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The technique of impedance cardiography

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Introduction

Impedance cardiography has been studied for the past 30 years as a non-invasive, harmless and cost effective method of monitoring stroke volume and other indicators of cardiac function. As a measure of stroke volume it has attracted the most interest. Since impedance cardiography has the potential to supply cardiovascular variables on a beat-to-beat basis, its possible clinical applications are unique, e.g. continuous monitoring of systolic time intervals, stroke volume and systemic vascular resistance, when combined with non-invasive blood pressure measurement. Therefore, such a technique would be very useful in patients with acute myocardial injury and in other critical care settings.

In 1966 Kubicek *et al.*[1] described their method of calculating stroke volume from the thoracic impedance signal. Today, the method has been subjected to various refinements and alterations. In order to establish its validity, impedance cardiography has been extensively compared to several other methods which measure stroke volume in both man and animals. The technique of impedance cardiography, however, has not yet been accepted world wide as a reliable method of assessing cardiac output. In the present review the current status and the various aspects of the impedance methodology are summarized and discussed.

Basic principles of impedance cardiography

Impedance cardiography is founded on Ohm's law $R = V/I$, where R is resistance (Ohm), V is voltage (volt) and I is current (ampere). Resistance in an alternating current is called impedance (Z) and can also be calculated as $Z = V/I$ in impedance cardiography. This law is applied to an electrical model generally used for the human body: the parallel conductor model. This model assumes that the impedance of thoracic tissue is parallel to that of blood. The validity of this assumption has been shown by various investigators[2–4].

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Other than fluctuations caused by respiration thoracic tissue impedance is constant. Blood-related impedance changes repeat themselves with every heart beat and are linked to cardiac activity.

The electrode configuration

Cardiac-related impedance changes are measured by passing a sinusoidal current of 50–100 kHz between two electrodes on the thorax and measuring the resulting voltage between two other electrodes. As current strength is known, the impedance can be calculated.

The conventional method according to Kubicek *et al.*[1] uses a tetrapolar band electrode configuration (Fig. 1(a)). The band electrodes, however, are not practical for use; they are difficult to place in clinical settings[5], uncomfortable to wear and expensive. Therefore, many investigators have tried to replace them with disposable spot electrodes, which would be far more practical.

Penny *et al.*[6] were the first to replace the band electrode array with four disposable spot electrodes. However, there was a considerable discrepancy between the stroke volume calculations using the Kubicek equation[1]. In 1986 Bernstein[7] altered Sramek *et al*'s. newly proposed methodology[8] and proposed a new eight disposable spot electrode array (lateral spot electrode array, Fig. 1(b)). This array became very popular; many studies have been performed comparing other techniques of estimating stroke volume with Sramek and Bernstein's method (Table 2). However, Woltjer *et al.*[9] showed that the original band electrode array and the lateral spot electrode array do not give the same results. Furthermore, it has currently been proven that with the lateral spot array a highly inhomogeneously electrical field is created[10]. This implies that values found for baseline thoracic impedance (Z_0), necessary for stroke volume calculations, are not comparable between individuals and therefore might affect the validity of the method.

Recently a promising new nine disposable spot electrode array has been proposed by Woltjer *et al.*[10] (modified semi-circular array, Fig. 1(c)). This array is a modification of Bernstein's array[7], but creates a far better homogeneous electrical field and is interchangeable with the original band electrode array. Future

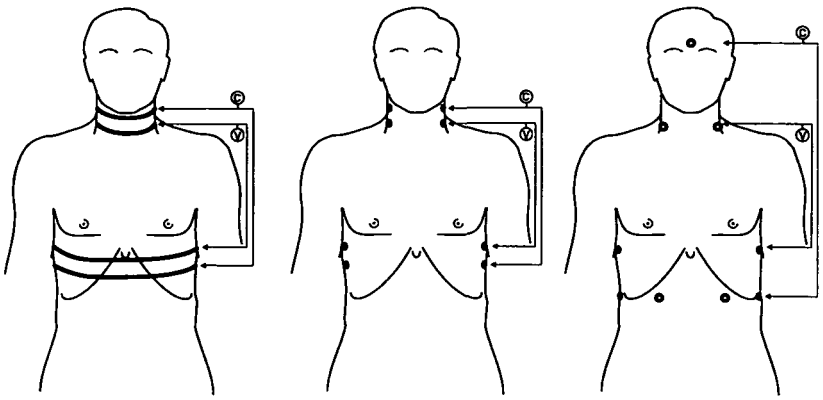

Figure 1 **Illustration of the electrode arrays as frequently used in impedance cardiography, where C are the current injecting electrodes and V the voltage measuring electrodes. The spot electrodes at one horizontal level are always electrically connected. LS=lateral spot; MSC=modified semi-circular array.**

research should indicate whether this array can be used for stroke volume measurement.

