INSTITUTE OF PHYSICS PUBLISHING PHYSIOLOGICAL MEASUREMENT

Physiol. Meas. **27** (2006) 817–827 doi:10.1088/0967-3334/27/9/005

Impedance cardiography revisited

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Received 7 February 2006, accepted for publication 9 June 2006
Published 5 July 2006
Online at stacks.iop.org/PM/27/817

Abstract

Previously reported comparisons between cardiac output (CO) results in patients with cardiac conditions measured by thoracic impedance cardiography (TIC) versus thermodilution (TD) reveal upper and lower limits of agreement with two standard deviations (2SD) of approximately ± 2.2 l min^{-1}, a 44% disparity between the two technologies. We show here that if the electrodes are placed on one wrist and on a contralateral ankle instead of on the chest, a configuration designated as regional impedance cardiography (RIC), the 2SD limit of agreement between RIC and TD is ± 1.0 l min^{-1}, approximately 20% disparity between the two methods. To compare the performances of the TIC and RIC algorithms, the raw data of peripheral impedance changes yielded by RIC in 43 cardiac patients were used here for software processing and calculating the CO with the TIC algorithm. The 2SD between the TIC and TD was ± 1.7 l min^{-1}, and after annexing the correcting factors of the RIC formula to the TIC formula, the disparity between TIC and TD further declined to ± 1.25 l min^{-1}. Conclusions: (1) in cardiac conditions, the RIC technology is twice as accurate as TIC; (2) the advantage of RIC is the use of peripheral rather than thoracic impedance signals, supported by correcting factors.

Keywords: cardiac output measurements, thoracic bioimpedance, whole-body bioimpedance, impedance cardiography

Introduction

Three basic technologies are currently in use for impedance cardiography (ICG): (1) the thoracic ICG (TIC), where the electrodes are placed on the root of the neck and the lower part of the chest, being the dominant method in the market (Patterson *et al* 1964, Kubicek

et al 1966, 1974); (2) the whole-body ICG (ICG_{WB}), where four pairs of electrodes are used, one pair on each limb (Tischenko 1973, Koobi *et al* 1999); (3) the regional ICG (RIC), a technology which is used by the NICaS (noninvasive cardiac system). In this technology, which is the subject of this report, only two pairs of electrodes are used, performing best when placed on one wrist and on the contralateral ankle (Cohen *et al* 1998, Cotter *et al* 2004, Torre-Amione *et al* 2004).

Two comprehensive reviews of the literature on clinical experience in measuring the cardiac output (CO) by TIC determined that in patients with cardiac conditions the TIC-CO results are unreliable (Raaijmakers *et al* 1999, Handelsman 1991). According to Patterson (1985) and Wang *et al* (2001), a number of sources in the chest, such as the lungs, vena cava, and systemic and pulmonary arterial vasculatures, generate systolic impedance reductions, while the heart generates signals of increased impedance. In addition to these multifarious sources of ΔZ,[4] variations in the electrical conductivities between the sources of impedance changes and the TIC electrodes (Kim *et al* 1988, Kauppinen *et al* 1998), and between the various impedance sources (Wtorek 2000) have been described. These model experimentations indicated that the thoracic ΔZ is not a reliable signal for calculation of the SV due to the multiple sources of dZ/dt (Kim *et al* 1988, Wang and Patterson 1995, Kauppinen *et al* 1998, Wtorek 2000), providing the explanations for the above-mentioned unsatisfactory clinical results obtained by TIC (Raaijmakers *et al* 1999, Handelsman 1991).

In this report, an attempt is made to define the differences between the peripheral and thoracic impedance signals, and based on this, to explain the differences in the performance of RIC and TIC.

As we are capable of saving raw data from the wrist–ankle (peripheral) impedance signals, we were able to use the peripheral impedance waveforms and base impedance values to calculate stroke volumes, using various algorithms that have been associated with TIC calculations. This enabled us to prove that (1) the performance of RIC is twice as accurate as reported TIC results; (2) the reasons for this are as follows: (a) the impedance changes which are yielded by the limb electrodes are more suitable than the impedance changes of the thoracic electrodes for calculating the stroke volume and (b) the use of properly designed coefficients improved the accuracy of the CO results by at least an additional 25%.

