Cardiac output by Portapres®

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A B S T R A C T

Portapres® derives continuous estimates of cardiac output from the peripheral pulse and has the potential to be an extremely valuable physiological and clinical tool. We assessed Portapres® estimates of cardiac output in healthy subjects at rest, during maximal treadmill exercise ($n = 8$) and during decreases caused by orthostatic stress ($n = 8$). Comparison with a rebreathing method indicated that Portapres® tended to overestimate cardiac output. The random errors of the estimates (precision), expressed as ± 2 S.D. of the differences between paired estimates during steady states, ranged between 1.2 and 2.6 litres/min. We conclude that these errors indicate that the method is probably only useful for assessing changes in individual subjects where large changes are anticipated, as during exercise. When smaller changes occur, as during orthostasis, the errors preclude the use of individual subject data and only permit group average data to be examined.

INTRODUCTION

An accurate, simple and non-invasive method for the continuous estimation of cardiac output in humans would be a valuable tool both for clinical investigation and research. Several methods, based mainly on the Fick principle, have been developed. These have involved equilibration of CO_2 by rebreathing [1–3] or slow prolonged expirations [4–6], or have involved the uptake of inert gases such as acetylene [7,8]. All of those methods seem to provide reasonable estimates provided that extreme care is taken; however, all are complex and require considerable subject cooperation. Furthermore, they provide only intermittent estimates and require prolonged steady-state periods.

In 1993, Wesseling and co-workers [9] described a method for the continuous estimation of cardiac stroke volume/cardiac output from the pulse contour of a peripheral artery. Pulse contour depends mainly on the stroke volume of the left ventricle and on the vascular resistance and compliance of the major arteries. Wesseling et al. [9] described a mathematical model that predicts stroke volume from the pulse contour based on assumptions of arterial distensibility, which varies with age [10,11] as well as with the subject's sex, height and weight. This is the Modelflow® and is incorporated into the software installed with the Portapres® finger photoplethysmographic device.

There have been a small number of comparisons of Modelflow® estimates with values obtained by thermodilution in ill patients [12–14] and these have provided variable results. In a recent study involving healthy old people [15], it was reported that there was no significant correlation between estimates obtained by Modelflow® and thermodilution. However, such inaccuracies are to be expected for two main reasons. Firstly, thermodilution itself carries errors of approx. ± 15 % [16]. These errors may be reduced by averaging several estimates or timing injections to particular phases of the respiratory cycle [17] but, nevertheless, comparisons of absolute values inevitably involve errors from both methods. Secondly, values of cardiac output in similar subjects, made only at rest, are unlikely to be very different. Therefore a combination of the errors of both methods and the lack of spread of the data inevitably leads to a poor correlation.

All of these previous studies have been concerned with the estimation of cardiac output in various

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Abbreviation: LBNP, lower body negative pressure.
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Table 1 Subject data

Exercise study				Orthostatic stress study			
Sex	Age (years)	Height (cm)	Weight (kg)	Sex	Age (years)	Height (cm)	Weight (kg)
F	21	172	70.0	F	21	165	66.0
F	20	165	65.2	F	26	168	67.5
F	20	168	62.0	M	63	181	78.2
M	21	178	69.2	M	38	174	93.5
F	25	167	66.2	M	46	180	68.6
M	37	184	71.3	M	32	180	69.9
F	23	166	54.4	M	35	175	75.0
M	35	175	75.0	M	31	180	65.0
Mean ± S.E.M.	25.5 ± 2.4	171.9 ± 2.4	66.7 ± 2.3	Mean ± S.E.M.	36.5 ± 4.6	175.5 ± 2.2	73.0 ± 3.3

groups of subjects only under resting conditions. There is little information on the suitability of the pulse contour method for assessing changes in cardiac output during various physiological manoeuvres. We, therefore, undertook the present study, using healthy subjects, to investigate the suitability of Portapres® for determining changes in cardiac output during increases effected by exercise and during decreases due to orthostatic stress. Systematic errors were assessed by comparison with a non-invasive respiratory method, which has been shown to correlate well with thermodilution [18]. Random errors (precision) were assessed as differences between paired data during steady-state conditions [19].