The impedance signal and its origin

A typical impedance signal (*dZ*), its first derivative (*dZ/dt*) with marks on the important points of the wave form, and the ECG are shown in Fig. 2. Since Kubicek *et al.* introduced their methodology for stroke volume calculation, the first derivative of the impedance signal has extensively been studied by many investigators to discover its physiological correlates and origin.

Karnegis *et al.*[11] first showed that the A-wave follows the P wave of the ECG, and the C-wave is associated with ventricular contraction. During diastole, they noticed another upward deflection of the *dZ/dt* signal: the O-wave. Lababidi *et al.*[12] compared the *dZ/dt* signal with simultaneously performed phonocardiography in 91 subjects. They found that the B-point coincides with the aortic valve opening and the X-point with aortic valve closure. These observations have been confirmed by several investigators using echocardiography and aortic pressure recordings[13,14]. Today the *dZ/dt* signal is highly sensitive for systolic time intervals[15–17].

The origin of the impedance cardiographic signal appears to be complex and the exact physiological and anatomical basis still needs further explanation. Many investigators have dealt with this subject in the past. In general, evidence to support the origin of the impedance cardiographic signal has been derived from studies, which tried to correlate physiological parameters to the *dZ/dt* signal, modelling studies and studies performed in animals.

The A-wave

Lababidi *et al.*[12] and Karnegis *et al.*[11] found convincing evidence that the A-wave is linked to the contraction

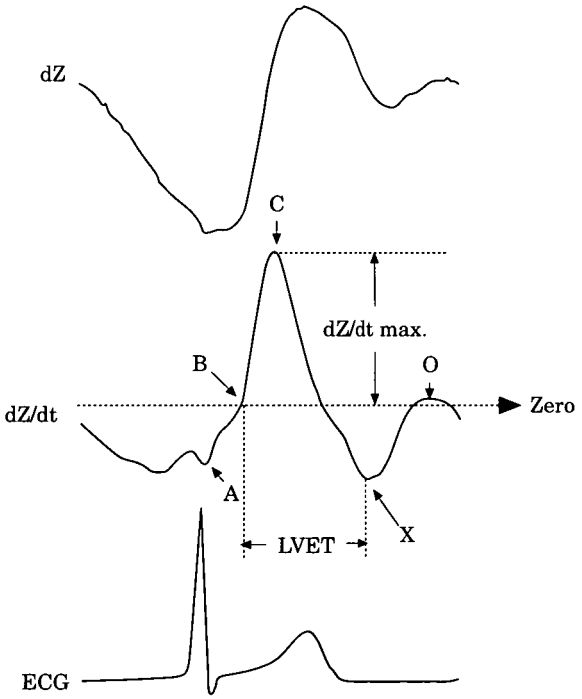

Figure 2 **Characteristic *dZ*, *dZ/dt* and ECG signal, where A is the downward deflection due to the contraction of the atria, B is the start of ejection of blood by the left ventricle, C the major upward deflection occurring during systole, X the closure of the aortic valve, O the diastolic upward deflection, LVET the left ventricular ejection time (s) and dZ/dt_{max} the maximal impedance change during systole (Ω/s).**

of the atria. Lamberts *et al.*[18] raised the hypothesis that this wave has its source in the back flow of blood from the atria into the central veins. Takada *et al.*[19] found evidence that the left atrium might be the main contributor to this wave. He showed that the left atrial ejection fraction is highly correlated to the relative height of the

A-wave (r=0·91). The exact contributions of the right and left atria to the A-wave, however, are not known.

