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Noninvasive assessment of cardiac output from arterial pressure profiles during exercise

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Abstract The stroke volume of the left ventricle (SV) was assessed in nine young men (mean age 22.2, ranging from 20 to 25 years) during cycle ergometer upright exercise at exercise intensities from 60 to 150 W (about 20% to 80% of individual maximal aerobic power). The SV was calculated from noninvasive tracings of the arterial blood pressure, determined from photoplethysmograph records and compared to the SV determined simultaneously by pulsed Doppler echocardiography (PDE). Given the relationship $SV = A_s \cdot Z^{-1}$ in which A_s is the area underneath the systolic pressure profile (in millimetres of mercury and second), and Z (in millimetres of mercury and second per millilitre) is the apparent hydraulic impedance of the circulatory system, a prerequisite for the assessment of SV from the photoplethysmograph tracings is a knowledge of Z. The experimental value of Z (hereafter defined Z^*) was calculated by dividing A_s (from the finger photoplethysmograph) by SV as obtained by PDE. When the whole group of subjects was considered, Z^* was not greatly affected by the exercise intensity: it amounted to 0.089 (SD 0.028; $n = 36$). The Z was also estimated independently of any parameter other than heart rate (HR), mean (MAP) and pulse (PP) arterial blood pressure obtained from the photoplethysmograph. A computerized statistical method allowed us to interpolate the experimental values of Z^*, HR, PP and MAP by the equation $Z_m = a \cdot (b + c \cdot HR + d \cdot PP + e \cdot MAP)^{-1}$, thus obtaining the coefficients a to e. The mean percentage error between Z_m (calculated from the coefficients obtained and Z^* was 21.8 (SD 14.3)%. However, it was observed that, in a given subject, Z^* was significantly affected by the exercise intensity. Therefore, to improve the estimate of Z a second algorithm was developed to update the experimental value of Z determined initially at rest (Z_{in}). This updated value (Z_{cor}) of Z was calculated as $Z_{cor} = Z_{in} \cdot [(f/(i + g \cdot (HR/HR_{in}) + h \cdot (PP/PP_{in}) + 1 \cdot (MAP/MAP_{in})]$, where HR_{in}, PP_{in}, MAP_{in}, HR, PP, MAP are the above parameters at rest and during exercise, respectively. Also in this case, the coefficients f to 1 were determined by a computerized statistical method using Z^* as the experimental reference. The values of Z_{cor} so obtained allowed us to calculate SV from arterial pulse contour analysis as $SV_F = A_s \cdot Z_{cor}^{-1}$. The mean percentage error between the SV_F obtained and the values simultaneously determined by PDE, was 10.0 (SD 8.7)%. It is concluded that the SV of the left ventricle, and hence cardiac output, can be determined during exercise from photoplethysmograph tracings with reasonable accuracy, provided that an initial estimate of SV at rest is made by means an independent high quality reference method.

Key words Stroke volume · Pulse contour · Pulsed Doppler echocardiography · Exercise · Finger photoplethysmograph

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Introduction

The measurement of cardiac output (CO) during exercise is essential in evaluating the capability of the human body to cope with the increased oxygen needs of the working muscles. However, several methods commonly used for clinical purposes, e.g. the direct Fick or the thermodilution methods, are invasive and have employed the use of centrally positioned catheters (Swan et al. 1970; Conway and Lund-Johansen 1990).

As such they are far from ideal for use with exercising subjects. A further limitation to their use is the need to assess CO over several consecutive heart beats. Some of these drawbacks can be overcome by using indirect (rebreathing) Fick methods. The rebreathing methods, however, have suffered from another limitation, i.e. that of affecting to a certain extent the CO by the rebreathing manoeuvre itself (Reybrouck and Fagard 1990; Sackner 1987). All these limitations would seem to be overcome by pulsed Doppler echocardiography (PDE), which permits beat-by-beat determination of the stroke volume (SV) of the left ventricle. Widespread use of PDE has nevertheless been limited by the cost of the instrumentation and by the need for highly skilled operators (Loeppky et al. 1981; Shaw et al. 1985; Coats 1990).