Methods

The data for this project were gathered from two patient series. In both, comparisons were made between cardiac output results measured by the NICaS versus thermodilution. One series, which was studied in hospital A, consisted of 30 patients who were studied immediately upon arrival at the ICU following an open heart operation. In 11 (36%), despite the intravenous administration of adrenalin, cardiac index (CI) was lower than 2.5 l min^{-1} m^{-2}. The second series included 13 cases of acute heart failure that were studied in hospital B. CI was lower than 2.5 l min^{-1} m^{-2} in seven (54%), and in the combined group of 43 cases of the two hospitals, it was lower than 2.5 l min^{-1} m^{-2} in 18 (43%).

The purpose of this study was to use peripheral impedance waveforms to calculate stroke volume by means of four different ICG algorithms and to compare each of these SV values with the thermodilution SV result.

Of the 55 and 31 studies conducted in hospitals A and B, respectively, raw data were successfully retrieved from only the last 30 consecutive patients of hospital A and the last 13

[4] In the ICG_{WB} and RIC, where the impedance changes are depicted in the periphery, the impedance value is automatically converted into the real parts (R_0 and ΔR) of the measured impedance signals (Lamberts *et al* 1984).

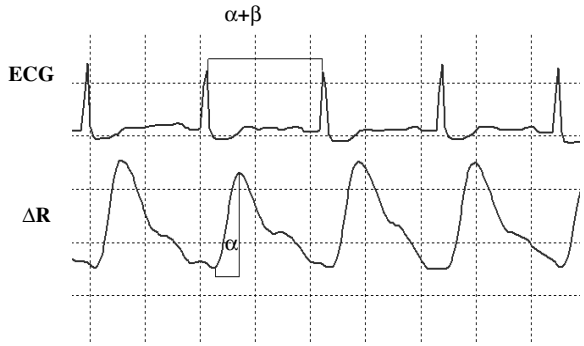

Figure 1. Unedited print of the ECG and ΔR waveforms to demonstrate the definitions of α and β.

consecutive cases of hospital B. It quickly became apparent that these 43 source data were retrieved from only one of the two NICaS devices that were being used in the two hospitals. The reason for this was that we did not realize that the software designed for source data retrieval was not implemented in one of the two NICaS devices that were used interchangeably during these trials.

Measuring the CO

Thermodilution. The standard techniques for measuring the thermodilution CO (TDCO) used in these two hospitals have been reported elsewhere (Cotter *et al* 2004).

RIC (NICaS). To measure the CO with the NICaS (NICO), which is a tetrapolar device, two electrodes are placed on a wrist above the radial pulse and two on the contralateral ankle above the posterior tibialis arterial pulse. If the arterial pulses in the legs are either absent or of poor quality, the second pair of electrodes is placed on the contralateral wrist. The NICaS device calculates the SV by means of the following Frinerman formula[5] (Cohen *et al* 1998):

$$\mathrm{SV} = \frac{\Delta R \rho L^2 (\alpha + \beta) K_\mathrm{w} \times \mathrm{HF}}{R R_\mathrm{i} \beta}, \tag{2}$$

where SV is the cardiac stroke volume (ml), ΔR is the resistance change during the cardiac cycle (Ω), R is the basal resistance (Ω), R_i is a corrected basal R (Ω), ρ is the blood electrical resistivity (Ω cm), L is the patient's height (cm), K_w is a correcting factor for the body weight, HF is the hydration factor related to the body water composition and $(\alpha + \beta)/\beta$ is the ratio of the systolic time plus the diastolic time divided by the diastolic time of the ΔR waveform (figure 1).

