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Validation of impedance cardiography measurements of cardiac output during limited exercise in heart transplant recipients

J. Pepke-Zaba[1], T. W. Higenbottam[1], A. T. Dinh Xuan[1], J. P. Scott[1], T. A. H. English[2], and J. Wallwork[2]

[1] Department of Respiratory Physiology and [2] Department of Cardiothoracic Surgery, Papworth Hospital, Papworth Everard, Cambridge CB3 8RE, UK

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Abstract. Twenty-one patients were studied at rest and during exercise after heart transplantation to compare cardiac output measured by thermodilution and impedance cardiography. Exercise was performed on a bicycle ergometer over a limited range of work load (25 and 50 watt) whilst metabolic gas exchange was recorded. One patient was studied at rest whilst his circulation was maintained by a Jarvik-7 artificial heart. The values of cardiac output measured by impedance cardiography corresponded closely with the flow rate from the artificial heart. There was also close agreement between the impedance and thermodilution measurements of cardiac output at rest and during exercise. Both measurements followed the changes in heart rate and oxygen consumption. Both thermodilution and impedance cardiography methods elicited good reproducibility of cardiac output measurements at rest and during exercise. These observations suggest that the noninvasive and continuous record of cardiac output obtained by impedance cardiography can be used for the postoperative monitoring of heart transplant recipients.

Key words: Impedance cardiography, in cardiac transplantation – Cardiac output, in cardiac transplantation, impedance – Thermodilution and cardiac impedance, in cardiac transplantation

Cardiac output measurement offers a means of assessing global cardiac function. As cardiac output rises linearly with work load [3, 13], its measurement during exercise offers an ideal means of determining the response of the cardiovascular system to demand.

Heart transplant recipients experience episodes of rejection that depress cardiac function at rest [26]. This has led to attempts to detect rejection noninvasively at an early stage [26] by measuring the changes in cardiac output in response to exercise [7].

Offprint requests to: T. W. Higenbottam

We have measured cardiac output, both at rest and during limited exercise, with impedance cardiography in orthotopic heart transplant recipients who had no evidence of cardiac rejection. These measurements were then validated by comparison with those obtained with the thermodilution method. To complete our validation we have also included a study at rest of a patient with a Jarvik-7 artificial heart [14].

Patients and methods

Patients

Twenty-two male patients were studied. All gave informed consent and the study was approved by the local ethical committee. Twenty-one patients, aged 30–57 years (mean 46 years), had undergone allogenic heart transplantation. The time after the operation ranged from 2 to 6 years (mean 3.3 years). One patient was studied 2 years after retransplantation. No patient had a concurrent endomyocardial biopsy positive for rejection. The procedure was part of the routine follow-up after transplantation.

A 40-year-old patient was studied whilst supported by a Jarvik-7 artificial heart [14].

Methods

Impedance cardiography measurement of cardiac output. The noninvasive measurements of cardiac output were obtained using the impedance cardiograph (NCCOM3 monitor, Bomed Medical Manufacturing, Irvine, Calif). Four pairs of silver-silver chloride electrocardiograph (ECG) electrodes were applied bilaterally to the neck and chest. Two internal pairs were sensing electrodes and two acted as the electrodes supplying the current. All the electrodes were interfaced to the computer. Through each pair of injecting electrodes, a constant magnitude alternating current of ±2.5 mA at 70 kHz was applied. In addition, a pair of electrodes was placed on the chest to obtain a clear ECG signal.

This technique makes use of the change in potential difference between the sensing and current-carrying electrodes (dZ/dt) associated with the cardiac cycle to calculate stroke volume. The calculations derived by Sramek have been reported elsewhere [10, 17, 18]. The only additional measurement required is the patient's thoracic