In recent years, the so-called pulse contour methods (PCM) have permitted yet another step forward in the study of CO during exercise. The PCM have stemmed from the original concepts of Frank (1899) and have actually been implemented by Nichols (1973) and Wesseling et al. (1983). The PCM are based on the relationship between SV of the left ventricle and the area subtended by the systolic part of the peripheral arterial pressure profile. Therefore, for CO to be obtained, the relationship between these two variables, a quantity dimensionally equal to the mean impedance of the arterial tree, defined as Z, must be known or calculated. However, Z has been shown to change with the age and with the cardiovascular condition [heart rate (HR) and blood pressure] of the subject (Bader 1967; McDonald 1974; Wesseling et al. 1974). Therefore, even if Z is initially assessed by other methods, in subjects whose haemodynamic conditions change, its value must be continuously updated. To do this, Wesseling et at. (1983) have proposed an algorithm that was verified in subjects in whom the arterial pressure profile was measured invasively by intra-arterial catheters (Sprangers 1990; Jansen et al. 1990). Subsequently, several authors (Gratz et al. 1992; Stok et al. 1993; Antonutto et al. 1994) have applied Wesseling (or similar) algorithms to calculate CO by PCM, determining the arterial pressure profile by means of the photoplethysmographic volume clamp method of Peñaz (1973). This approach, rendered possible by the development and validation of the Finapres apparatus (Kurki et al. 1987; Hildebrandt et al. 1991) seems very promising, allowing the assessment of CO to be made noninvasively beat-by-beat. Indeed, in the above cited studies, the correlation coefficient between CO estimated by PCM and by a reference standard method gave a result between 0.75 and 0.96.

The aim of this study was to verify the validity of CO assessment by Finapres and to determine experimentally an algorithm for the correction of Z in subjects whose haemodynamic conditions change. To do this we compared the ventricular SV measured by PDE with those measured by Finapres in subjects exercising on a cycle ergometer.

Methods

Subjects

The experiments were performed on nine healthy young men, aged 20–25 years [mean 22.2 (SD 1.9) years]. All subjects were familiar with the experimental procedure and gave informed consent to study. Their physical characteristics are shown in Table 1. The individual maximal aerobic exercise intensity estimated from the HR/exercise intensity relationship extrapolated to $HR_{max} = 220 -$ subject's age (Åstrand and Rodahl 1986; p. 189) is also indicated in Table 1.

Experimental protocol

The subjects reported in the laboratory in the afternoon, after a light meal, and sat at rest on the cycle ergometer for about 10 min. During this period, the diameter of the ascending aorta was determined by M-mode echocardiography and the blood velocity in the ascending aorta was measured twice by PDE (see below). Two 20-s

Table 1 Physical characteristics of subjects. Body surface area was calculated from the equation of Du Bois and Du Bois (1916)

Subject	Age (years)	Height (cm)	Body mass (kg)	Body surface area (m^2)	Aortic diameter (cm)	Maximal aerobic exercise intensity (W)
UB	21	180	75	1.94	2.4	268
ER	20	183	74	1.95	2.9	276
NP	21	180	90	2.10	2.6	259
MB	25	171	66	1.77	2.7	184
IT	22	180	72	1.91	2.6	350
FC	21	178	65	1.81	2.2	342
GI	25	173	68	1.81	2.8	178
FG	21	182	68	1.88	3.0	193
RM	24	181	75	1.95	2.9	269
Mean	22.2	178.6	72.5	1.90	2.7	257.7
SD	1.9	3.8	7.1	0.10	0.3	63.4

Finapres recordings were also taken simultaneously with the blood velocity determination. Then the subjects pedalled for about 6 min, at a constant frequency (1 Hz) indicated by a metronome, at each of three different exercise intensities (range 60–150 W, i.e. from 21.7% to 77.7% of maximal aerobic intensity) on an electromagnetically braked cycle ergometer (Ergomed 840 L, Siemens). After 4 min of exercise, the blood velocity in the ascending aorta was measured by PDE twice at 1-min intervals. For each PDE measurement, 20 s of arterial pressure profile was also recorded by Finapres.

