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A new impedance cardiograph device for the non-invasive evaluation of cardiac output at rest and during exercise: comparison with the "direct" Fick method

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Abstract The objectives of this study were to evaluate the reliability and accuracy of a new impedance cardiograph device, the Physio Flow, at rest and during a steady-state dynamic leg exercise (work intensity ranging from 10 to 50 W) performed in the supine position. We compared cardiac output determined simultaneously by two methods, the Physio Flow ($\dot{Q}_{cPF}$) and the direct Fick ($\dot{Q}_{cFick}$) methods. Forty patients referred for right cardiac catheterisation, 14 with sleep apnoea syndrome and 26 with chronic obstructive pulmonary disease, took part in this study. The subjects' oxygen consumption values ranged from 0.14 to 1.19 $l \cdot min^{-1}$. The mean difference between the two methods ($\dot{Q}_{cFick} - \dot{Q}_{cPF}$) was 0.04 $l \cdot min^{-1}$ at rest and 0.29 $l \cdot min^{-1}$ during exercise. The limits of agreement, defined as mean difference ± 2SD, were −1.34, +1.41 $l \cdot min^{-1}$ at rest and −2.34, +2.92 $l \cdot min^{-1}$ during exercise. The difference between the two methods exceeded 20% in only 2.5% of the cases at rest, and 9.3% of the cases during exercise. Thoracic hyperinflation did not alter $\dot{Q}_{cPF}$. We conclude that the Physio Flow provides a clinically acceptable and non-invasive evaluation of cardiac output under these conditions. This new impedance cardiograph device deserves further study using other populations and situations.

Key words Impedance cardiography · Cardiac output · Fick principle · Exercise · COPD

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Introduction

The accurate evaluation of a patient's haemodynamic status, which includes knowledge of cardiac output, is important for clinicians in many situations. In intensive care units, the assessment of cardiac output is essential for the monitoring of patients with heart failure or shock, enabling the precise adjustment of cardiac treatments or pacing. In addition to the continuous monitoring of the electrocardiogram (ECG) blood pressure and pulse oxymetry, cardiac output monitoring during exercise and recovery periods would be of interest for assessing patient tolerance and safety. Finally, the measurement of cardiac output in patients with shortness of breath can yield useful diagnostic information.

Most of the techniques that are currently available for measuring cardiac output, such as dye dilution, thermodilution and methods based on the Fick principle (direct Fick), are invasive and require adhesion to strict conditions for accurate measurements. Doppler-echocardiography and measurement of cardiac output by CO_2 rebreathing are the most widely used non-invasive techniques, but their accuracy during exercise remains debatable (Coates 1992; Lumb 1993). All of these techniques require an experienced operator. Two groups of methods allow the non-invasive and simple evaluation of cardiac output. The pulse contour methods are based on the relationship between stroke volume (SV) and the area subtended by the systolic part of the peripheral arterial profile, determined from finger plethysmography. SV calculated with these methods during cycle ergometer exercise showed reasonably good agreement with that obtained using Doppler echocardiography (Antonutto et al. 1995). The measurement of changes in electrical bioimpedance during the cardiac cycle has been used to estimate beat-to-beat changes in cardiac output for more than 30 years (Kubicek et al. 1966). This technique, which provides an automated and continuous measurement, is non-invasive and simple to perform. The original Kubicek equation that is used to calculate SV has been modified by Sramek and Berstein (Berstein 1986; Sramek et al. 1983). Different devices operating on the basis of these formulae have been tested against reference methods, with divergent results. For some authors, impedance cardiography provides a reasonable estimate of the directional changes in cardiac output, but for others, impedance cardiography remains controversial with regard to its accuracy and reliability (Bloch and Russi 1997; Critchley 1998; Fuller 1992; Jensen et al. 1995; Pennock 1997). Indeed, it is likely that none of the impedance devices provide the same results. However, both the Kubicek and Sramek and Berstein equations need an evaluation of the basal thoracic impedance (Z_0). Z_0 is one of the two components of the impedance cardiography waves, and represents the steady-state mean thoracic impedance. The second component is the pulsatile variation in impedance (ΔZ), which is mainly a function of variations in the volume and velocity of the thoracic aorta blood flow (Jensen et al. 1995). Z_0 depends upon multiple factors such as thorax morphology, homogeneity of thorax perfusion, and fluid and gas content (Berstein 1986; Jensen et al. 1995; Kubicek et al. 1966; Penney 1986; Sramek et al. 1983). The precise measurement of this variable is critical, and can be altered by perspiration, subcutaneous adiposity, and poor electrical contact (Jensen et al. 1995). Large and rapid exercise-induced variations of this parameter make its estimation more difficult in this situation (Warburton et al. 1999).

In the study presented here, we test a new impedance cardiograph device, the Physio Flow PF-03 (Manatec Biomedical, Macheren, France). The development of this device has resulted from technical improvements in both the hardware (a new generation of analog technology allows the Physio Flow to improve signal filtering and stability, and provides better data processing) and software. The basic equation for calculating SV has been modified profoundly in order to overcome the difficult evaluation of variables such as blood resistivity (ρ), the distance between recording electrodes (l), and the Z_0 used in the Kubicek and Sramek-Berstein equations. The direct Fick method, considered to be one of the most reliable methods for cardiac output measurement, was chosen as the reference technique. Cardiac output was measured simultaneously by the Physio Flow ($\dot{Q}_{\mathrm{cPF}}$) and by the direct Fick ($\dot{Q}_{\mathrm{cFick}}$) methods at rest and during a mild exercise in patients who were referred to our department for right cardiac catheterisation. The patients had either chronic obstructive pulmonary disease (COPD) or sleep apnoea syndrome (SAS). Since impedance cardiography has been considered to be inaccurate in patients with emphysema, we also examined the effects of thoracic hyperinflation on the impedance cardiography measurement of cardiac output.