The C-wave

Much research has been performed to unravel the source of the systolic C-wave in the impedance cardiogram, since the absolute height (dZ/dt_{max}, Fig. 2) of this wave is used to calculate stroke volume. The first report on this subject has been published by Bonjer *et al.*[20]. In anaesthetized dogs they encased the heart in an insulating sheet of rubber. From this experiment they concluded that the volume changes in the heart itself generally play a very minor role. Geddes and Baker[21] showed that contraction of both the right and the left ventricle can cause a change in the thoracic impedance. However, the impedance changes were relatively small. The impedance changes from the ascending aorta were much larger. Ito *et al.*[22] performed a study in anaesthetized dogs in which the aorta and the pulmonary artery were perfused with a controlled pulsatile flow. From this experiment they concluded that less than 30% of the thoracic impedance signal originates from the pulmonary artery. Saito *et al.*[23] also showed that the pulmonary circulation is reflected in the thoracic impedance cardiographic signal. Kubicek *et al.*[24], however, published signals of a dog whose left ventricle pumped only once every two ejections of the right ventricle. Only when the left ventricle contracted was there a change in the thoracic impedance. He also showed that the peak value of the dZ/dt signal appeared precisely at the peak of the left ventricular ejection velocity. These results were confirmed by Lamberts *et al.*[18]. Spinale *et al.*[25] correlated the left and right ventricular fractional shorting as determined with echocardiography, to the dZ/dt_{max} in pigs during positive inotropic stimulation and preload reduction. This study showed that dZ/dt_{max} was highly correlated to the left ventricular fractional shortening (r=0·88) and moderately to the right ventricular fractional shortening (r=0·54). They also concluded that the systemic circulation must be the largest contributor to the impedance cardiogram.

Welham *et al.*[26] related dZ/dt_{max} to peak aortic flow velocity in anaesthetized dogs which inspired an increasing halothane concentration. A high correlation was noted between these two variables (r=0·95). Ohashi[27] correlated the dZ/dt_{max} and peak aortic flow velocity, measured in 30 human subjects. This study showed a high correlation between these variables (r=0·84). Kizakevich *et al.*[13] repeated this experiment in 31 human subjects during exercise and used Doppler echocardiography to measure peak aortic flow velocity. They also found a high correlation (r=0·86).

In order to unravel a more detailed description of the origin of the C-wave, some investigators have tried to simulate impedance cardiographic changes in a model[28–31]. However, these are far from consistent, and most fail to explain the frequently found relationship between dZ/dt_{max} and other physiological variables, e.g. aortic peak flow velocity. More research is needed on the contributors of dZ/dt_{max} as predicted by a model.

The O-wave

The O-wave is the diastolic upward deflection of the dZ/dt signal. Lababidi *et al.*[12] showed that the maximum of this wave coincides with the opening snap from the mitral valve in patients with mitral stenosis. Most evidence for its origin has been derived from impedance measurements in patients with cardiac abnormalities. An elevated O-wave has been noticed in patients with mitral and aortic valve pathology[18,32–34], in patients with heart failure[35], and in patients with acute myocardial injury[36]. Because of the early diastolic appearance and the specific elevation in mitral and aortic valvular disorders, the origin of the O-wave has been strongly linked to the pulmonary venous return to the left side of the heart. Pickett *et al.*[37] found a significant relation between peak Doppler early diastolic velocity, obtained at the mitral valve tips, and the relative height of the O-wave (r=0·64).

Stroke volume equations and validation

Signal processing techniques

Heart cycle-related impedance changes are superimposed on impedance changes caused by respiration. Therefore, these effects have to be separated in order to obtain data that are only related to the first phenomenon. Previous investigators have tried this by measuring the thoracic impedance changes during end-expiratory apnoea. However, this manoeuvre significantly influences the haemodynamic process itself[38].

In the last decade new refinements have been applied to the impedance signal processing technique. In 1986 Muzi *et al.*[39] introduced the computer supported ensemble averaging technique, which has been refined by Kim *et al.*[40]. This is a simple technique, which totally eliminates the effects of respiration on the impedance signal. However, it also eliminates the possibility of measuring stroke volume beat by beat. Therefore, several investigators worked on digital filtering techniques[41–43]. These techniques preserve the beat-by-beat information, but are far more complex. One of the greatest problems are the movement artifacts, whose spectra are unknown and may sometimes overlap the impedance signal spectrum. Barros *et al.*[44] recently claimed that this problem might be solved by an adaptive filtering technique. Today, digital filtering techniques are still in development.

Stroke volume equations

To explain the pulsatile variations of the impedance signal, some assumptions were made: (1) the impedance of thoracic tissue is parallel to that of intrathoracic blood; (2) the resistivity of blood is constant during the cardiac cycle; (3) the thorax, from base of the neck to the

xiphoid process, is a cylinder which encompasses an elastic cylindrical tube of the same length: the aorta; (4) the electric current distribution in this cylinder is homogeneous; (5) the maximal change in impedance (dZ/dt_{max}) multiplied by the left ventricular ejection time (left ventricular ejection time) is directly proportional to the systolic pulsatile change in aortic blood volume.

