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Comparison of Impedance Cardiography and Thermodilution-Derived Measurements of Stroke Volume and Cardiac Output at Rest and During Exercise Testing

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Summary. Background: **Non-invasive evaluation of haemodynamic variables remains a preferable and attractive option in both pharmacologic research and clinical cardiology.**

Objectives: **The objective of this study was to evaluate the correlation, feasibility and diagnostic value of haemodynamic measurements by ICG with the thermodilution (TD) method at rest and during exercise testing.**

Methods: **We measured stroke volume (SV) and cardiac output (CO) with both methods in 20 patients with suspected coronary artery disease (CAD). All measurements were performed simultaneously at rest and during bicycle exercise.**

Results: **There was a highly significant correlation ($p < 0.001$) for measurements of SV between both methods at rest ($r = 0.83$) and during exercise ($r = 0.85$–0.87) with 50–100 watts. For measurements of CO, the respective correlations were $r = 0.85$ at rest and $r = 0.92$–0.94 during exercise. The mean difference for measurements of SV were 3.8 ± 12.6 ml at rest and 6.5 ± 11.4 ml during exercise. For measurements of CO, the mean difference between both methods was 0.9 ± 1.0 l/min at rest and 1.0 ± 0.8 l/min during exercise. Compared to TD measurements, ICG had a bias to overestimate SV and CO of approximately by 5–10%. One patient had to be excluded because of inappropriate quality of the ICG signals during exercise.**

Conclusions: **ICG is a feasible and accurate method for non-invasive measurements of SV and CO. Haemodynamic measurements by ICG were correlated highly significant to simultaneous measurements by the TD method.**

Key Words. **impedance cardiography, electrical bioimpedance, haemodynamic monitoring, exercise testing, cardiac output**

Introduction

Non-invasive and continuous evaluation of haemodynamic variables such as stroke volume and cardiac output is a preferable and attractive option in both pharmacologic research and clinical cardiology. Impedance cardiography allows (ICG) allows non-invasive monitoring of cardiac function by measuring pulse-synchrone changes in thoracic electrical bioimpedance via simple surface electrodes together with a conventional electrocardiogram (ECG). Derived from the first derivative of the thoracical bioimpedance curve, the impedance cardiogramme (ICG), stroke volume (SV) and cardiac output (CO) can be calculated via various formula [1–4]. In comparison to other non-invasive methods for monitoring cardiac function and haemodynamics such as Doppler-echocardiography which demands highly skilled investigators [5–7], ICG has the advantage of being an user-independent and less time consuming method with a portable device which can therefore be simply applied in cardiovascular research and clinical routine. Compared to invasive methods for measuring cardiac function and output such as the thermodilution (TD) method or the direct Fick-method, ICG has the inherent advantages of any non-invasive method, namely of being free of any typical potential risks and complications associated with an interventional procedure i.e. right heart catheterization [8].

Due to substantial progress in the development of computerized, ICG systems which provide online and continuous availability of various haemodynamic parameters, ICG has recently regained attention. The validity and reliability of impedance cardiography (ICG) has been reviewed by several authors [9–11]. ICG was reported as a reliable and accurate method for non-invasive measurement of SV and CO. The correlation of ICG versus standard invasive methods at rest has been extensively studied in healthy volunteers, pharmacologic research and various clinical settings including applications in the intensive care unit [12,13], the intra- and peripostoperative setting [14,15] and pharmacologic stress testing [16,17]. The largest meta-analysis including 27 studies comparing ICG versus the TD method [10] reported a correlation of $r = 0.81$ between both methods. However, only one study [20] examined the validity and correlation of ICG versus the TD during exercise testing in patients with cardiac disease. All other available validation studies of ICG during exercise have been

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conducted versus the direct or indirect Fick method which has several methodological limitations for its use during exercise [18,19–24]. In addition, there are no data on the diagnostic value of ICG in patients with left ventricular dysfunction during exercise, a condition which is kown to reduce the accuracy of ICG.

The primary objective of our study was to evaluate the correlation of measurements of SV and CO by ICG versus with the respective measurements by the TD method at rest and at various stages of bicycle exercise. Secondary objectives were to assess the feasibility of ICG during exercise to assess its potential value for future applications in patients with suspected coronary artery disease.