Methods

Subjects

Forty patients who were referred to our department for right cardiac catheterisation agreed to participate in this study, which was approved by the Institutional Review Board. Twenty-six (65%) patients had COPD, and among those, 16 had emphysema. Fourteen patients (35%) had severe SAS without other respiratory symptoms. After measurement of their physical characteristics, spirometry was performed to measure the subjects' vital capacity (VC) and forced expiratory volume in 1 s (FEV_1). Functional residual capacity was measured using the helium dilution technique, and/or thoracic gas volume was measured with the aid of a total-body plethysmograph (Bodyscope, Ganshorn Medizin Electronic, Münnerstadt/Niderlauer, Germany). Total lung capacity (TLC) and residual volume (RV) were then calculated. Pulmonary function tests are expressed as percentage of the predicted values based on age, height and gender (Quanjer et al. 1993). The patients' characteristics are presented in Table 1.

Protocol

Measurements were performed in the morning, 2–3 h after breakfast, in an air-conditioned room. The patient remained supine throughout the preparation for cardiac catheterisation. Direct Fick and Physio Flow measurements were recorded simultaneously by two investigators in a blind fashion. Two cardiac output measurements were performed, one at rest, and one during a mild exercise carried out in a supine position on an electromechanically braked bicycle ergometer. The workloads were low, ranging from 10 to 50 W according to the patient's fitness, so as to stay below the patient's ventilatory threshold and to allow the patient to reach a steady-state condition. Cardiac output measurement was performed during the 6th min of the exercise test, a steady-state condition [e.g. stable oxygen consumption, ($\dot{V}O_2$) and cardiac frequency (f_c)] being obtained in most patients at the 3rd min. To test the repeatability of the cardiac output measurement at rest, in ten patients, a second evaluation by the two methods was performed 5 min after the first.

Measurement of $\dot{Q}_{\mathrm{cFick}}$

A catheter (Flexopulmocath Plastimed, 4F) was inserted under sterile conditions into the pulmonary artery via the antecubital vein or, rarely, via the femoral vein. The catheter was advanced while monitoring simultaneously ECG and intravascular pressure (Physiogard SM 785). A Potts-Cournand needle was inserted into the brachial artery for arterial blood gas analysis. Expired gas was

Table 1 Characteristics of the subjects. Values are expressed as means (SD). Predicted values are those of the European Respiratory Society. (*VC* Vital capacity, *FEV₁* forced expiratory volume during 1 s, *TLC* total lung capacity, *RV* residual volume, *COPD* chronic obstructive pulmonary disease, *SAS* sleep apnoea syndrome, *M* male, *F* female)

Disease	Number of subjects	Gender (M/F)	Age (years)	Body mass (kg)	Height (cm)	VC (% predicted)	FEV_1/VC (%)	TLC (% predicted)	RV/TLC (%)
COPD	26	22/4	58.9 (10.6)	70.6 (13.3)	168 (6)	80.6 (22.7)	57 (25)	107.7 (16.4)	51.8 (13.5)
SAS	14	13/1	54.7 (4.3)	94.1 (24.1)	169 (8.7)	106.0 (12.4)	89 (9)	100.9 (9.7)	32.1 (5.2)
Total	40	35/5	56.8 (9.5)	78.5 (20.7)	168 (7)	88.9 (23.1)	71 (23)	105.1 (14.2)	44.3 (14.7)

analysed with a commercially available system (breath-by-breath metabolic measurement chart, Medi-soft, Dinant, Belgium). Calibration of the expired gas analysis device was made and the flowmeter checked with a calibration syringe. $\dot{V}O_2$ CO_2 production ($\dot{V}CO_2$), expired minute ventilation ($\dot{V}_E$) and respiratory exchange ratio were measured continuously throughout the study. Measurements of cardiac output were made when $\dot{V}O_2$ and f_c had been stable for 3 min and the respiratory exchange ratio was below 1.0. Blood was sampled over a period of 10 s. Blood gases were measured immediately with a blood gas analyser (Ciba-Corning 270–278) located in an adjacent room. Arterial and mixed venous oxygen content (caO_2 and $c\bar{v}O_2$, respectively, $ml \cdot dl^{-1}$) were calculated from the measurements of the arterial partial pressure of O_2 (P_aO_2, mmHg), arterial O_2 saturation (S_aO_2), haemoglobin concentration (Hb, $g \cdot dl^{-1}$) and the theoretical O_2-carrying capacity of Hb ($1.34\ mlO_2 \cdot g^{-1}$ Hb). For instance, for arterial blood: $c_aO_2 = (Hb \times 1.34 \times S_aO_2) + (P_aO_2 \times 0.003)$. Cardiac output was then obtained as: $\dot{Q}_{cFick} = \dot{V}O_2/(c_aO_2 - c\dot{V}O_2) \times 10^2$ ($\dot{V}O_2\ l \cdot min^{-1}$ STPD, time average during 1 min, $\dot{Q}_{cFick}$, $l \cdot min^{-1}$).