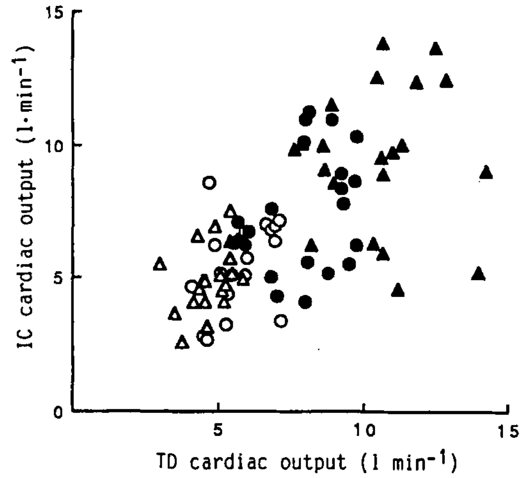

Fig. 1. Correlation between individual values of cardiac output measured by thermodilution (TD) and impedance cardiography (IC) at rest and during exercise. Each individual value represents the mean of four measurements of cardiac output obtained with the two methods. ○, Rest (supine); △, rest (sitting); ●, exercise (25 watt); ▲, exercise (50 watt). $r = 0.65$; $P < 0.01$

length, which can be derived from a nomogram using weight and height.

Recordings were made continuously, stroke by stroke, throughout the study, average results being taken for each 10-s period.

Thermodilution measurement of cardiac output. Thermodilution cardiac output was measured with a balloon-tipped flow-directed catheter (Edwards model 93A-131-7F) placed under fluoroscopic control in the pulmonary artery. Ten milliliters of 5% dextrose at 4°C was injected into the pulmonary artery. Cardiac output was calculated from the standard equation [6] using an on-line computer (Edwards 9025A Cardiac Computer, Edwards Laboratories, Irvine, Calif). Cardiac output was recorded every minute at rest and during exercise.

Metabolic gas exchange measurement. Metabolic gas exchange rate was continuously recorded as previously described [8]. The mixed expired oxygen and carbon dioxide concentrations were continuously recorded from the mixing box with a mass spectrometer (MGA 200, Airspec, Westerham, Kent, UK). Expired volume was measured with a Fleisch pneumotachograph (No 2 Statham, P K Morgan MK2, UK). All these variables were recorded on a multichannel recorder (W & W Electronic Recorder 404, Basel, Switzerland). The rates of ventilation ($1.min^{-1}$), oxygen consumption ($\dot{V}O_2$; $mmol.min^{-1}$), and carbon dioxide output ($1.min^{-1}$) were calculated in a standard fashion [8]. These measurements were obtained concurrently with the measurement of cardiac output by thermodilution.

Exercise. The 21 patients were first studied at rest in a supine position. They were then studied in a sitting position, first at rest, and then during cycle exercise (Body-guard ergometer 990, Iona Ogland AS, Sandros, Norway) whilst the metabolic gas exchange was continuously recorded as described above. The patients were assessed at two levels of work load, 25 and 50 watt, each of which lasted for 4 min.

Cardiac output measurement in the patient with the Jarvik-7 artificial heart. The patient was studied in a supine position on six separate occasions over a 2-day period. The ECG triggering signal for the NCCOM3 was obtained directly from the Jarvik-7 artificial heart. An average of four determinations of cardiac output with impedance cardiography were compared with the Jarvik-7 artificial heart output. No estimates of metabolic rate were made in this patient.

Statistical analysis

The coefficient of variation for cardiac output was calculated for impedance or thermodilution measurements [1].

We have used two methods to compare cardiac output measurements with impedance cardiography and thermodilution. First, individual data obtained with both methods, at rest and during exercise, are plotted along the line of identity, whereby coefficients of correlation were calculated in the usual way [1]. To avoid systematic biases that may be introduced by this method [4], we have subsequently calculated differences between the mean of the two determinations of cardiac output with thermodilution and impedance cardiography at rest, and plotted them against the average value of the two [4].

To calculate the mean response of cardiac output during exercise, we performed factorial analysis of variance [4], where the factors were stage of exercise (time in minutes), subjects, and the two types of measurement (i.e., impedance cardiography and thermodilution). The residual error from the factorial analysis of variance was used to calculate the least significant difference at $P = 0.05$ [4].

The same form of analysis was performed on $\dot{V}O_2$ and heart rate. The residual variance was used to calculate standard deviation (SD).

Results

A total of 381 measurements of cardiac output by simultaneous impedance cardiography and thermodilution was made.