Patients and Methods

Patients and study protocol

We examined serial 20 patients (13 males, 7 females, mean age 58.4 ± 6.4 years) who where referred to our institution for cardiac catheterization. The indication for cardiac catherization was based on either suspected CAD because of a positive exercise electrocardiographic (ECG) test, typical anginal symptoms, a known history of manifest CAD (previous myocardial infarction, CABG or PTCA) or atypical symptoms including dyspnea on exertion. After selective coronary angiography (Judkin's technique) and left ventricular angiography, right heart catheterization was performed together with exercise testing. Simultaneous haemodynamic measurements by ICG and the TD method were performed at rest and at the different stages of exercise. The baseline characteristics of all study patients are given in Table 1.

All ICG-derived haemodynamic data were evaluated after completion of the invasive studies by coronary angiography or right heart catheterisation by investigators blinded to the results of the two invasive methods. Informed consent for participation in the study was obtained from all patients. The study was approved by the appropaite nstitutional ethical review board.

Table 1. *Baseline characteristics*

Previous CV history	
Hypertension (n)	16
Previous MI (n)	8
Previous CABG (n)	3
Previous PTCA (n)	4
Angiographic findings*	
LV ejection fraction	62 ± 5%
No significant CAD (n)	7
Single vessel disease (n)	6
Two vessel disease (n)	3
Three vessel disease (n)	4

CV: cardiovascular; MI: myocardial infarction; CABG: coronary artery bypass grafting; PTCA: percutaneous transluminal coronary angioplasty; CAD: coronary artery disease;

*LV: left ventricular; Significant CAD was defined as more than 50 % lumen narrowing by quantitative coronary angiography.

Exercise testing

All patients underwent exercise testing in a semi-supine position in the catherization laboratory in a supine position after coronary angiography. Exercise testing was routinely started at 25 watts with increasing 3-minute stages of 50 watts until the age-predicted heart rate (85% of 220 minus age) was achieved. Other criteria for the termination of the exercise test were the presence of angina pectoris, significant ST depression, dyspnea, significant arrhythmias, hypertension (systolic blood pressure ≥220 mmHg, diastolic blood pressure ≥110 mmHg), other cardiac or circulatory symptoms (palpitations) or peripheral exhaustion.

Right heart catheterization

All patients underwent right heart catherization using a conventional pulmonary artery catheter (Baxter Inc., Irvine, California, USA) which was positioned in the pulmonary artery. The correct position was controlled by confirmation of the typical pressure curves and radiographic control. TD measurements were obtained by manual bolus injections of iced water (4–6 degrees Celsius) independently from the respiratory cycle into the right atrium and detection by the thermistor probe at the distal end in the pulmonary artery. The first of four consecutive measurements was routinely skipped to avoid incorrect measurements. The thermodilution curve confirming correct injection was visible on a control screen. The calculations of SV and CO derived from the thermodilution curves were automatically performed by the haemodynamic microcomputer (Edwards Laboratories Inc., Madison, Wisconsin, USA) connected to the pulmonary catheter using the respective standard formula.

Impedance cardiography

Continuous haemodynamic monitoring during the bicycle exercise test was performed by an automated ICG system (cardioscreen professional, Medis GmbH, Ilmenau, Germany). The ICG system consisted of a conventional laptop computer with the ICG signal processing software and a transmitting unit. Four pairs of electrodes positioned (one pair at the left and right neck in the sternocleidomastoid region, one pair at the left and right side of the lower thoracic aperture in the medioclavicular line) were used for recording the thoracic bio-impedance field ("four pair method"). The ECG was monitored by three conventional electrodes. Correct identification of the points B (opening of the aortic valve), P (maximum systolic flow) and X (closure of the aortic valve) on the ICG curves were confirmed by marker channels. The modified Bernstein formula (4) was used for automated calculation of stroke volume (SV) and derived thereof, cardiac output (CO). The

ICG-system was programmed to average and calculate five consecutive beats at each prespecified timepoint at rest and at the different exercise stages (50 watts, 75 watts, 100 watts). The system permitted continuous on-line monitoring the ICG and ECG signals including the programmed haemodynamic variables. All ICG data were digitally stored and evaluated blinded to the haemodynamic findings obtained by right heart catherization.