Measurement of $\dot{Q}_{cPF}$

The bioimpedance method of cardiac output determination uses changes in transthoracic impedance during cardiac ejection to calculate SV. The Physio Flow emits a high-frequency (75 kHz) and low-amperage (1.8 mA) alternating electrical current via electrodes. Two sets of two electrodes (Ag/AgCl, Hewlett Packard 40493 E), one "transmitting" electrode, one "sensing" electrode, are applied above the supraclavicular fossa at the left base of the neck and along the xiphoid, respectively. Positioning of the electrodes is not critical, since Z_0 evaluation is unnecessary. No specific skin preparation is needed, except shaving. Another set of two electrodes is used to monitor a single ECG lead (V1/V6 position). Verification of the correct signal quality is accomplished by visualization of the ECG and its first derivative (dECG/dt), the impedance waveform (ΔZ) and its first derivative (dZ/dt). Autocalibration is achieved after having entering the patient's age, height, body mass, and systolic/diastolic blood pressure assessed using a standard mercury-column sphygmomanometer. To achieve this autocalibration, which provides the basic curves and data necessary to measure SV variations according to ΔZ and dZ/dt variations, patients have to be immobile and relaxed. Values for SV obtained over a 12-beat period are averaged, the Physio Flow deleting unacceptable curves (Olympic filter level 2). For this experiment, cardiac output determinations made with Physio Flow during 1 min were averaged. Examples of waveforms processed by the Physio Flow device are shown in Fig. 1. Physio Flow methodology is described by the designer in Appendix I.

Data analysis

The coefficient of repeatability was calculated for both the Physio Flow and direct Fick methods (Bland and Altman 1986) by remeasurement of the cardiac output using both methods after a 5-min delay in ten resting subjects. Comparisons between the two methods were made separately for the sets of measurements taken at rest and during exercise, except for the $\dot{Q}_{cPF}/\dot{V}O_2$ relationship. Linear regression analysis was carried out first with $\dot{Q}_{cPF}$ plotted against $\dot{V}O_2$, and next against $\dot{Q}_{cFick}$. To compare the two types of measurement and evaluate whether there was agreement or bias, we used the method of Bland and Altman (1986), where the difference between bioimpedance and $\dot{Q}_{cFick}$ for each set of simultaneous determinations ($\dot{Q}_{cFick} - \dot{Q}_{cPF}$) is plotted against the mean of the two measurements [$(\dot{Q}_{cFick} + \dot{Q}_{cPF})/2$]. The differences in cardiac output are expressed both in absolute terms ($l \cdot min^{-1}$) and as a percentage of the mean value. Limits of agreement are defined as means $\pm(1.96 \times SD)$.

To test the effect of thoracic hyperinflation on thoracic impedance, we carried out the regression of the difference ($\dot{Q}_{cFick} - \dot{Q}_{cPF}$) as a function of the RV/TLC ratio.

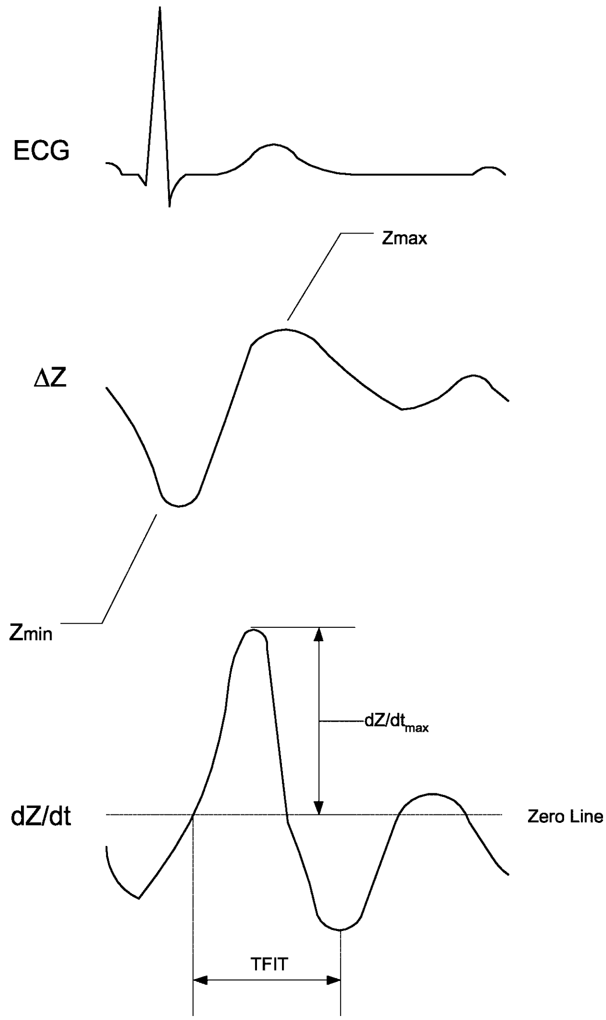


Fig. 1 Waveforms obtained with Physio Flow. The *upper trace* is the electrocardiogram (*ECG*). The *middle* and *bottom* traces are impedance (ΔZ) and its first derivative, dZ/dt, respectively. Thoracic fluid inversion time (*TFIT*) and dZ/dt_{max} are indicated on the first derivative waveform

Results

The repeatability of cardiac output measurements was determined from the second measurements made on ten resting subjects. The coefficients of repeatability were $0.94\ l \cdot min^{-1}$ and $0.96\ l \cdot min^{-1}$ for the Physio Flow and the direct Fick methods, respectively.