The validity of the first assumption has been shown by various investigators[2–4]. About the second there has been much debate, since it is known that, besides volume changes, flowing blood itself can cause an impedance change. This is caused by a change in the orientation of the erythrocytes[18,45]. Various investigators have tried to estimate the relative contributions of these two phenomena (the orientation of erythrocytes and blood flow) to the dZ signal. The first reports estimated these contributions about equal[18,45,46]. Shankar *et al.*[47], however, reported that the signal caused by the change in blood resistivity, due to orientation of erythrocytes during the cardiac cycle, is not in phase with the signal caused by the volume changes. Therefore, orientation of the erythrocytes does not affect the magnitude of the dZ/dt peak. They showed that the erythrocyte orientation effect only accounts for less than 5·5% of the total magnitude of the dZ/dt_{max}. More research is needed on this subject.

The third assumption is a simplification and has often been criticized from an anatomical point of view. Recently, Raaijmakers *et al.*[48] showed that a two-cylinder model might be a better reflection of the electrical behaviour of the thorax, instead of the one-cylinder model as applied by Kubicek *et al.*[1]. Validation of this model is lacking at the moment. Although Guha *et al.*[49] claimed that the current densities vary over the thoracic cross-section, Lamberts *et al.*[18] showed, in vivo, that the basic thoracic impedance (Z_0) is ultimately linear related to the inner distance between the voltage detecting electrodes. The fifth assumption has also often been questioned. Recently Faes *et al.*[50] showed that this assumption is mathematically correct. However, the exact origin of the impedance signal still remains to be explained.

Several equations have been developed in the past to calculate stroke volume from the impedance cardiographic signal. However, the two equations most commonly used are the Kubicek[1] and the Sramek-Bernstein[7,8] equations.

Taking the earlier mentioned assumptions into account, the Kubicek equation[1] runs:

$$SV = \rho \cdot \frac{L^2}{Z_0^2} \cdot dZ/dt_{max} \cdot LVET$$

where stroke volume is stroke volume (ml), ρ the resistivity of blood ($\Omega \cdot$ cm), L the distance between the voltage measuring electrodes (cm), Z_0 the basic thoracic impedance (Ω), dZ/dt_{max} the maximal impedance change (Ω/s) and $LVET$ the left ventricular ejection time (s).

No consensus exists about the value for ρ in this equation. Controversial reports have been published in the past about this subject. According to Kubicek *et al.*[1], this variable is dependent on the patient's haematocrit. However, when a normal haematocrit is assumed, a mean value of 150 $\Omega \cdot$ cm might be used. Hill *et al.*[51] showed the importance of adjusting ρ dependent on the haematocrit when patients with a low haematocrit are measured. This was also advocated by Kobayashi *et al.*[52] in normal healthy subjects during exercise, and by Costeloe *et al.*[53] in babies during the neonatal period. In 1981 however, Quail *et al.*[55] claimed, based on in vitro and in vivo investigations, that ρ might be considered virtually constant at a value of 135 $\Omega \cdot$ cm. More research is needed on this subject.

Sramek *et al.*[8] developed a new equation in which they substituted ρ, in Kubicek's equation, for a value dependent on Z_0, L and V, where V is the volume of the electrical conductor. For the determination of V, Sramek *et al.* claimed that L equals about 17% of a person's height (H), and that V can be estimated as $L^3/4{\cdot}25$, based on chest roentgenograms from 30 anatomically normal, adult volunteers. Furthermore they assumed that the volume of the electrically participating tissue in the thorax is a truncated cone instead of a cylinder as in the Kubicek's equation. Bernstein[7] added a weight correction factor, δ, to Sramek's equation; however, no evidence has been published about the validity of δ. The Sramek–Bernstein equation runs:

$$SV = \delta \cdot \frac{(0.17 \cdot H)^3}{4.25} \cdot \frac{dZ/dt_{max}}{Z_0} \cdot LVET$$

Validation

In the past 30 years many validation studies have been performed comparing the impedance cardiographic method according to Kubicek *et al.*[1], and according to Sramek *et al.*[8] and Bernstein[7], with other methods to assess stroke volume. The results of these studies using Kubicek's method are shown in Table 1. Table 2 shows the results of the studies using Sramek and Bernstein's method.

It is noteworthy that Sramek and Bernstein's method is by far the most frequently used impedance cardiographic method since 1986. This is probably the result of the implication of this method in a practical, commercially available set-up (the NCCOM, BoMed Medical Manufacturing Ltd., Irvine, CA, U.S.A.).