Statistical analysis

All data are presented as mean values ± standard deviation (SD) if not indicated otherwise. The Mann-Whitney u-test was used for comparison of haemodynamic variables between the patients groups. The Wilcoxon test was used for comparisons within the groups. A p-value of $p < 0.05$ was interpreted as significant. The Pearson method was used for calculating the correlations between the measurements of SV and CO by ICG versus the TD method. The accuracy of ICG measurements versus the TD method was compared using the Bland-Altman method [25] defining the limits of agreement as mean ± (2SD). Despite the coefficients of correlation all measurements were rounded to one decimal.

Results

Exercise testing and coronary angiography

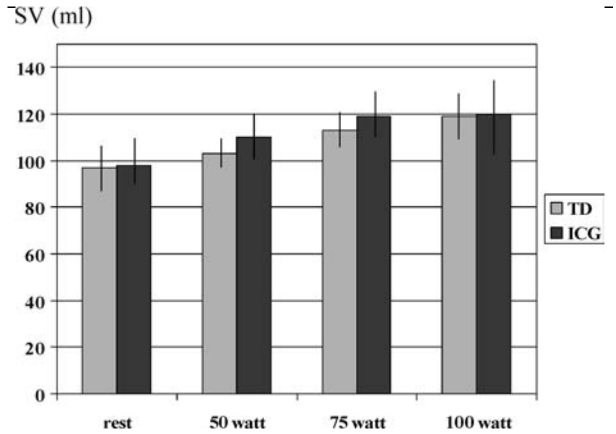
Seven of 20 patients had no significant coronary artery disease, in 13 patients significant coronary angiography was diagnosed (defined as ≥50% lumen narrowing by quantitative coronary angiography). The results of coronary angiography are included in Table 1 (baseline characterictics). All patients had a normal left ventricular ejection fraction at baseline was (mean 62 ± 5%). An exercise level of 50 watts was achieved by all patients, 18 of 20 patients achieved 75 watts. Eleven of 20 patients were able to achieve 100 watts of exercise for 2 minutes before exercise testing was stopped. Only 7 of 20 patients were able to achieve the age-predicted target heart rate. In the remaining 13 patients, the exercise test was stopped either due to dyspnea ($n = 7$), anginal symptoms ($n = 3$) or a typical pathologic ST-depression in the ECG ($n = 3$).

Comparison of stroke volume and cardiac output by thermodilution and impedance cardiography

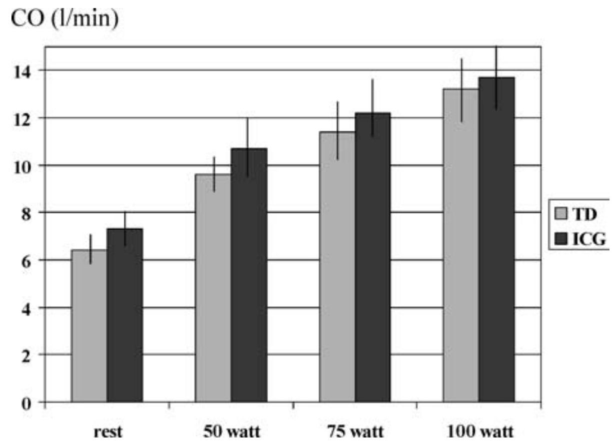
One patient had to be excluded from automated ICG-analysis because of inappropriate quality of the recorded ICG-curves. The results of 19 patients in whom simultaneous measurements of SV and CO by either TD or ICG were compared at rest (baseline) and at each exercise stage are given in Table 2. Bicycle exercise resulted in an significant increase of SV and CO versus baseline starting already at 50 watts in all patients ($p < 0.01$). There were no significant differences between the TD and ICG measurements of SV and CO at the different stages (50, 75 and 100 watts, respectively) of exercise (Figs. 1 and 2). There was a highly significant correlation between both methods ($p < 0.0001$) for measurements of SV and CO at rest ($r = 0.83$ and $r = 0.85$) and at each stage of exercise ($r = 0.82 - -0.87$ and $r = 0.85$–0.92). Regression plots of SV and CO by ICG versus the TD method at baseline and 100 watts are depicted in Figures 3–6. The comparison of both methods using the Bland-Altmann method showed a total mean difference for measurements of SV of 3.8 ± 12.6 ml (95% limits of agreement −20.9 ml, ± 28.6 ml) at rest and 6.5 ± 11.4 ml (95% limits of agreement −15.8 ml, +28.9 ml) during exercise. This corresponded to an average difference of 4.7 ± 13.6% at rest and 9.8 ± 10.2% during exercise between both methods. For measurements of CO, the total mean difference between both methods was 0.9 ± 1.0 l/min at rest (95 % limits of agreement −1.0 ml, +2.7 l/min) and 1.0 ± 0.8 l/min (95% limits of agreement −2.6 ml, +3.6 l/min) during exercise corresponding to an average difference of