Thirty-two patients were able to perform the exercise at between 10 and 50 W, with 17 (53%) of them pedalling at a 30-W workrate. The 72 cardiac outputs measured at rest (40) and during exercise (32) ranged from 4.34 to $14.84\ l \cdot min^{-1}$ for the Physio Flow, and from 3.60 to $15.03\ l \cdot min^{-1}$ for direct Fick. $\dot{V}O_2$ ranged from 0.14 to $1.19\ l \cdot min^{-1}$. The regression of $\dot{Q}_{cPF}$ ($l \cdot min^{-1}$) against $\dot{V}O_2$ ($l \cdot min^{-1}$) is shown in Fig. 2. The regression equation, based on 72 measurements, is $\dot{Q}_{cPF} = 7.2 \times \dot{V}O_2 + 4.2$. Individual values of cardiac output obtained simultaneously by the two methods are plotted in Fig. 3. The correlation coefficient was 0.89 ($P < 0.001$) for resting values and 0.85 ($P < 0.001$) for exercising values. There was no difference between average cardiac outputs measured by the two methods, either at rest [mean $\dot{Q}_{cPF}$ = 6.25 (1.14) $l \cdot min^{-1}$, mean $\dot{Q}_{cFick}$ = 6.32 (1.42) $l \cdot min^{-1}$, NS] or during exercise [mean $\dot{Q}_{cPF}$ = 9.89 (2.17) $l \cdot min^{-1}$, mean $\dot{Q}_{cFick}$ = 10.15 (2.35) $l \cdot min^{-1}$, NS].

A comparison of the two techniques with the Bland and Altman method is shown in Fig. 4. At rest, the mean difference ($\dot{Q}_{cFick} - \dot{Q}_{cPF}$) was 0.07 $l \cdot min^{-1}$ [95% confidence interval: −0.23, +0.27 $l \cdot min^{-1}$], which represents 0.29% of the mean resting cardiac output. The $\dot{Q}_{cFick} - \dot{Q}_{cPF}$ difference did not vary significantly with the mean of $\dot{Q}_{cFick}$ and $\dot{Q}_{cPF}$. The limits of agreement are (−1.18, +1.32 $l \cdot min^{-1}$) at rest. Thus, in 95% of the paired measurements, the difference between $\dot{Q}_{cFick}$ and $\dot{Q}_{cPF}$ is within a (−19%, +19%) interval. During a mild effort, the mean of the $\dot{Q}_{cFick} - \dot{Q}_{cPF}$ difference is 0.26 $l \cdot min^{-1}$ (2.44% of the mean exercising cardiac output) with a (−0.17, +0.69 $l \cdot min^{-1}$) 95% confidence interval. The limits of agreement during exercise are −2.16 and +2.68 $l \cdot min^{-1}$ (−21%, +26% of cardiac output). At rest, $\dot{Q}_{cFick}$ differed by 20% or more in only one patient among the 40 (2.5%). During exercise, two $\dot{Q}_{cFick} - \dot{Q}_{cPF}$ differences among the 32 measurements (6.2%) were equal to or greater than 20%.

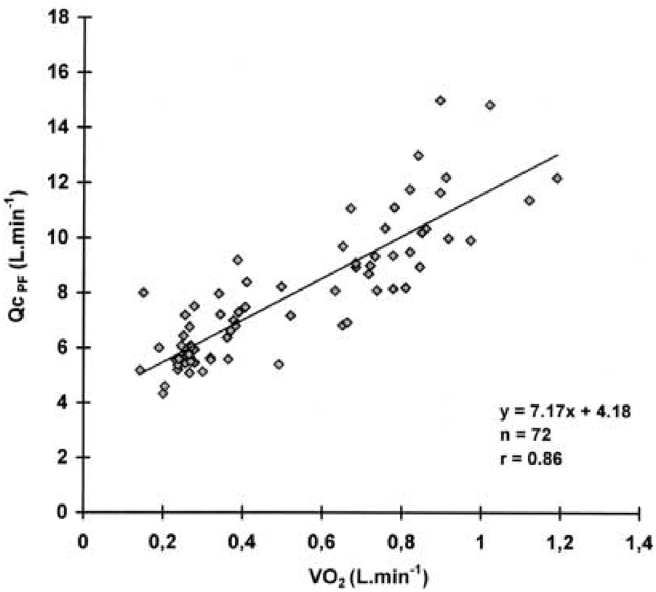


Fig. 2 Plot of cardiac output measured by impedance cardiography ($\dot{Q}_{cPF}$, Physio Flow device) versus O_2 consumption ($\dot{V}O_2$)

Measurement of the RV was performed by the helium dilution technique in 18 patients, by the body plethysmography method in 13 patients, and by both methods in 9 patients. The ratio of RV/TLC obtained by body plethysmography ranged from 32 to 71%, with a mean value of 49 (11)%. Helium dilution RV/TLC ranged from 22 to 66%, with a mean value of 39 (12)%. Regression of the difference between $\dot{Q}_{cFick}$ and $\dot{Q}_{cPF}$ against RV/TLC is shown in Fig. 5. The difference between $\dot{Q}_{cFick}$ and $\dot{Q}_{cPF}$ does not vary with increasing RV/TLC.