Measurements

Aortic diameter (DA) was measured during systole in the ascending aorta by M-mode echocardiography with the subject at rest. Blood velocity in the ascending aorta was measured by PDE (2.5 MHz, Sonos 1000, Hewlett Packard). The probe was positioned in the supersternal notch and directed towards the ascending aorta during all the experimental sessions. The Doppler beam was considered to be aligned with the blood flow when the Doppler signals were maximal. At the end of each exercise intensity period, about ten cardiac cycles were recorded on videotape, during a very short apnoea, for off-line analysis. The echocardiograph left ventricular SV (SV_E in cm^3) was then estimated on the cardiac cycle yielding the best blood velocity curve by means of the following equation:

$$SV_E = S_a \cdot v_{int} \quad (1)$$

where $S_a = \pi \cdot (DA/2)^2$ is the ascending aorta cross-sectional area (cm^2) and v_{int} (cm) (Coats 1990) is the time integral of the systolic phase of blood velocity in ascending aorta. The echocardiograph cardiac output (CO_E) was then calculated from SV_E multiplied by average HR over the five cardiac cycles preceding and the five following the cardiac cycle analysed by PDE as obtained by the Finapres tracings. In every subject the arterial blood pressure wave, measured by the Finapres device simultaneously with PDE analysis, was recorded on tape (Teac-MR 30) and the cardiac cycles analysed by PDE were identified by a voice mark. The Finapres traces were then digitized by an A-D converter (NB-MIO 16) at a sample rate of 200 Hz and analysed by Lab View software (Natl. Instr. USA). Five Finapres cardiac cycles were analysed for each PDE measure and the mean values of the five cycles of systolic, diastolic and mean pressure were calculated, together with the area of the systolic portion of the arterial blood pressure curve (A_s) (Wesseling et al. 1974; Antonutto et al. 1994), i.e. that corresponding to the ejection phase of the cardiac cycle. The number of cycles on which A_s was calculated was standardized to 5, due to the fact that the dicrotic notch could not be clearly identified on all cycles, especially at the highest exercise intensities.

Pulse contour analysis

As proposed by Wesseling et al. (1983) the SV of the left ventricle was calculated from the equation:

$$SV = A_s \cdot Z^{-1} \quad (2)$$

where SV is in millilitres, A_s is measured in millimetres of mercury and second and Z in (millimetres of mercury and second per millilitre) is a calibration factor dimensionally equal to the aortic impedance.

An obvious prerequisite for the assessment of SV from Eq. 2 is a knowledge of Z. We therefore developed two algorithms to estimate this. Of these, the first (A) was based on haemodynamic data [HR, mean arterial pressure (MAP) and pulse arterial pressure (PP)] obtained from the Finapres only, without any independent assessment of Z. The other (B) made it possible to update an initial value of Z from the exercise values of HR, MAP and PP obtained by Finapres, thus yielding the values of Z presumed to apply at exercise. In turn, the initial Z values were determined in all subjects from measurements of SV_E (by PDE, see Eq. 1) and of A_s (by Finapres) at rest before exercise.

Two sets of values of Z were therefore obtained and used to calculate SV from the Finapres pressure profile using Eq. 2. The resulting two sets of SV values (defined SV_F) were compared with the set measured by PDE (SV_E, Eq. 1) during the same experimental session.

Results and discussion

The mean values and standard deviations of PDE and Finapres measurements for all the subjects investigated and experimental conditions are reported in Table 2. The calculated values of Z, reported in Table 2 as Z^*, were obtained by dividing SV_E by A_s, as obtained by Finapres on the five preceding beats. The HR and echocardiograph left ventricular stroke volume index (SVI_E) values are also reported in Fig. 1 as a function of the exercise intensities expressed as a percentage of the maximal aerobic intensity (see Methods and Tables 1, 2). This figure shows that, as expected: (1) SVI_E attained a plateau for intensities equal to or greater than about 35% maximal intensity (WL_{max}) and (2) HR was an approximately linear function of the intensity (Åstrand and Rodahl, 1986, pp. 188–191).