Table 2. *Results and correlation of simultaneous measurements of stroke volume (SV) and cardiac output (CO) by either the thermodilution method (TD) or impedance cardiography (ICG). The last column gives the coefficient of correlation (r) between the two methods. Significant differences versus measurements at rest of p ≤ 0.01 are indicated by **

Parameter	TD	ICG	Δ mean difference (ICG-TD)	P (TD vs ICG)	Coefficient of correlation (r)
Stroke volume (SV)					
Rest (ml)	97.0 ± 20.8	98.5 ± 22.2	3.8 ± 12.6	n.s.	0.83
50 Watt (ml)	103.3 ± 13.1*	110.6 ± 18.8*	7.4 ± 9.8	n.s.	0.85
75 Watt (ml)	113.6 ± 16.3*	119.8 ± 21.5*	8.3 ± 11.6	n.s.	0.82
100 Watt (ml)	119.8 ± 18.2*	120.1 ± 27.9*	6.5 ± 11.4	n.s.	0.87
Cardiac output (CO)					
Rest (l/min)	6.4 ± 1.1	7.3 ± 1.7	0.9 ± 0.9	n.s.	0.85
50 Watt (l/min)	9.6 ± 1.8*	10.7 ± 2.3*	1.1 ± 0.8	n.s.	0.94
75 Watt (l/min)	11.4 ± 2.3*	12.2 ± 2.4*	0.8 ± 1.2	n.s.	*0.93
100 Watt (l/min)	13.2 ± 2.6*	13.7 ± 2.8*	0.5 ± 1.6	n.s.	0.92



(Fig. 1)



(Fig. 2)

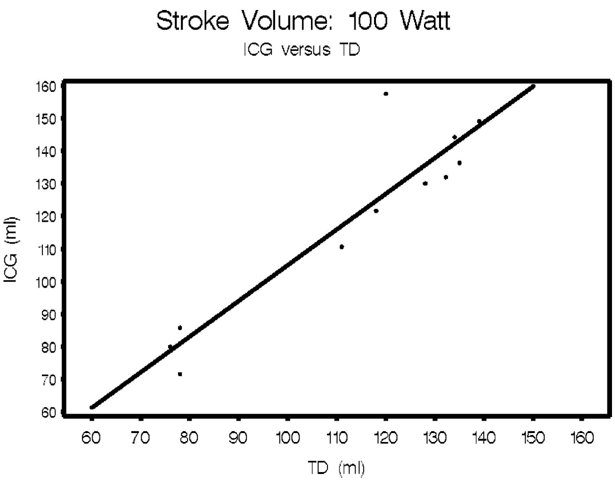
Figs. 1 and 2. *Comparison of stroke volume (SV) and cardiac output (CO) at baseline and 50, 75 and 100 watts of bicycle exercise by either the thermodilution method (TD) or impedance cardiography (ICG). There were no significant differences between both methods at baseline and the various exercise stages (compare Table 2).*

6.4 ± 8.8% at rest and 11.4 ± 14.8% during exercise. Systematically higher values for SV and CO were calculated by ICG as compared to TD.