The means of cardiac output measurements ranged from 3 to 14.2 $1.min^{-1}$ and from 2.6 to 13.9 $1.min^{-1}$ with the thermodilution and impedance methods, respectively. The coefficients of variation of both methods of measurements at rest, in the supine and sitting positions, are shown in Table 1.

Measurements of cardiac output at rest and during exercise by impedance cardiography were significantly related ($r = 0.65$; $P < 0.01$) to those obtained with the thermodilution method (Fig. 1).

There was a small mean difference between the two measurements of cardiac output at rest. One SD of the differences was 1.5 $1.min^{-1}$ and 1 $1.min^{-1}$ in the supine and sitting positions, respectively (Figs. 2, 3). The impedance cardiography values tended to become greater than the thermodilution values as cardiac output increased.

Table 1. Range of coefficient of variation (%) of cardiac output

	Heart transplant patients at rest	
	Supine position	Upright position
Impedance cardiography	1.75–13.38	1.19–13.22
Thermodilution	0.50–20.88	0.47–21.00

Table 2. Comparison of Jarvik-7 artificial heart cardiac output ($l \cdot min^{-1}$) and bioimpedance method (NCCOM3)

Jarvik-7 heart	6.7	7.4	7.3	7.2	6.7	6.7
NCCOM3 (mean)	6.5	6.3	6.4	6.2	6.7	5.5
± SEM	0.3	0.1	0.1	0.1	0.1	0.1

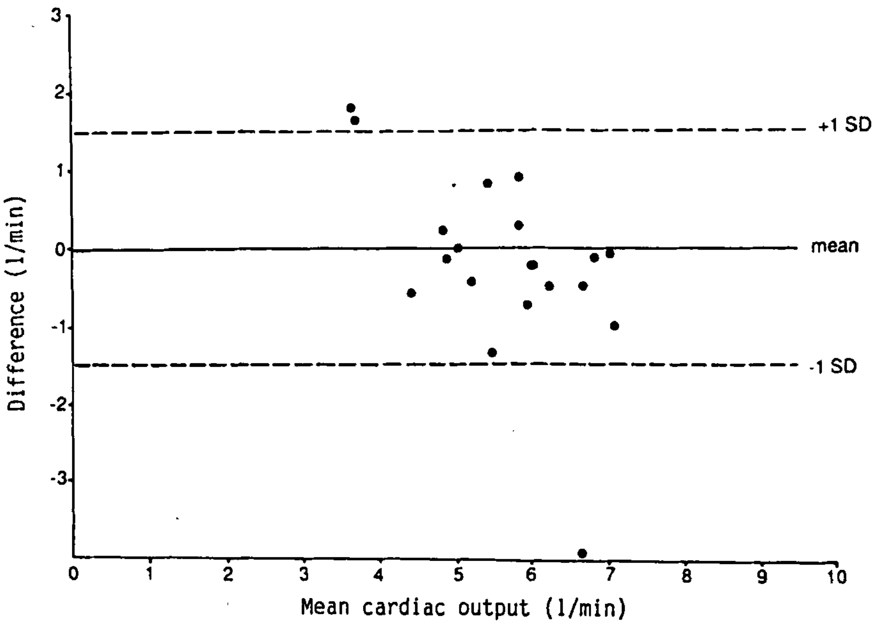

Fig. 2. Differences between means of four values of cardiac output obtained with thermodilution (TD) and impedance cardiography in supine patients ($n = 19$) are plotted against the average of the two. *Lines* show the mean and standard deviation *(SD)* of the differences. Only one TD measurement of cardiac output was obtained in two patients whose results are, therefore, not shown here