[5] The present formula is principally the same as the formula in Cohen *et al* (1998), but is written differently. The original formula was

$$\mathrm{SV} = \frac{\mathrm{Hct_{corr}}}{K_\mathrm{sex}} \times K_\mathrm{el} \times K_\mathrm{weight} \times \frac{\mathrm{IB} \times H^2_\mathrm{corr} \Delta R}{R} \times \frac{(\alpha + \beta)}{\beta}. \tag{1}$$

The values of the hematocrit (Hct) and Na((el) are now represented by ρ, which is the electrical resistivity of the blood. $K_{\mathrm{sex\ age}}$, which affects the basal resistance (R), is now represented by R_i, and IB (index body) is now represented by HF (hydration factor). The correction of H^2 is no longer included in the formula, but in patients whose arms are disproportionately long, the electrodes should be placed 5 cm proximally to their regular position.

Definition and principles of the correcting coefficients of the Frinerman formula

The basic impedance part of Frinerman's formula consists of the following Bonjer equation (1950):

$$\mathrm{SV} = \frac{\mathrm{d}R\rho L^2}{R^2}, \tag{3}$$

to which Frinerman's correcting factors were added. These coefficients were designed to neutralize the individual effects of gender, age, body water composition and anthropomorphic variabilities of each patient.

According to RIC studies, the basal R_0 is higher in females than in males, a fact which is in accordance with the literature (Organ *et al* 1994, Lukaski *et al* 1986, Hoffer *et al* 1970, Lamberts *et al* 1984, Ward *et al* 2000), and it tends to rise with age (Organ *et al* 1994).

Based on reported values of basal resistances related to sex and age (Organ *et al* 1994, Lukaski *et al* 1986, Ward *et al* 2000), a coefficient is calculated to determine an ideal value of R_0 for the studied patient. Ideal here means an ideal weight compared to height in healthy condition. By dividing the measured R_0 of the patient by the calculated ideal R_0, a correcting coefficient is obtained. By multiplying the measured R by the correcting coefficient, the R_i variable is determined and placed in the denominator of the formula.

Similarly, a correcting coefficient (K_w) for the body weight is calculated by dividing the measured weight by the calculated weight according to Hamwi's formula (1964) of ideal weight. K_w is required for compensation of the reduced electrical conductance in the fat, and this coefficient is placed in the numerator of the formula, affecting the value of ΔR. In a similar fashion, the hydration factor, HR, is calculated by the patient's body water composition, and this coefficient is placed in the numerator of the formula, either to reduce or to increase ΔR in over- or under-hydrated patients, respectively.

The variable $(\alpha + \beta)/\beta$ is based on the Windkessel principle (Frank 1926, Faes *et al* 1999), where a distinction is made between the aortic inflow α, which is incurred by the systolic left ventricular ejection, and the aortic outflow $(\alpha + \beta)$, which extends throughout the cardiac cycle (figure 1).

Comparative calculation of CO by software simulation

The impedance raw data of the compiled 43 investigative patients were retrieved and their CO were calculated by the following formulae: (1) Frinerman's formula, as measured by the NICaS; (2) Bonjer's equation of 1950 (Bonjer 1950), which was expressed differently by Patterson's first version of the TIC formula (Patterson *et al* 1964):

$$\Delta V = \rho \left(\frac{L}{Z}\right)^2 \Delta Z; \tag{4}$$

(3) Patterson's formula of the first derivative (Patterson 1965):

$$\mathrm{SV} = \frac{\mathrm{d}Z}{\mathrm{d}t} \times T \times \rho \times \left(\frac{L}{Z}\right)^2, \tag{5}$$

where SV is the cardiac stroke volume (cm), $\mathrm{d}Z/\mathrm{d}t$ is the peak of the first derivative of the impedance change during systole ($\Omega\ \mathrm{s}^{-1}$), T is the cardiac ejection time (s), L is the length between voltage pick-up electrodes (cm) and Z is the base impedance value (Ω), which is still used by the TIC technology (Kubicek *et al* 1974); (4) a combined formula which includes Patterson's equation together with Frinerman's correcting factors (table 1, figures 2 and 3):