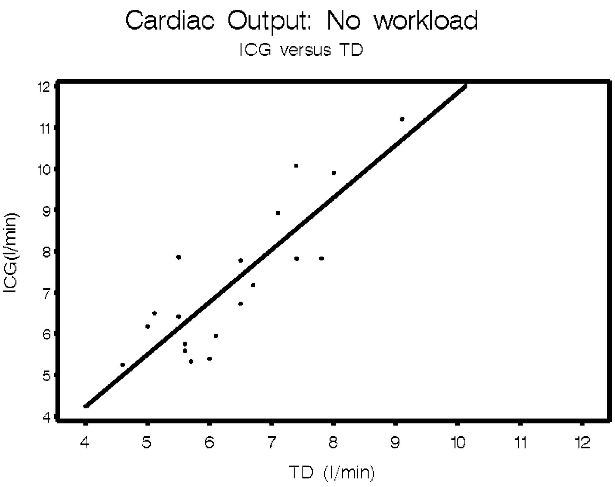
Discussion

The results of this study demonstrate that ICG is an accurate and feasible method for non-invasive haemodynamic evaluation not only at rest but also during exercise testing. There was a highly significant correlation ($p < 0.001$) for measurements of both SV and CO measured by either ICG or the TD method at rest and at various stages of bicycle exercise. This is of particular importance since the correlation of both methods and thus the validity of ICG for haemodynamic evaluation during exercise has so far been only poorly studied [18–24]. In contrast to all other previous studies which despite

(Fig. 3)

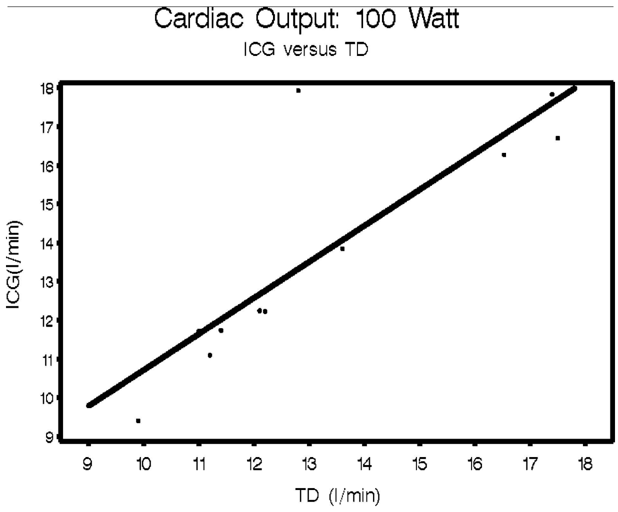


(Fig. 4)



(Fig. 5)

Figs. 3 to 6. *Regression plots of stroke volume (SV) and cardiac output (CO) at baseline and 100 watts of bicycle exercise by either the thermodilution method (TD) or impedance cardiography (ICG). (Continued on next page.)*



(Fig. 6)

Figs. 3 to 6. *(Continued).*

one study [20] included only healthy volunteers or patients without cardiac disease, all patients in our study underwent coronary catheterization to assess coronary status including left ventricular angiography. The presence or absence of significant coronary artery disease becomes important when the correlation and validity of ICG measurements during exercise versus another standard method should be assessed since left ventricular dysfunction may reduce the accuracy of ICG measurements due to difficulties in the automated identification of aortic closure [11,26]. Therefore, correlations reported for ICG versus other standard methods resulting from comparative studies with healthy volunteers cannot regarded applicable and valid for assessing the accuracy of ICG in clinical situations or pharmacologic studies in with exercised-induced left ventricular dysfunction might occur.

Comparison with previous studies examining impedance cardiography during exercise

The reported correlation between ICG and the direct Fick method used in previous exercise studies ranged from $r = 0.82$–94 at rest and $r = 0.85$–95 during exercise [18–24]. In the first study comparing haemodynamic measurements by ICG with the Fick method during exercise, 6 healthy males and 20 patients with suspected CAD were studied by Teo and collegues [18]. The authors reported no significant differences for between both methods but highly significant correlations. ICG, the TD method and measurements obtained by the Fick method were compared in a study by Belardinelli and collegues [20] in a series of 25 consecutive patients with coronary artery disease. Consistent with the results of our study, no significant differences between measurements of SV and CO by TD or ICG were found. The correlation of ICG versus TD was reported high at rest ($r = 0.94$–0.98) and during exercise ($r = 0.90$). The results of our study confirm that ICG-based calculations seem to have a tendency to slightly overestimate SV and CO compared to other standard methods such as the TD- or the Fick method [5,9–11,20,24,25]. However, importantly, this trend towards an overestimation does not increase during exercise and a stable correlation between both methods was maintained until 100 watts (Table 2, Figs. 1 and 2). When interpreting results of comparative studies on haemodynamic parameters such as SV and CO it has also to be considered that the "true" SV "true" CO can in fact never be—and will never be—measured by any of the currently available or future methods but all respective data represent rather an estimated by method-specific formulas based on certain physiological and mathematical assumptions. From this perspective, a relative mean difference between 5–10% for ICG-based measurements of SV and CO versus the respective TD-based measurements (which usually have a variability of at least this size as well) as shown in this study together with a highly statistically significant and stable correlation between ICG- and TD-based measurements represents a rather assuring and encouraging finding for future applications in both pharmacologic studies and clinical routine.