In general, most investigators found a significant correlation between stroke volume measured with impedance cardiography and stroke volume measured with other methods. However, various investigators also reported a wide dispersion of the impedance stroke volume data. This has especially been reported by investigators using Sramek–Bernstein's method in the last decade[66,68,75,77,79,82–85]. It also appears from these studies that the impedance method is not equally valid

Table 1 Comparison between Kubicek's impedance cardiographic method and other methods to assess cardiac output in man

Authors	Year	Population	n	ρ	Signal process technique	Reference method	Results
Sova[55]	1970	20, healthy adults	20	145	UK; M; B	DD	0·78; UK; UK; UK
Lababidi[56]	1971	21, children left to right shunts	21	Hct	4; M; B	PF	0·96; UK; UK; UK
Lababidi[56]	1971	13, children aortic insufficiency	13	Hct	4; M; B	DF	−0·31; UK; UK; UK
Naggar[57]	1975	14, DHC	14	135	>5; M; BH	DF	0·91; UK; UK; UK
Hill[51]	1975	20, hypertension and haemodialysis	20	Hct	UK; M; UK	^{131}I	0·87; UK; −0·73; UK
Keim[58]	1976	3, healthy adults and 14, hypertensive patients	122	Hct	3; M; BH	DD	0·46; <0·001; UK; UK
Gabriel[59]	1976	10, after myocardial infarction	86	135	5; M; UK	DD	0·85; ns; 0·42; UK
Costeloe[53]	1977	32, healthy neonates	109	Hct	8–12; M; B	N_2O	0·88; UK; UK; UK
Kobayashi[52]	1978	10, healthy adults	UK	Hct	5; M; BH	VO_2	0·95; UK; UK; UK
Lamberts[18]	1984	53, valvular pathology	53	Hct	3; M; B	DD	0·64; UK; 0·2; 3·8
Ebert[60]	1984	14, DHC	47	135	1; M; BH	LVG	0·79; UK; UK; 6·8*
Muzi[61]	1985	14, CI	14	135	100–300; CSA; B	TD	0·87; UK; UK; UK
Koon-Kang[62]	1985	20, DHC	40	Hct	5; M; BH	DF	0·93; ns; UK; UK
Donovan[5]	1986	27, CI	120	150	10; M; B	TD	0·63; UK; 0·17; 4·8
Goldstein[63]	1986	19, CI	19	Hct	<10; M; B	TD	0·85; ns; 0·1; UK
Miles[64]	1988	37, children various congenital heart defects	37	135	10; M; UK	DF	0·84; ns; 0·05; UK
Ekman[65]	1990	10, major vascular surgery	50	Hct	32; CSA; B	TD	0·88; ns; 2·6*; UK
Pickett[66]	1992	43, various cardiac diseases	201	fixed value	UK; CSA; B	TD	0·75; ns; 0·1–3, 2·1
Demeter[67]	1993	10, after CABG	10	Hct	3; M; B	TD	0·84–0·97; ns; 0·2; UK
Woltjer[68]	1995	37, after CABG	37	Hct	20; CSA; B	TD	0·90; ns; 0·5*; 16*

n=Number of measurements; ρ=resistivity of blood; Hct=haematocrit; M=manual; CSA=computer supported averaging; B=breathing; BH=breath holding; DD=dye dilution; DF=direct Fick; PF=pulmonic flow Fick; ^{131}I=radioisotopic cardiac output determination; N_2O=N_2O rebreathing; VO_2=oxygen uptake; EC=echocardiography; CO_2=CO_2 rebreathing; LVG=left ventriculography; DHC=diagnostic heart catheterization; CI=critically ill; Hct=haematocrit; H=L taken as 17% of the patient's height (cm); D=determined; UK=unknown; ns=not significant (P>0·05).

The signal processing technique is given in the following order: number of heart beats used; manner of averaging; respiration during the measurements. The results are given in the following order: the correlation coefficient for the relation between impedance cardiography and the reference method, the value of significance for the mean difference between the two methods (Student's t-test), mean difference between the two methods (l . min^{-1}) and the standard deviation of this difference × 2 (l . min^{-1}) (*=ml).

under all physiological conditions. Aortic valvular pathology[18,56], the first 12 h after coronary artery surgery[81,84] and sepsis[85] appear to be less favourable conditions for impedance cardiography.