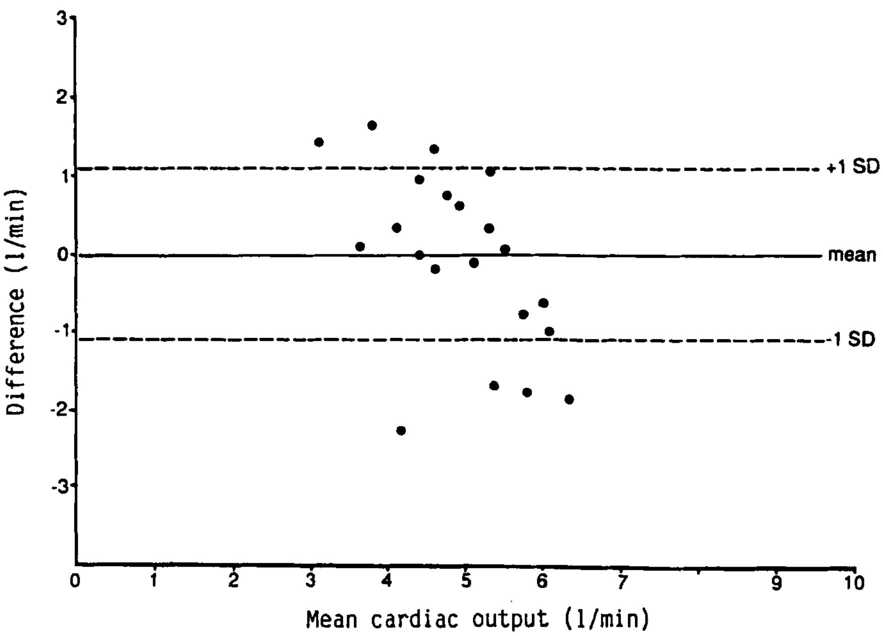

Fig. 3. Differences between means of four values of cardiac output obtained with thermodilution and impedance cardiography in resting upright patients ($n = 21$) are plotted against the average of the two. *Lines* show the mean and standard deviation *(SD)* of the differences

In the patient with the Jarvik-7 artificial heart, the average difference between the impedance cardiography and artificial heart output was 0.8 $1.min^{-1}$, cardiac output measured by impedance cardiography being equal to, or below, that of the Jarvik-7 artificial heart (Table 2).

The mean values for cardiac output measured by impedance cardiography or thermodilution during exercise followed closely the change in $\dot{V}O_2$ (Fig. 4) and heart rate (Fig. 5). There was little difference in the mean values for heart rate and $\dot{V}O_2$ obtained on the two occasions.

Discussion

These observations demonstrate that impedance measurement of cardiac output gives comparable values to those obtained with thermodilution, with reasonable reproducibility and an ability to follow the changes in cardiac output with exercise. The impedance method also accurately reflects the cardiac output from an artificial heart.

The reference method of measurement of cardiac output is the Fick determination [23]. This requires right heart catheterisation and carries an error of 10%, which can even exceed 19% in low cardiac output states [23]. Alternatively, the thermodilution method can be used and is widely available [6, 11]. This, however, also requires cardiac catheterisation. As it records pulsatile flow, the thermodilution method can sometimes be associated with error as high as 16% [19, 21].

A number of noninvasive methods are available, such as aortovelography using a Doppler technique [12, 20, 22]. This method elicits reproducible results at rest [12]. However, it cannot be performed in patients with thick necks

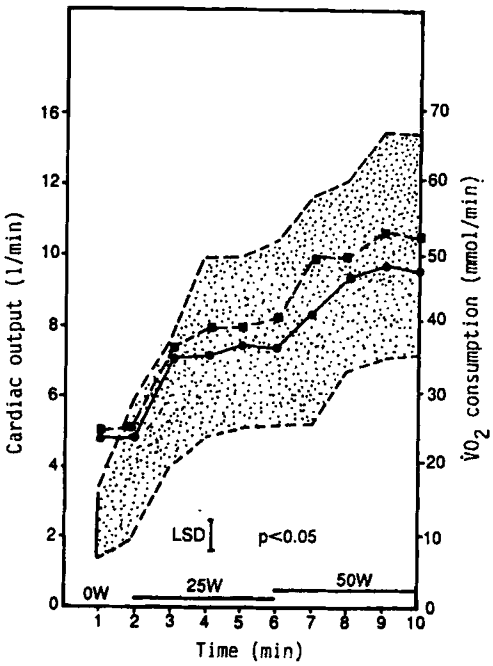

Fig. 4. Comparison of cardiac output values obtained with thermodilution (■) and impedance cardiography (●) at rest and during exercise. The *bar* represents the least significant difference *(LSD)* for $P < 0.05$. The *stippled area* represents the mean and one standard deviation for oxygen consumption *($\dot{V}O_2$)* in the 21 patients