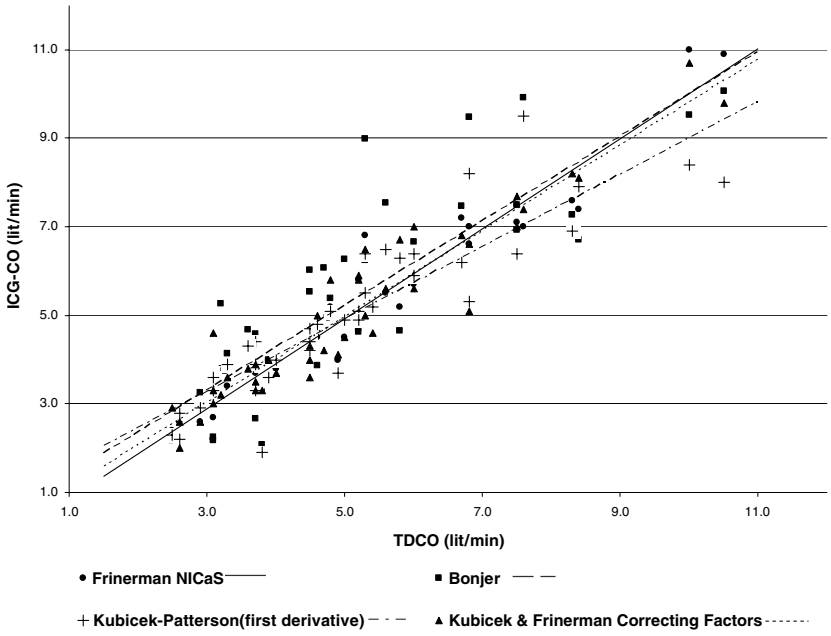

Figure 2. Scatter plot comparing CO results calculated by four impedance algorithms versus thermodilution.

Table 1. Correlations and limits of agreement between four algorithms versus TD. Comparison of four different algorithms in 43 patients for measuring cardiac output (CO) of the same raw data: (a) Frinerman (NICaS); (b) Bonjer; (c) Patterson–Kubicek; (d) Patterson–Kubicek–Frinerman. Each of these was compared with thermodilution.

	TD	Frinerman NICaS	Bonjer	Patterson–Kubicek	Patterson–Kubicek–Frinerman
Average CO (l min^{-1})	5.12	5.05	5.33	5.00	5.09
SD	1.952	2.043	2.218	1.781	1.986
Correlation with TD		0.969	0.841	0.897	0.950
p value versus NICaS[a]		–	<0.001	<0.0005	0.33
Bias		−0.0698	0.2107	−0.1116	−0.0302
SD of Bias		0.509	1.203	0.864	0.624
LL agreement		−1.088	−2.196	−1.840	−1.277
UL agreement		0.949	2.617	1.617	1.217

SD = standard deviation; LL agreement = lower limit of agreement; UL agreement = upper limit of agreement.

[a] Bonferroni adjusted p values for testing equality of correlation NICaS TD as compared with Bonjer TD (<0.0001), Patterson–Kubicek TD (<0.0005), Patterson–Kubicek–Frinerman TD (0.33).

$$\mathrm{SV} = \frac{\mathrm{d}R \times T}{\mathrm{d}t \times R} \times \frac{\rho \times L^2(\alpha + \beta)}{R_\mathrm{i}\beta} \times K_\mathrm{w} \times \mathrm{HF}, \tag{6}$$

where Frinerman's ΔR was replaced by $\mathrm{d}Z/\mathrm{d}t \times T$ and $(\alpha + \beta)/\beta$ was deleted.

Patient selection

Restlessness, aortic insufficiency, abdominal aneurysm, heart rate above 130 beats min^{-1}, arrhythmia with significant irregular heart rate, severe peripheral vascular disease, two or more