Discussion

All methods considered as a reference for cardiac output evaluation are invasive. Non-invasive procedures would, however, be more appropriate in situations such as sleep, exercise, or ambulatory. Impedance cardiography presents many advantages, since this method does not require experienced operators, is simple, involves only the application of electrodes onto the skin, and can provide a continuous estimation over a long period. However, its reliability and accuracy is still not established. Many variants of the initial method described by Kubicek et al. (1966), including changes in the model of the human thorax, electrode configuration, and equations, have been tested, none of them being accepted universally. In this study, we have tested a new imped-

Fig. 3A, B Plot of $\dot{Q}_{cPF}$ versus cardiac output measured using the direct Fick method ($\dot{Q}_{cFick}$) in the same individuals. The identity line is represented. **A** Cardiac output measured at rest. The regression equation is: $\dot{Q}_{cPF} = 0.69 \times \dot{Q}_{cFick} + 1.92$, ($r = 0.89$). **B** Cardiac output measured during mild exercise. The regression equation is: $\dot{Q}_{cPF} = 0.76 \times \dot{Q}_{cFick} + 2.14$ ($r = 0.85$)

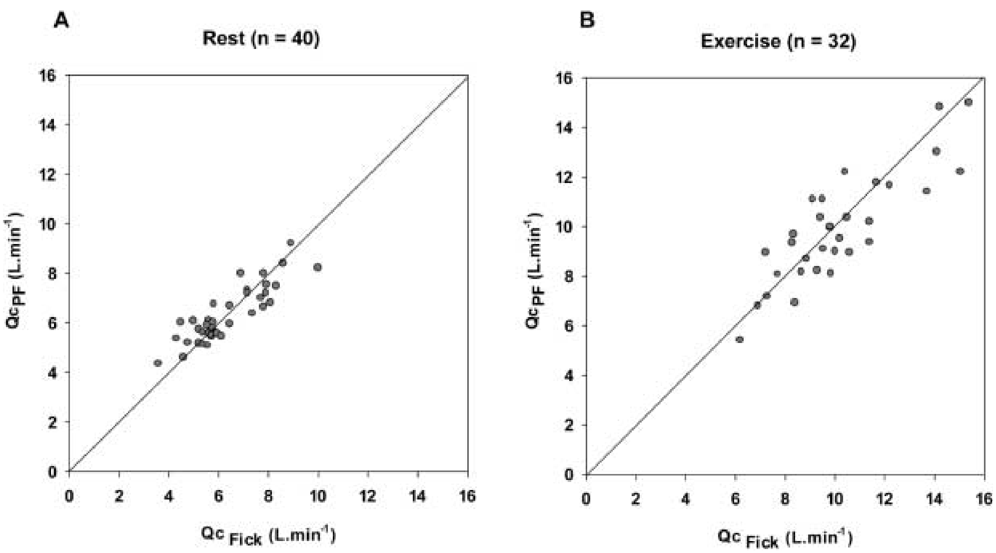
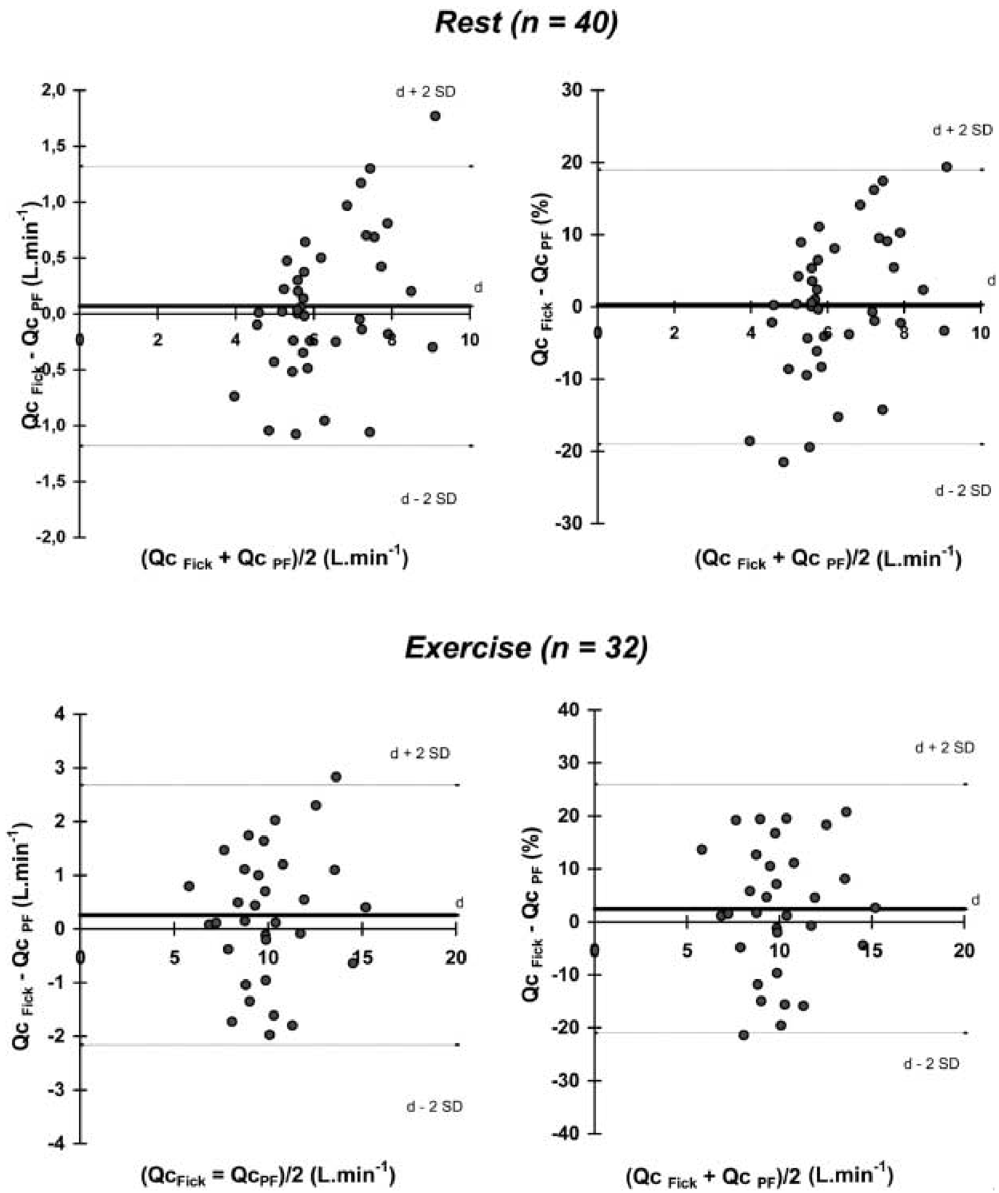