Clinical implications

A valid and feasible method for evaluation of left ventricular function in patients with suspected or previous history of coronary artery disease would not only allow reliable and accurate haemodynamic measurements at rest and during exercise, but should also be simple to use, cost-effective and be suited for serial evaluations. In this context, the major finding of this study comparing ICG versus TD is that we demonstrated that the previously reported high and significant correlation between ICG- and TD based measurements of SV and CO at rest can be maintained not only in healthy volunteers but also in patients with a high prevalence of coronary artery disease and exercise-induced ischaemia ($p < 0.001$) together with a high feasibility of ICG. In contrast to other studies, by the design of our study, we clearly differentiated between resting and exercise measurements and the respective correlations at each exercise stage in order to exclude a progressive loss of correlation between both methods during increasing stages of exercise. Our results are therefore important for both cardiovascular research and clinical cardiology and because they extend the potential for future applications of the new generation of ICG systems from measurements at rest towards their use during exercise testing.

Study limitations

The conduct of left and right heart catheterization in the catherization laboratory required exercise testing in a semi-supine position. This might, due to the increased venous return and consecutively increase thoracic blood volume, have resulted in a different thoracical bioimpedance at baseline as compared to exercise testing in an upright position since posture has been shown to have an impact on form and detection of the ICG signal. Applying other formula than the Bernstein formula [4] we used for calculating SV or other electrode positions than in the present study might also impact results of ICG [31]. However, comparing different mathematical approaches for calculating estimates of SV and CO were not the objective of the present study.

Conclusions

The results of our study demonstrate that ICG is accurate and feasible method for non-invasive measurements of SV and CO not only at rest but also during bicycle which is highly and significantly correlated with invasive measurements by the TD. There was a non-significant but systematic overestimation of SV and CO by ICG compared to the TD method. Our results support the use of ICG in both pharmacologic and clinical research in exercise studies in which non-invasive haemodynamic monitoring is desired.