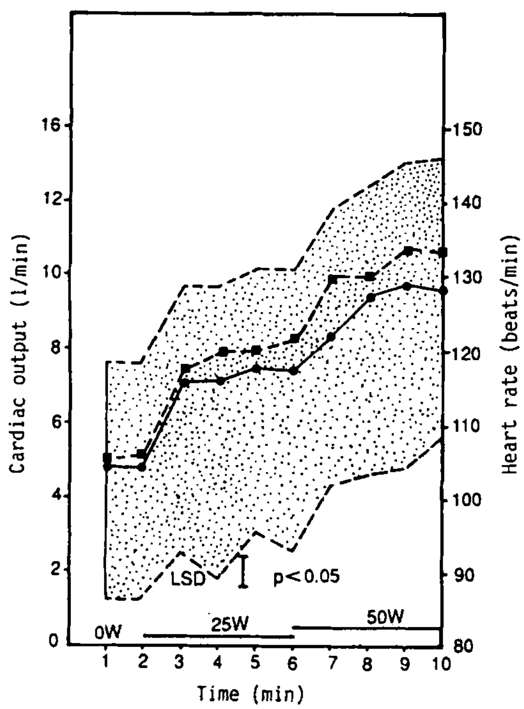

Fig. 5. Comparison of cardiac output values obtained with thermodilution (■) and impedance cardiography (●) at rest and during exercise. The *bar* represents the least significant difference *(LSD)* for $P < 0.05$. The *stippled area* represents the mean and one standard deviation for heart rate in the 21 patients

and may produce error as high as 30% during exercise [22].

Thoracic impedance cardiography provides a beat-by-beat noninvasive measurement of stroke volume [9, 10, 16]. Objections to the original method based on Kubicek et al.'s calculation [17, 18] include an overestimation of stroke volume and poor correlation with other methods of measurement of cardiac output, in both healthy and diseased subjects [9, 10]. Furthermore, without an on-line computer, analysis of the data is time-consuming [25]. The NCCOM3 incorporates the calculation of Sramek et al. [24, 25], which avoids many of the errors of the original Kubicek method of calculating stroke volume from dZ/dt [2].

It is now thought that dZ/dt is derived from changes in volume of the aorta with cardiac systole [5, 15]. The patient with the Jarvik-7 artificial heart developed values for dZ/dt equivalent to the other patients'. Yet, this patient had no active cardiac muscle, and cardiac output was determined externally by the setting of the mechanical pump [14]. Support is therefore provided for the suggested aortic volume change mechanism for dZ/dt. The precision of cardiac output measurement from the mechanical pump of the Jarvik-7 artificial heart provides reliable reference values. Therefore, the comparable results obtained in the same patient with the impedance cardiograph are strongly in favour of the reliability of the latter method.

We were able to demonstrate in patients at rest and during exercise, in a sitting position within a limited range of work load, that measurements of cardiac output with impedance cardiography could be obtained without major difficulty. The equipment is easily portable and can be applied with no greater difficulty than that for electrocardiography [26].

We applied the impedance method in heart transplant recipients who were in a stable phase of their clinical conditions. We do not know how accurate the impedance measurements in patients with pleural and cardiac fluid collections can be. Such patients probably need to be assessed in a separate study. Nonetheless, our comparison with the thermodilution method shows that impedance measurement of cardiac output produces very similar results in clinically well heart transplant recipients, even when using new statistical methods to demonstrate the size of the difference [4]. During exercise, both measurements of cardiac output closely followed the level of work as determined by the rate of oxygen consumption.

In conclusion, impedance measurement of cardiac output can be used with ease in heart transplant recipients. Furthermore, this method gives reproducible measurements, at rest and even during exercise. Thoracic impedance cardiography could, therefore, be used to detect early cardiac dysfunction. Since the latter also reflects cardiac rejection in many instances, its detection by a noninvasive and easily performed method may provide valuable help in the postoperative management of heart transplant recipients.

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