Table 2 shows that Z^* was not greatly affected by the exercise intensity, if the whole group of subjects is considered. However, a one-way analysis of variance showed that, for a given subject, Z^* was significantly different at different intensities (Table 3). In an attempt

Table 2 Values of main parameters investigated and during exercise at different exercise intensities (WL). The SVI_E and CI_E are the stroke volume index and cardiac index as obtaine by pulsed Doppler echocardiography. For further details see text. MAP Mean arterial pressure PP pulse pressure, HR heat rate, WL_{max} percentage maximal exercise intensity Z^* experimental value of Z (apparent hydraulic impedence of circulatory system

WL (w)	%WL_{max} %		Subjects (n)	HR (beats·min^{-1})		SVI_E (ml·m^{-2})		CI_E (l·min^{-1}·m^{-2})		MAP (mmHg)		PP (mmHg)		Z^* (mmHg·s·ml^{-1})	
	Mean	SD		Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Rest	Rest		9	79	12	36.4	8.8	2.9	0.8	97	15	42	9	0.083	0.017
60	25.8	5.2	7	103	9	43.0	14.1	4.4	1.5	117	19	62	14	0.101	0.025
90	33.9	6.9	7	115	17	52.1	15.2	5.9	1.7	120	24	67	12	0.093	0.028
120	46.6	9.2	9	133	18	50.7	10.4	6.7	1.4	114	21	64	14	0.084	0.022
150	52.0	10.6	4	143	23	48.3	9.4	6.8	1.3	115	15	67	11	0.086	0.018

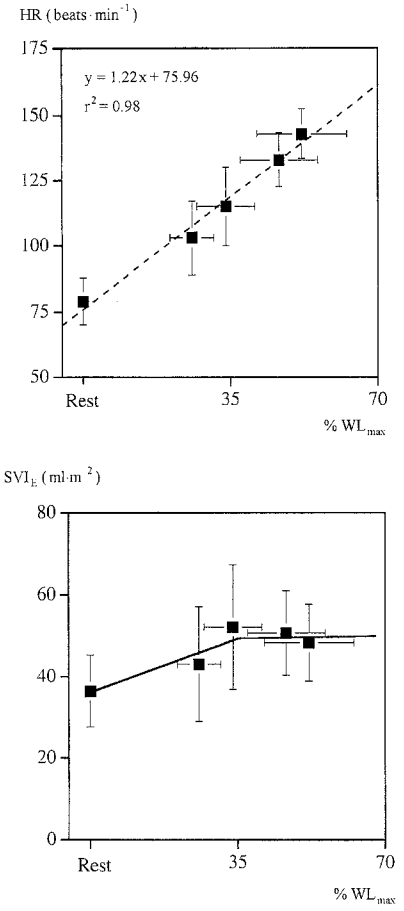

Fig. 1 Heart rate (*HR*, *upper panel*) and stroke volume index measured by pulsed Doppler echocardiography (SVI_E, *lower panel*) as a function of exercise intensity in percentage of the maximal aerobic intensity (% WL_{max}). The SVI_E values are interpolated by *the continuous line*. *Bars* indicate ± 1 SD. *Dashed line*, described by $y = 1.22x + 75.9$, $r^2 = 0.981$, $n = 36$, represents the regression line between *HR* and % WL_{max} values

to estimate Z and hence CO from Finapres data only, without the need for a previous independent assessment of SV (as in Table 2), it was assumed that, as previously shown for subjects at rest (Antonutto et al. 1994), also during mild exercise, the relationship between Z (dependent variable) and HR, PP and MAP (independent variables) could be described by:

$$Z = \mathrm{a}\cdot(\mathrm{b} + \mathrm{c}\cdot HR + \mathrm{d}\cdot PP + \mathrm{e}\cdot MAP)^{-1} \quad (3)$$

The five coefficients (a–e) were determined by a statistical package (Systat 5.2, Systat Inc.) inserting into Eq. 3 the values of Z^* determined experimentally in all subjects (see Table 2), together with the corresponding values of HR, MAP and PP. The statistical analysis showed that the mean percentage absolute error (mean % error_{abs}) between the values of Z estimated from the Eq. 3 (Z_m) and those determined experimentally from $A_s/\mathrm{SV}_E(Z^*)$:

$$\mathrm{Mean\%\ error}_{abs} = (Z^* - Z_m)/Z^* \times 100 \quad (4)$$

Table 3 Experimental values of Z^* ($A_s \cdot SV_E^{-1}$ millimeters of mercury and second per millilitre, see Table 2) for each subject at different intensities of exercise where A_s is the area underneath the systolic pressure profile and SV_E is the stroke volume obtained by echocardiography