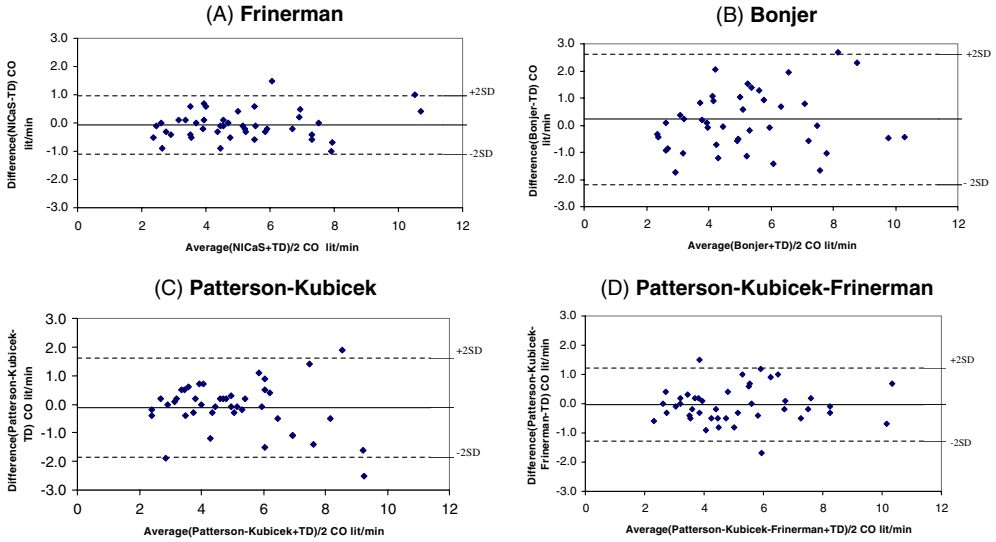

Figure 3. Scatter plots of Bland–Altman difference-against-average of the CO results calculated by the four impedance algorithms versus thermodilution results (based on table 1).

pitting edema and dialysis all interfere with the proper measurements of the SV; therefore, this patient population, which amounts to 15% of the candidates, is *a priori* excluded from the ICG studies. Also excluded are RIC measurements of the CO in thoracoabdominal operations, such as esophagectomies and pancreatectomies, where plasma loss and heavy intravenous volume loads due to significant bleeding undermine the stability of the basal R and the reliability of the CO results (Critchley *et al* 1996).

Statistical analysis

Thermodilution (TD) was used as the 'gold standard', and agreement between the four ICG formulae and TD was analyzed according to the Bland–Altman approach (Bland and Altman 1986).

Results[6]

The results of the four algorithms revealed a rather similar average of the NICO in the range of 5 l min^{-1} (table 1). The Pearson correlation coefficients were $r = 0.969$, 0.841, 0.897 and 0.950 with the formulae of Frinerman, Bonjer (1950), Patterson–Kubicek (Patterson 1965, Kubicek *et al* 1974) and the combined Patterson–Kubicek–Frinerman formula, respectively (table 1, figures 2 and 3). The Bland–Altman 2SD lower and upper limits of agreement with TD were −1.088 and 0.949, −2.196 and 2.617, −1.840 and 1.617, and −1.277 and 1.217, according to the same order of formulae as above (table 1, figure 3).

[6] To calculate the SV with the Bonjer, Patterson–Kubicek and Patterson–Kubicek–Frinerman formulae, the raw data of the 43 patients were e-mailed to Professor Robert Patterson, the inventor of the TIC technology (Patterson *et al* 1964, Patterson 1965), who made these calculations at the University of Minnesota.

Discussion

To compare the performance of the currently used TIC technology with RIC, we used three recent reports representing TIC results in patients with chronic stable congestive heart failure, which revealed similar values (Drazner *et al* 2002, Van De Water *et al* 2003, Leslie *et al* 2004) and could serve as a paradigm of the performance of TIC in the presence of cardiac conditions. A relatively recent publication by Sageman *et al* (2002) could not be included here because (a) only CI values were provided, (b) these values are characteristic of patients with normal cardiac functions and (c) the patients' CO results were averages of up to 20 measurements, an approach which is not used clinically.

The average cardiac output in each of the three TIC series was in the range of 5 l min^{-1}. Comparison in each series of the results with thermodilution (TD) revealed a Bland–Altman limit of agreement with a 2SD of approximately $\pm$2.2 l min^{-1}—a 44% deviation compared to TD (Drazner *et al* 2002, Van De Water *et al* 2003, Leslie *et al* 2004). Despite the fact that the present series did not include cases of chronic congestive heart failure, it is comparable with the TIC studies because (a) the patients were actively managed for cardiac conditions, (b) a CI $<$ 2.5 l min^{-1} m^{-2} was observed in 43% of the cases and (c) the average CO was in the range of 5 l min^{-1}, as in the TIC paradigm.