Fig. 4 Graphic representation of the difference between the two measurements ($\dot{Q}_{cFick} - \dot{Q}_{cPF}$) versus the mean of the two measurements [$(\dot{Q}_{cFick} + \dot{Q}_{cPF})/2$] for each individual, according to Bland and Altman (1986). *Horizontal lines* indicate the mean difference or bias (*d*) and limits of agreement (d − 2SD and d + 2SD)



ance cardiography device, the Physio Flow, which was developed as a result of an improvement in equipment and using a basically modified algorithm. We have measured cardiac output at rest and during mild exercise at a constant work rate (30 W in most patients) and have compared the results to Fick-derived measurements performed concomitantly. Measurements of $\dot{Q}_{cFick}$ were performed under strict conditions (e.g. achievement of steady-state, measurement of $\dot{V}O_2$ over at least a 1-min period, slow blood sampling midway in the measurement period of $\dot{V}O_2$, and accurate measurement of HbO_2). When these conditions are respected, direct Fick is considered to be the most reliable technique available, with a very good reproducibility (Fagard and Conway 1990; Visshher and Johnson 1953).

During submaximal exercise, cardiac output increases linearly with $\dot{V}O_2$. This relationship is stable and predictable for a wide variety of subjects, and is thus an interesting variable to look at when cardiac output evaluation during exercise is required. The slope of the $\dot{Q}_{cPF}$ versus $\dot{V}O_2$ regression equation obtained in this study (equal to 7.2) does not differ from those published in the literature, which range from 5.4 to 7.8 (Ekelund and Holmgren 1967; Yamaguchi et al. 1986). All paired values ($\dot{Q}_{cPF}$, $\dot{V}O_2$) but one fall in the confidence interval defined by authors who also studied supine subjects (Ekelund and Holmgren 1967; Yamaguchi et al. 1986).

According to the Bland and Altman analysis, the mean difference between the values obtained using the direct Fick and Physio Flow methods is only $0.07\ l \cdot min^{-1}$ at rest and $0.26\ l \cdot min^{-1}$ during exercise. The difference ($\dot{Q}_{cFick} - \dot{Q}_{cPF}$) does not vary in any systematic way over the range of measurements. The limits of agreement [mean ± 2SD] represent 19% and 26% of cardiac output at rest and during exercise, respectively. For most authors, a 20% variability between two cardiac

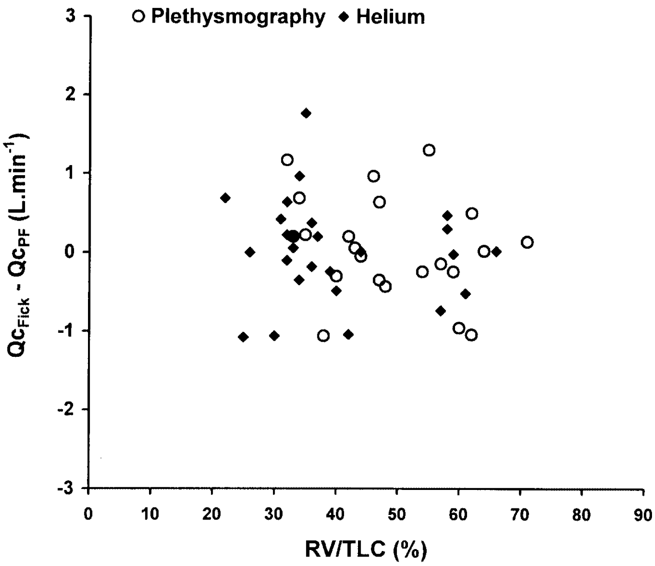


Fig. 5 Plot of ($\dot{Q}_{cFick} - \dot{Q}_{cPF}$) versus the residual volume/total lung capacity ratio (*RV*/*TLC*), which is an index of thoracic distension. Measurement of the residual volume was performed by the helium dilution technique in 18 patients (*closed diamonds*), by the body plethysmography method in 13 patients (*open circles*), and by both methods in 9 patients

output evaluation methods is clinically acceptable (LaMantia et al. 1990; Stetz et al. 1982). We found that only 2.5% of resting and 6.2% of exercising $\dot{Q}_{cPF}$ values differed from $\dot{Q}_{cFick}$ values by more than 20%.