Subjects	Rest	60 W	90 W	120 W	150 W
UB	0.089	0.119	0.097	0.085	
ER	0.079	0.068	0.065	0.066	
NP	0.085	0.141	0.146	0.063	
MB	0.079	0.098	0.082	0.072	
IT	0.063		0.066	0.095	0.068
FC	0.085		0.111	0.106	0.096
GI	0.087	0.193	0.098	0.114	
FG	0.052	0.088		0.052	0.057
RM	0.110	0.080		0.078	0.106
Mean	0.083	0.101	0.093	0.084	0.086
SD	0.017	0.025	0.028	0.022	0.018

was equal to 21.8 (SD 14.3)%. The five coefficients a to e, equal to 8.92, 167.87, 0.31, -0.53 and -0.62, respectively, can therefore be used to estimate Z in male subjects comparable to our group, without the need for any previous measurements. The values obtained can then be used to calculate SV, and hence CO, from Finapres measurements only. Obviously, however, the CO data obtained will suffer by the same mean percentage error reported above for the difference between Z_m and Z^*.

As suggested by the work of Wesseling et al. (1983), we therefore set out to determine an algorithm to estimate a value of Z applying to any subject during exercise based on an initial experimental assessment of Z^* (Z^*_{in}) at rest. The exercise value (Z_{cor}), is then obtained from Z^*_{in} from HR, MAP and PP measurements during exercise. Using an iterative statistical package (Systat 5.2, Systat Inc.), we found that the following equation minimised the differences between Z^* and Z_{cor}:

$$\begin{aligned} Z_{cor} &= Z^*_{in}\cdot F_{cor} \\ &= Z^*_{in}\cdot\{\mathrm{f}/[\mathrm{i} + \mathrm{g}\cdot(HR/HR_{in}) + \mathrm{h}\cdot(PP/PP_{in}) \\ &\quad + 1\cdot(MAP/MAP_{in})]\} \end{aligned} \quad (5)$$

where F_{cor} is the correction factor, HR in beats per minute, PP in millimetres of mercury and MAP in millimetres of mercury are the cardiovascular parameters measured by Finapres during exercise at a steady state and HR_{in}, PP_{in}, MAP_{in} are the corresponding parameters measured during the pre-exercise assessment of Z^*_{in}. The coefficients of Eq. 5 obtained were f = 50.16, g = 35.3, h = -19.51, i = 35.5 and 1 = -12.07. The mean values of F_{cor} decreased from 1.39 at the lowest exercise intensity (25.8% to WL_{max}) to 1.04 at the highest intensity (52% of WL_{max}). Inserting Z_{cor} into Eq. 2, the corresponding values of the SV of the left ventricle (SV_F) and of cardiac output from the

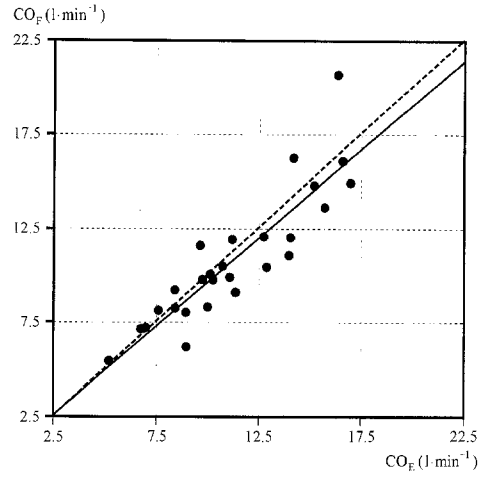

Fig. 2 Cardiac output as calculated from Eq. 8 (CO_F) is plotted as a function of the values obtained simultaneously by pulsed Doppler echocardiography (CO_E). Regression equation (*continuous line*) is described by: $CO_F = 0.24 + 0.94 \cdot CO_E$ ($r = 0.88$). The *identity line* is also shown (*dashed line*)