When the Patterson–Kubicek algorithm was fed by impedance raw data yielded by the peripheral wrist–ankle rather than by thoracic electrodes, the disparity compared to TD was $\pm$1.7 l min^{-1}, which is a 34% difference (figures 2 and 3). When the Patterson–Kubicek algorithm was reinforced by the correcting factors of the NICaS formula and the peripheral raw data were used, there was a further decline in the disparity between ICG and TD to the range of $\pm$1.25 l min^{-1}, a 25% difference. This is almost as good as the 20% disparity between the NICaS and the TD.

Judging by the 20% deviation between the NICaS and TD CO results, and by the 44% deviation between the reported TIC and TD CO results, it is evident that the accuracy of the NICaS is higher by a factor of more than 2, than the reported values of TIC (Raaijmakers *et al* 1999, Handelsman 1991, Drazner *et al* 2002, Van De Water *et al* 2003, Leslie *et al* 2004).

Moreover, according to the FDA standard of bioequivalence (Guidance for Industry 2001), the comparative results of new and gold-standard technologies should be contained within a range of 20% disparity. This 20% range is determined by the 10% repeatability rate of each of the two methods. Judging by figure 3(A), the agreement between the NICaS and the TD is in very close proximity to the FDA standard bioequivalence.

About the validity of correcting coefficients

To appreciate the competence of the correcting factors, it is suffice to compare the CO results of Frinerman's and Bonjer's formulae (figures 3(A) and (B)). As stated earlier, the only difference between these two equations is the addition of Frinerman's correcting factors to Bonjer's formula. R_{i}, for example, which is the corrected R_0, may reach twice the value of the measured R_0. K_{w} may increase the measured ΔR by up to 45%. The HF may either reduce or increase the value of ΔR by only slight to moderate degrees. Thus, it can be discerned that when using Bonjer's equation alone (figure 3(B)) the 2SD limits of agreement are approximately $\pm$2.4 l min^{-1}, and when Frinerman's variables are added (figure 3(A)) the 2SD limits of agreement are $\pm$1.0 l min^{-1}. There is a 20% disparity between the NICaS and the TD, and a 45% improvement of Bonjer's reinforced performance.

Similarly, annexing the Frinerman correcting coefficients to the TIC $\mathrm{d}Z/\mathrm{d}t \times T$ formula dramatically improved the calculated CO results, from 2SD limits of agreement of

approximately $\pm 1.7\,\mathrm{l\,min^{-1}}$ (table 1, figure 3(C)) to 2SD limits of agreement of approximately $\pm 1.25\,\mathrm{l\,min^{-1}}$ (table 1, figure 3(D)).

It has been repeatedly shown by Hoffer *et al* (1970), Lukaski *et al* (1986), Organ *et al* (1994), Ward *et al* (2000) and others that the body is not a homogeneous conductor, and its basal resistance, and consequently the spatial distribution of conductivities, is a function of the body composition. It is also recognized that the two main factors which determine the impedance variabilities are the percentages of body water and fat. As shown here, by using the RIC approach, the variabilities of age, sex, height and weight can be quantitated and translated to the effective correcting coefficients.

About the validity of the wrist–ankle electrodes

The most significant advantage of RIC in comparison to TIC is the use of the peripheral impedance signal for calculation of the SV. According to Kauppinen *et al* (2000), 75% of the peripheral (RIC) impedance waveform is borne by the systolic blood volume pulsations of the arterial vasculature of the upper and lower limbs, and the remaining 25% arrives from the trunk (thorax). Still, the sole source of the peripheral signal is generated by the blood volume pulse of the arterial vasculature.

It must be borne in mind that the aorta and its peripheral ramifications comprise a single anatomophysiological structure, and the pulse waveform, which evolves throughout its length, occurs almost at the same time. This is possible only because the velocity of the pulse wave is so rapid that the arterial expansion is completed before the termination of the left ventricular contraction (Guyton and Hall 2000). The mean value of the pulse wave velocity (PWV) from the thorax to the calves is approximately 7–10 $\mathrm{m\,s^{-1}}$ (Guyton and Hall 2000).[7] Similarly, the impedance volume pulse travels at approximately the same rate as reported by Risacher *et al* (1995).