Impedance cardiography has been compared to the direct Fick method in only a few studies. Most of those articles were published in the 1980s and do not refer to the Bland and Altman analysis, but provide only correlation coefficients (Braden et al. 1990; Hetherington et al. 1985; Miles et al. 1988; Salandin et al. 1988; Teo et al. 1985). These range from 0.63 to 0.84 and from 0.89 to 0.93, when the Kubicek equation and the Sramek-Berstein equation were used, respectively. More recently, Yakimets and Jensen (1995), who studied patients undergoing a coronary angiogram or after heart surgery, found that impedance cardiography underestimated Fick measurements by [mean (SD)] 1.05 (1.53) $\mathrm{l \cdot min^{-1}}$ at rest, and by 1.50 (2.20) $\mathrm{l \cdot min^{-1}}$ during exercise. This means that impedance cardiography may be 4.1 $\mathrm{l \cdot min^{-1}}$ below or 2.01 $\mathrm{l \cdot min^{-1}}$ above Fick at rest, and 5.9 $\mathrm{l \cdot min^{-1}}$ below or 2.9 $\mathrm{l \cdot min^{-1}}$ above Fick during exercise, differences that are clinically unacceptable for evaluating cardiac performance. Bellardinelli et al. (1996), using similar equipment and methods, obtained smaller levels of error with a mean difference of -0.03 $\mathrm{l \cdot min^{-1}}$ (limits of agreement: -1.20 and $+0.7$ $\mathrm{l \cdot min^{-1}}$) at rest and -0.31 $\mathrm{l \cdot min^{-1}}$ (limits of agreement: -1.55 and $+1.80$ $\mathrm{l \cdot min^{-1}}$) during exercise in patients with ischaemic cardiomyopathy. Comparison of impedance cardiography to dye dilution and thermodilution, the latter being used more frequently than the Fick method, has also resulted in conflicting results that have been widely discussed in the literature (Fuller 1992; Jensen et al. 1995). The lack of reliability of impedance cardiography observed in some of the previous studies may be due to the difficulty of accurately measuring Z_0, as emphasised earlier. The major advance of Physio Flow has been to overcome the evaluation of this variable, which then leads to more reproducible and reliable measurements.

Impedance cardiography is influenced by changes in thoracic blood and gas content. In addition, differences in chest wall configuration and the surface area of the thoracic cavity can modify thoracic electrical impedance. It has been demonstrated previously that breathing with increased resistive loads, which increases pleural pressure swings and chest wall movements, does not influence cardiac output measurement by impedance cardiography (Edmunds et al. 1982). Bogaard et al. (1997), comparing impedance cardiography to CO_2 rebreathing in patients with COPD, found limits of agreement of 2.56 $\mathrm{l \cdot min^{-1}}$, identical to these observed in healthy subjects. Rebreathing of CO_2 was also used as a reference method to validate impedance cardiography at rest and during exercise in children with cystic fibrosis (Pianosi 1997). The mean bias was -0.09 (0.94) $\mathrm{l \cdot min^{-1}}$, and in 83% of the cases, the difference between the two methods did not exceed 20%. In the present work, we have studied the impact of thoracic hyperinflation, as defined by an increased RV/TLC ratio, on $\dot{Q}_{cPF}$. The difference between the Fick value and the Physio Flow value did not increase with increasing RV/TLC (Fig. 5). Evaluation of $\dot{Q}_{cPF}$ is thus not altered by thoracic hyperinflation.

To summarise, we have shown that the Physio Flow, a new impedance cardiograph device, can provide cardiac output evaluation at rest and during submaximal exercise with clinically acceptable accuracy in patients with a normal cardiorespiratory function, as well as in patients with airway obstruction and thoracic hyperinflation. This new device deserves further investigation in other populations such as critically ill patients, or children, and in other situations such as maximal exercise, tilt testing or pharmacological tests.

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Appendix I

Physio Flow methodology

Physio Flow PF-03 (Manatec Biomedical, Macheren, France)

All formulae that are used currently in impedance cardiography make use of the impedance baseline values

(Z_0). For instance, the Kubicek formula (Kubicek et al. 1966) for stroke volume (SV) is the following:

$$SV = \rho \times l^2/Z_0^2 \times dZ/dt_{max} \times t \quad (1)$$

where ρ is blood resistivity ($\Omega \cdot cm^{-1}$), l is the distance between the two sensing electrodes (cm), dZ/dt_{max} is the maximal rate of decrease in impedance for a given heart beat ($\Omega \cdot s^{-1}$), and t is the ventricular ejection time (s), which is usually measured by phonocardiography. The first derivative of thoracic impedance variations (dZ/dt_{max}) was shown to be proportional to SV.