References

1. Kubicek WG, Karnegis JN, Patterson RP, Witsoe DA, Mattson RH. Development and evaluation of an impedance cardiography output system. *Aerospace Med* 1966;37:1208–1212.
2. Kubicek WG, Kottke FJ, Ramos MU, et al. The Minnesota impedance cardiograph—theory and applications. *Biomed Eng* 1974;9:410–416.
3. Sramek BB. Electrical bioimpedance. *Med Electron* 1983;14:95–103.
4. Bernstein DP. Continuous noninvasive real-time monitoring of stroke volume and cardiac output by thoracic electrical bioimpedance. *Crit Care Med* 1986;14:898.
5. Acton G, Broom C. A comparison of attenuation compensated volume flow based Doppler echocardiography and impedance cardiography in healthy volunteers. *Am J Noninvasiv Cardiol* 1990;4:290–297.
6. Breithaupt K, Erb A, Neumann B, Wolf GZ, Belz GG. Comparison of four noninvasiv Techniques to measure stroke volume: Dual-beam Doppler echoaortography, electrical bioimpedance Cardiography, Mechanosphygmography and M-mode echocardiography of the left ventricle. *Am J Noninvas Cardiol* 1990;4:203–209.
7. Ng HW, Walley T, Tsao Y, Breckenridge AM. Comparison and reproducibility of transthoracic bioimpedance and dual beam Doppler ultrasound measurement of cardiac function in healthy volunteers. *Br J Clin Pharmacol* 1991;32:275–282.
8. Robin ED. Death by pulmonary artery flow-directed catheter: Time for amoratorium? *Chest* 1987;92:727–31.
9. Fuller HD. The validity of cardiac output measurement by thoracic impedance: A meta-analysis. *Clin Invest Med* 1992;15:103–112.
10. Jensen L, Yakimets J, Teo KK. Issues in cardiovascular care. A review of impedance cardiography. *Heart Lung* 1995;24:83–93.
11. Woltjer HH, Bogaard HJ, de Vries PMJM. The technique of impedance cardiography. *Eur Heart J* 1997;18:1396–1403.
12. Clancy TV, Norman K, Reynolds R. Cardiac output measurement in critical care patients: Thoracic electrical bioimpedance versus thermodilution. *J Trauma* 1991;31:1116–1121.
13. van der Meer M, de Vries P. The reliability and applicability of impedance cardiography in the ICU. *Intensivmed* 1996:33:495–500.
14. Spahn DR, Schmid ER, Tornic EM, et al. Noninvasive versus invasive assessment of cardiac output after cardiac surgery: Clinical validation. *J Cardiothorac Anesth* 1990;4:46–59.
15. Perrino AC, Lippman A, Ariyan C, O'Connor TZ, Luther M. Intraoperative cardiac output monitoring: Comparison of impedance cardiography and thermodilution. *J Cardiothorac Vasc Anesth* 1994;8:24–29.
16. Goldstein DS, Cannon RO, Ziemlichman R, Keiser HR. Clinical evaluation of imdedacne cardiography. *Clinical Physiology* 1986;6:235–251.
17. Scherhag A, Pfleger S, de Mey C, Schreckenberger AB, Staedt U, Heene DL. Continuous measurement of hemodynamic alterations during pharmacologic cardiovascular stress using automated impedance cardiography. *J Clin Pharmacol* 1997;37:21–28.
18. Teo KK, Hetherington MD, Haennel RG, Greenwood PV, Rossall RE, Kappagoda T. Cardiac output measured by impedance cardiography during maximal exercise tests. *Cardiovasc Res* 1985;19:737–743.
19. Thomas SH. Impedance cardiography using the Sramek-Bernstein method: Accuracy and variability at rest and during exercise. *Br J Clin Pharmacol* 1992;34:467–476.
20. Belardinelli R, Ciampani N, Costantini C, Blandini A, Purcaro A. Comparison of impedance cardiography with thermodilution and direct Fick methods for noninvasive measurement of stroke volume and cardiac output during incremental exercise in patients with ischemic cardiomyopathy. *Am J Cardiol* 1996;77:1293–1301.
21. Charloux A, Lonsdorfer-Wolf E, Richard R, et al. A new impedance cardiograph device for the non-invasive evaluation of cardiac output at rest and during exercise: Comparison with the "direct" Fick method. *Eur J Appl Physiol* 2000:82:313–320.
22. Tordi N, Mourot L, Matusheski B, Hughson RL. Measurements of cardiac output during constant exercises: comparison of two non-invasive techniques. *Int J Sports Med* 2004;25:145–149.
23. Richard R, Lonsdorfer-Wolf E, Charloux A, et al. Non-invasive cardiac output evaluation during a maximal progressive exercise test, using a new impedance cardiograph device. *Eur J Appl Physiol* 2001;85:202–207.
24. Christensen TB, Jensen BV, Hjerpe J, Kanstrup IL. Cardiac outpur measurement by electrical bioimpedance compared with the CO2 rebreathing technique at different levels of exercise. *Clin Physiol* 200:20:101–105.
25. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986;(I):307–310.
26. Capan LM, Bernstein DP, Patel KP, Sanger J, Turndof H. Measurement of ejection fraction by bioimpedance method. *Crit Care Med* 1987;15:402.

27. Salandin V, Zussa C, Risica G, et al. Comparison of cardiac output estimation by thoracic electrical bioimpedance, thermodilution and Fick methods. *Crit Care Med* 1988;16:1157–1158.
28. Wong DH, Tremper KK, Stemmer EA, et al. Noninvasive cardiac output: Simultaneous comparison of two different methods with thermodilution. *Anesthesiology* 1990;72:784–92.
29. Pickett BR, Buell JC. Validity of Cardiac Output Measurement by Computer-Averaged Impedance Cardiography, and comparison with simultaneous thermodilution determinations. *Am J Cardiol* 1992;69:1354–1358.
30. Yung GL, Gedullo PF, Kinninger K, Johnson W, Channick RN. Comparison of impedance cardiography to direct fick and thermodilution cardiac output determination in pulmonary arterial hypertension. *CHF* 2004;10(2 suppl. 2):7–10.
31. De Mey C, Enterling D. Noninvasive assessment of cardiac performance by impedance cardiography: disagreement between two equations to estimate stroke volume. *Aviat Space Environ Med* 1988;59:57–62.