Thus, in accordance with the existing knowledge of the cardiac role in the formation of the pulse (McVeigh *et al* 2002), the RIC peripheral volumetric signal is borne throughout the length of the arterial tree beginning with the left ventricular stroke volume ejection.

In contrast, the thoracic (TIC) waveform is generated by multiple sources, including the aorta, lungs, atria, vena cava and artifacts due to heart movements (Wang *et al* 2001, Kauppinen *et al* 1998, Wtorek 2000). In normal people, some studies have shown that TIC gives reasonably reliable CO results (Raaijmakers *et al* 1999), but in the presence of cardiac conditions, distortions of the TIC waveforms were already observed in the earliest days of the emergence of this technology (Kubicek *et al* 1974). This is contrary to RIC, where we see very few changes, if any, in the waveform shape incurred by the different cardiac conditions.

The immunity of the peripheral impedance waveform to the distorting influence of cardiac conditions is reflected by the results of the present study. The average disparity between TIC-CO and TD-CO measured in cardiac patients is 44%. In the present trial, the average disparity between TD-CO and ICG-CO, which was calculated by the combination of the TIC algorithm and a peripheral impedance waveform, was 34%. This 23% higher accuracy, which is obtained by the standard TIC algorithm, can be attributed only to one factor, the reliance for calculation of the SV on the peripheral, rather than the thoracic, impedance signal.

The fact that the RIC region consists of only part of the whole body but can be used to calculate the CO of the whole body is explained by the electrophysiological relationships which exist between RIC and $\mathrm{ICG_{WB}}$. In the $\mathrm{ICG_{WB}}$ technique, electrodes are placed on all four limbs, and yet, despite the fact that the head which consumes 13% of the CO is not

[7] Significant differences exist in these values, depending on the elasticity of the arterial vasculature.

included in the electrical field, the reliability of the CO results of this technology has been validated (Tischenko 1973, Koobi *et al* 1999).

The common electrophysiological denominator of RIC and ICG_{WB} is in that the same basal *R* of a body that is measured by RIC is twice the value measured by ICG_{WB}. As measured in this series, and by and large as measured by others (Kauppinen *et al* 2000, Lukaski *et al* 1986, Organ *et al* 1994), the basal *R* of the region between the wrist and the ankle is approximately 450 Ω.[8] This, when the value of the basal *R* of ICG_{WB} is in the range of 200–250 Ω (Tischenko 1973, Lamberts *et al* 1984, Kauppinen *et al* 2000). The 2:1 ratio of the basal *R* in RIC versus ICG_{WB} is attributed to the fact that in ICG_{WB} the two upper and the two lower limbs are measured in parallel. Consequently, the cross-sectional area of the limbs is twice as large in ICG_{WB}, resulting in the reduction of the electrical resistance to one-half. Thus, it is the same physiological mechanism which facilitates the appropriate measurement of the total CO by ICG_{WB}, which also holds for the exceptionally accurate RIC results.

Conclusions

The present CO results measured by the NICaS device indicate that, with regard to accuracy of measuring the CO, the RIC technology outperforms any other ICG technology, being twice as accurate as TIC.

The peripheral systolic impedance changes are more reliable than the TIC impedance changes for calculating the cardiac stroke volume.

The main disadvantage of the RIC technology is that in approximately 15% of the patients who need the test, there are exclusion criteria which preclude the use of the NICaS, a problem which is also shared by other impedance technologies.

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[8] It should be borne in mind that in females the electrical resistance between the wrist and the ankle is higher than in males by 80–100 Ω (Organ *et al* 1994, Lukaski *et al* 1986, Hoffer *et al* 1970). Furthermore, there are differences in the basal *R* values of different ethnic populations (Ward *et al* 2000), where different antropometric characteristics exist. In the present series, the average basal R of the postoperative cases was lower by 100 Ω compared to the non-operative cardiac patients, and this is attributed to the over-hydration induced during the surgery.

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