All of the formulae that include Z_0 can contribute to a significant error in SV evaluation. Z_0 depends upon experimental variables such as electrode position and quality, skin thickness and perspiration, and pathologies that modify thorax electrical properties such as oedema and emphysema. Movements, including respiration, and perspiration induced by exercise, cause a significant imprecision in the measurement of Z_0. The evaluation of SV can also be affected by an imprecise measurement of l, which depends upon the electrode positions, and by an inaccurate evaluation of t. To determine values of t, phonography can be used during resting periods, but it can give poor results during exercise.

The analysis of an extensive database of improved impedance cardiography signals with the Physio Flow prototype has led to the introduction of a different and original approach to impedance cardiography, based on the analysis of the signal waveform and its variations. The database was collected from patients with a variety of cardiocirculatory statuses, ranging from severe heart failure to hyperthyroidism, and at rest as well as during exercise. The haemodynamic status of these patients was assessed by echography or angiography. The most important result is that evaluation of Z_0, and as a corollary, the evaluation of thorax height, distance between sensing electrodes and blood resistivity, are unnecessary for the calculation of SV.

Cardiac output measurement by the Physio Flow device is based on the following formula:

$$\dot{Q}_c = f_c \times SVi \times BSA \quad (2)$$

where $\dot{Q}_c$ is cardiac output ($l \cdot min^{-1}$), f_c is the heart rate ($beats \cdot min^{-1}$; based on R–R interval measurement, determined on the ECG first derivative, $dECG/dt$, which provides a more stable signal than the ECG signal itself), BSA (m^2) is the body surface area, calculated according to the Haycock formula ($BSA = 0.024265 \times BM^{0.5378} \times H^{0.3964}$, where BM is body mass in kg and H is height in cm), and SVi is the SV index ($ml \cdot m^{-2}$; i.e. the SV divided by the BSA).

With the Physio Flow device, a first evaluation of SVi, called Svi_{cal}, is computed during a calibration procedure based on 24 consecutive heart beats recorded in the resting condition. This evaluation retains the largest impedance variation during systole ($Z_{max} - Z_{min}$), and the largest rate of variation of the impedance signal (dZ/dt_{max}, called the contractility index, CTI). The SVi calculation also depends on the ventricular ejection time (t). The ventricular ejection time is usually measured using echography or phonocardiography, but impedance cardiography can provide a very precise estimation of this variable (Mehlsen et al. 1990; Stern et al. 1985). The designers of the Physio Flow have chosen to use a related, but slightly different parameter, called the thoracic flow inversion time (TFIT, in ms). The TFIT is measured on the first mathematical derivative of the impedance signal. The TFIT is the time interval between the first zero value following the beginning of the cardiac cycle (beginning of the ECG's QRS) and the first nadir after the peak of the ejection velocity (dZ/dt_{max}). Afterwards, the TFIT is weighted [W(TFIT)] using a specific algorithm [alg(TFIT, f_c, PP)] which, in addition to the signal waveform, comprises two factors, the pulse pressure (PP, systolic arterial pressure – diastolic arterial pressure) and f_c. The impedance signal morphology is indeed affected by several phenomena that occur in the aorta. Aortic compliance contributes to the signal waveform; Chemla et al. (1998) have demonstrated the existence of a linear relationship between aortic compliance and the SV/PP ratio. In the [alg(TFIT, f_c, PP)], the PP, calculated from a sphygmomanometer measurement, is introduced at the end of the Physio Flow calibration phase. Similarly, certain oscillatory and resonance phenomena in relationship with f_c influence the signal morphology. Murgo et al. (1980) described a relationship between the pressure waveform and aortic impedance or f_c. f_c is the second factor entering into the algorithm.

As a result of the above concepts, SVi_{cal} is computed according to the following formula:

$$SVi_{cal} = k \times [(dZ/dt_{max})/(Z_{max} - Z_{min})] \times W(TFIT_{cal}) \quad (3)$$

where k is a constant, and the subscript "cal" indicates the parameters measured during the calibration phase. SVi_{cal} represents the baseline reference. During the data acquisition phase, the variations of the parameters described above are analysed and compared to those obtained during the calibration procedure. For instance, the designers demonstrated that the SV variations result mainly from a combination of contractility fluctuations (CTI or dZ/dt_{max}) and of TFIT variations, whereby:

$$SVi = SVi_{cal} \times \sqrt[3]{CTI/CTI_{cal} \times TFIT_{cal}/TFIT} \quad (4)$$

This concept is supported by a study by Moon et al. (1994), who showed that changes in SV, for example during exercise, are correlated with variations in dZ/dt, but inversely correlated with variations in left ventricular ejection time. In all equations used by other impedance cardiograph devices, these two parameters appear as a product.

To conclude, the Physio Flow methodology offers the following advantages compared to the previous impedance cardiograph devices:

1. There is no need to use multiple electrodes; four impedance electrodes and one ECG derivation

(two electrodes) are sufficient to obtain good quality signals.

2. Better reproducibility, even under non-optimal conditions (modification of electrode positions or type, or perspiration do not modify SV calculation).
3. Broader range of applications (better quality signals during cyclo-ergometer exercise).
4. There is no need to measure parameters related to thorax morphology (thorax height and diameter, the *l* factor). Nor is there any necessity to correct for blood resistivity using haematocrit values. These parameters are necessary only if direct measurements of blood volume changes are sought.
5. Increased reliability of the whole acquisition procedure by the introduction of a calibration phase.

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