Studies using Kubicek's method show better correlations with the reference method. Pickett *et al.*[66] and Woltjer *et al.*[68] seem to confirm this observation. These are the only studies comparing both methods with a reference method in the same group of patients. Nevertheless, Kubicek's method is far less standardized. A critical element of this method is the resistivity of blood (ρ). In recent studies of Demeter *et al.*[67] and Woltjer *et al.*[68], it was found that the best results are obtained when ρ is calculated dependent on the patient's haematocrit.

No consensus can be reached on the accuracy of impedance cardiography in the measurement of stroke volume based on the present studies. In some studies, the method is evaluated as highly accurate[51,59–62,80,86,87]; in others more dispersion between the two methods[5,18,79,81–85] is found. In most studies, however, the mean difference between the two methods and its standard deviation are not shown, which makes it difficult to draw conclusions about precision. In order to establish the validity of impedance cardiography, more research is needed on the latter, and more studies need to be performed comparing both impedance cardiographic methods with each other.

Conclusions

Although the exact source of the impedance cardiogram is still unknown, it is clear that this technique has the potential to become an accurate, non-invasive method to assess stroke volume. More research is needed on the following subjects in order to improve the accuracy of the method, and to decrease the substantial degree of methodological diversity that exists in its application today: (a) development of a reliable disposable spot electrode array which is practical in use; (b) more precise knowledge about the exact origin of the impedance cardiogram; (c) standardized methods to eliminate the effect of respiration and to analyse the impedance signal; (d) the effect of blood resistivity on the impedance signal; (e) the validity of the one cylinder or the truncated cone model; (f) the need to adjust the

Table 2 Comparison between Sramek–Bernstein's impedance cardiographic method and other methods to assess cardiac output in man

Authors	Year	Population	n	L	Signal process technique	Reference method	Results
Bernstein[69]	1986	17, CI	94	H	UK; CSA; B	TD	0·88; ns; UK; UK
Appel[70]	1986	16, CI	391	H	UK; CSA; B	TD	0·83; ns; UK; UK
Shoemaker[71]	1988	58, CI	587	H	UK; CSA; B	TD	0·83; ns; UK; UK
Smith[72]	1988	30, healthy adults	103	H	UK; CSA; B	CO_2	0·56; <0·05; UK; UK
Salandin[73]	1988	9, CAD and 15, valvular heart disease	108	H	UK; CSA; B	TD	0·83; ns; UK; UK
Spinale[74]	1988	10, after CABG	30	H	UK; CSA; B	TD	0·77; NS; UK; UK
Kalkat[75]	1988	53, CI	76	H	UK; CSA; B	TD	0·53; <0·01; UK; UK
Northridge[76]	1990	25, within 24 h after acute myocardial infarction	25	H	12; CSA; B	TD	UK; ns; −0·16; UK
Pepke-Zaba[77]	1990	21, after heart transplantation	381	H	UK; CSA; B	TD	0·65; UK; UK; UK
Spahn[78]	1990	25, after CABG	111	H	UK; CSA; B	TD	0·78; <0·05; UK; UK
Wong[79]	1990	67, CI	416	H	UK; CSA; B	TD	0·61; UK; −0·67; 3·44
Clancy[80]	1991	17, CI	51	H	UK; CSA; B	TD	0·91; UK; 0·23; 1·12
Thomas[81]	1991	28, after CABG first 12 h; second 12 h	28	H	12; CSA; B	TD	UK; <0·001; −1·08; 3·05 UK; ns; 0 09; 1·08
Walley[82]	1991	18, healthy male adults	UK	H	16; CSA; B	EC	0·69; ns; 0·0–3; 4·2
Woo[83]	1991	44, CI	80	H	UK; CSA; B	TD	0·51; UK; 0·12; UK
Pickett[66]	1992	43, with various cardiac diseases	201	H	UK; CSA; B	TD	0·66; UK; UK; UK
Sageman[84]	1993	50, after CABG	50	H	16; CSA; B	TD	0·49; UK; −0·33; 3·14
Young[85]	1993	19, sepsis	242	H	60; CSA; B	TD	0·36; UK; −1·69; 2·48
Shoemaker[86]	1993	68, CI	842	H	UK; CSA; B	TD	0·86; ns; 0·01; 1·4
Perrino[87]	1994	43, intraoperative	400	H	UK; CSA; B	TD	0·84; UK; −0·41; 2·0
Woltjer[68]	1995	37, after CABG	37	H	20; CSA; B	TD	0·64; ns; −2·7*; 29·3*

Abbreviations as in Table 1.

impedance-derived stroke volume for body weight; (g) comparison of the validity of the current methods in the same group of patients.

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