Finapres records (CO_F) were calculated from arterial pressure profile at the different exercise intensities:

$$SV_F = A_s \cdot Z_{cor}^{-1} \quad (7)$$

$$CO_F = SV_F \cdot HR \quad (8)$$

The values of CO_F are plotted in Fig. 2 as a function of the corresponding values measured by PDE (CO_E), for all subjects and all exercise intensities. The mean percentage error between the two measures, calculated as:

$$\text{Mean \% error}_{abs} = (CO_E - CO_F)/CO_E \times 100 \quad (9)$$

amounted to 10.0 (SD 8.7)%. This seemed satisfactory and supported the use of coefficients f to 1 for calculating CO under one set of conditions from the haemodynamic parameters indicated in Eq. 5. These can be obtained from the Finapres records only, once an initial assessment of Z_{in}^* has been made by any other method. We would also like to point out that, for the reasons explained in the Methods, the SV_E data were obtained on one cardiac cycle only, whereas HR and SV_F were measured on ten and five cycles, respectively. We feel that the mean % error_{abs} reported above, would be reduced further if this mismatching of the numbers of cycles could be avoided.

General Discussion

The aim of this study was to evaluate the possibility of estimating SV of the left ventricle from Finapres tracings in exercising subjects. To this aim, SV, assessed by Finapres, was compared to that obtained simultaneously by PDE. The methods of assessing SV and hence CO from Finapres tracings are extremely useful in practice, since they are noninvasive and give beat-by-beat information of SV of the left ventricle (Stok et al. 1993; Antonutto et al. 1994), which is different to other commonly used methods (e.g. thermodilution and rebreathing methods), which give only intermittent information on SV averaged over several heart beats (Sackner 1987; Conway 1990). In this study, we selected PDE as the reference method because it provides a reliable noninvasive beat-by-beat assessment of SV and CO (Loeppky et al. 1981; Christie et al. 1987; Coats 1990).

As pointed out previously, to calculate SV from arterial pressure tracings it is necessary to measure:

1. The area lying under the systolic part (and above the diastolic level) of the pressure profile of the heart beat considered (A_s) and
2. The value of the calibration factor Z (see Eq. 2).

We obtained the former from computer analysis of the Finapres arterial pressure profile. Indeed, it has been shown that A_s calculated at the finger level from Finapres tracings is not significantly different from the corresponding area obtained by a catheter positioned in the brachial artery (Imholz 1991).

As for the assessment of Z, we proceeded in two different ways. Firstly, Z was determined from the haemodynamic quantities obtained by Finapres only (HR, MAP and PP) on the basis of the empirical relationship described by Eq. 3 and the corresponding coefficients, as obtained by a statistical procedure (a-e, see above). The mean percentage error between the SV calculated from the Z obtained ($SV_F = A_s \cdot Z_m^{-1}$) and that directly determined by PDE (SV_E) was 21.8 (SD 14.3)%. This mean percentage error was substantially smaller than that obtained when SV_F was calculated from similar algorithms proposed by Wesseling et al. (1983), which amounted to 30 (SD 29)%.

To reduce further the mean percentage error between SV_E and SV_F, we adopted a second procedure, wherein a correction factor, again based on the same haemodynamic parameters (F_{cor}; Eq. 5), was applied to the value of Z experimentally determined at rest in the same subject. In this case, the mean percentage error between SV_E (determined by PDE), and SV_F (estimated using our algorithm) was substantially lower [10.0 (SD 8.7) %, for Eq. 5] than that calculated from the procedures mentioned above.

Equations 3 and 5 are similar to those proposed by Wesseling et al. (1983), but differ because:

1. They take into account also the pulse pressure as has also been suggested by Gratz (1992) and
2. They disregard the age of the subjects; an irrelevant variable in our case.

From the practical point of view, the use of Eq. 3 is to be preferred if Z cannot be calculated by any alternative method. In contrast, if a preliminary determination of Z can be performed, Eq. 5 has to be used. Obviously enough, the second procedure yields more accurate results.

Equations 3 and 5 are not based on any detailed theoretical analysis of the factors which are supposed to determine Z, rather they describe empirical relationships between the independent variables on which Z is assumed to depend and Z itself. The few paragraphs that follow will be devoted to discussing whether and to what extent a theoretical analysis is indeed possible and, if so, whether it fits the experimental data with reasonable accuracy. The Z has been shown to be conceptually and dimensionally equal to the hydraulic impedance of the circulatory system (Antonutto et al. 1994; Gratz et al. 1992). When dealing with electric circuits and alternating currents, the module of the impedance is described by:

$$Z^2 = R^2 + (\omega L - 1/\omega C)^2 \tag{10}$$

where R is the ohmic resistance of the circuit, ω ($= 2 \cdot \pi \cdot f$) is a function of the frequency (f) of the alternating current, L is the inductance and C the capacitance of the electric circuit. When dealing with hydraulic circuits with intermittent flow, as is the case of the circulatory system, as a first approximation these electrical quantities can be identified with the following parameters.

