be impossible using previous techniques.

The new device has certain limitations. First, it cannot measure *CO* while using diathermy. Second, the device is sensitive to movement so that the patient cannot be manipulated while the *CO* is being measured. These two factors require that the operation stop for the 20–30 s required to measure *CO*. Finally, the device measures *SV* and multiplies it by heart rate to measure *CO*. Arrythmias in which the heart rate varies significantly will result in a non-representative measurement of *CO*.

In summary, a new device using a semi-empirical equation relating *SV* to changes in the resistive portion of the patients' bioresistance has been developed. Information about specific patient data, blood components and body habitus inserted into the analytical software has significantly improved the ability to calculate *SV* from the bioresistance data. The device allows accurate, easy to obtain, non-invasive *CO* during cardiac surgery. Within the above stated limitations, we have confirmed the validity of the new bioresistance methodology in 31 patients who underwent CABG. Bioresistance measured cardiac output correlated well with *ThCO* during the CABG procedure and the immediate postoperative period.

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