1. The resistance R with the haemodynamic resistance, as given by the ratio of MAP to CO, in turn equal to the product of HR and SV;
2. The frequency of the alternating current (f) with HR;
3. The (L) with SV of the left ventricle;
4. The C with the compliance of the arterial system, which in turn can be assumed to be equal to the ratio of the SV to PP. Replacing these quantities into Eq. 10 and by rearrangement one obtains:

$$Z = \sqrt{\frac{1}{HR^2 \cdot SV^2} \cdot \left(MAP^2 + \frac{PP^2}{4 \cdot \pi^2} \right) + 4 \cdot \pi^2 \cdot HR^2 \cdot SV^2 - 2 \cdot PP} \tag{11}$$

It goes without saying that, several assumptions and approximations are implicit in the transformation of the *electrical* Eq. 10 into its *physiological* counterpart (Eq. 11). Suffice to point out here that:

1. The arterial pressure changes during the cardiac cycle are not sinusoidal, hence replacing ω in Eq. 10 with $2\pi \cdot$HR is somewhat artificial and
2. The quotient SV to PP is a rough approximation of the compliance of the ascending aorta. In addition,
3. As pointed out in previous papers, the arterial pressure profile determined at the peripheral level by Finapres has been described as a distorted representation of the events occurring in the aortic bulbus (O'Rourke et al. 1955; Wesseling et al. 1985; Hildebrandt et al. 1991).

Therefore, the compliance of the arterial system and the quantities that depend on it, such as PP can only be considered as integrated averages and, as a consequence, their direct use in Eq. 11 may be questionable. Nevertheless Eq. 11 shows that Z cannot be expected to change much during exercise. Indeed, the only parameter appearing in Eq. 11 to change substantially during exercise is CO ($CO = HR \cdot SV$). Inspection of Eq. 11 shows that an increase of CO leads, on the one hand to a reduction of the term $(MAP^2 + (PP^2/4\pi^2)) \cdot CO^{-2}$, and on the other to an increase of the quantity $4\pi^2 \cdot CO^2$. Since these changes cannot be very different from each other, the net effect is that an increase of CO has only very limited effects on Z, as found experimentally (see Tables 2, 3).

To assess to what extent Eq. 11 mimics physiological conditions, we interpolated, by means of the iterative statistical procedure Systat (Systat Inc.), the experimental variables Z^*, MAP, HR, PP and SV (at rest and during exercise) with an equation in the form of Eq. 11 to give a value for $Z(Z_{\text{theor}})$. The resulting regression was:

$$Z_{\text{theor}} = \sqrt{6.82 \cdot \frac{MAP^2}{HR^2 \cdot SV^2} + 1 \cdot 10^{-5} \cdot HR^2 \cdot SV^2 + 88.6 \cdot \frac{PP^2}{HR^2 \cdot SV^2 + 13 \cdot 10^{-5} \cdot PP - 3 \cdot 10^{-3}}} \tag{12}$$

($r = 0.90, n = 64$)

The goodness of fit of Eq. 12 was very satisfactory, in view of the great separations between theory and measurement. However, the mean percentage error between Z_{theor}, as estimated from Eq. 12, and the actual Z^* amounted to 30 (SD 24)%, too large a value for Eq. 12 to be of any practical use. It therefore remains somewhat unfortunate, that, for all practical purposes the empirically derived Eq. 5, which allowed us to estimate Z, and hence CO, with a mean percentage error of 10.0%, is to be preferred to Eq. 11 which we nevertheless consider theoretically sound.

Conclusions

The preceding results and discussion show that Finapres tracings, together with continuous assessments of arterial blood pressure and HR allowed us to calculate CO with reasonable accuracy. The assessment of CO in this way is particularly useful since:

1. It is relatively low-cost and non-invasive;
2. It does not interfere with the exercise performed by the subject, and
3. It permits beat-by-beat estimates of SV of the left ventricle, and thus would appear promising for the assessment of CO during metabolism transients.

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