METHODS

We determined cardiac output by Modelflow® using Portapres® and by a rebreathing method in eight healthy subjects during steady states seated at rest and during near-maximal treadmill exercise, and in eight subjects whilst supine and following head-up tilting with application of lower body suction. Details of the ages, heights and weights of the subjects for each part of the study are shown in Table 1.

Use of Portapres® to estimate cardiac output

The appropriate sized cuff was fitted to the middle finger of the left hand. The hand was supported at heart level using a sling and the sensor for reference pressure was fixed at the level of the fourth intercostal space in the mid-axillary line. The instrument's height calibration system was set and the subject data entered, i.e. age, sex, height and weight. It was then allowed to 'warm up' for 10 min. All estimates of cardiac output were calculated from the estimated values of stroke volume during 30 cardiac beats.

Rebreathing

The principle of rebreathing methods for determination of cardiac output is to cause the alveolar CO_2 level to increase until gas exchange ceases. Alveolar CO_2 tension is then assumed to be equal to that in mixed venous blood. The arterial value is estimated from the end-tidal value and cardiac output is estimated, using the Fick principle, from CO_2 output and arterial and mixed venous contents, determined using appropriate CO_2 dissociation curves. We used commercially available equipment (Medgraphics Cardio^2 Cardiopulmonary Exercise Testing System) and a rebreathing bag filled initially with 4 % CO_2, 35 % oxygen and 61 % nitrogen. Further details of this method have been reported previously [18]. Also, as before, we used an exponential function in the calculation of mixed venous P_{CO_2} (partial pressure of CO_2) during exercise [2,3] and the equilibrium value at rest [1].

Comparisons during peak exercise

Eight asymptomatic volunteers (three male), with a mean age of 25 years (range, 20–37 years), were used as subjects for this study. After obtaining resting values, subjects exercised on a treadmill (Quinton Q55) using the Bruce protocol [20] to determine peak exercise. Subsequently, after a period of 30 min rest, exercise was resumed at the previously determined peak level and, after 1 min, we determined cardiac output by Portapres®, then by rebreathing, followed by a second Portapres®, a second rebreathing, and finally a third Portapres® estimate. The average of the two estimates of cardiac output made by rebreathing was compared with the average of the three Portapres® values.

Comparisons during orthostatic stress

Comparisons with rebreathing during orthostatic stress tests were carried out on eight subjects (six male), with a mean age of 36 years (range, 21–63 years). Subjects lay supine on a combined head-up tilt/lower body

suction system [21]. After resting supine for 10 min, three estimates of cardiac output were made using Portapres® and two by rebreathing in the same order as in the exercise study. Subjects were then tilted head-up by 60° for 5 min and further estimates were made as described. Finally, lower body suction was applied at −20 mmHg for 5 min and further sets of estimates were made.

Ethics

This study was carried out in accordance with the Declaration of Helsinki (2000) of the World Medical Association, and has been approved by the Research Ethics Committee of the United Leeds Teaching Hospitals. All subjects provided informed written consent.

Statistics

Data were derived from averages of three estimates by Portapres® and two by rebreathing. Data were distributed normally and are presented as means ± S.D. or ± S.E.M. as indicated. Where the S.D.s of the cardiac output values were significantly different (F test: $P < 0.05$), statistical significance was assessed using alternate (Welch) t tests. All other comparisons of means were assessed by Student's paired t tests. Linear regression was performed on group data with more than two sets of data.

RESULTS

Comparison of Portapres® with rebreathing estimates at rest and during peak exercise

At rest, Portapres® estimates of cardiac output were higher than those by rebreathing (6.9 ± 0.49 compared with 5.1 ± 0.30 litres/min respectively; Welch test, $P < 0.01$). During maximal exercise, the difference increased further (19.1 ± 2.5 compared with 16.6 ± 1.2 litres/min; not significant). These findings are reflected in stroke volumes. When subjects were seated, the Portapres® overestimated stroke volume (85.0 ± 7.4 compared with 65.9 ± 5.6 ml; Student's paired t test, $P < 0.01$). The cardiac output values are compared in Figure 1 and this shows that, despite the significant difference, the mean values of both estimates changed proportionately. The individual comparisons are shown in Figure 2. Values from all subjects showed the same qualitative changes but, despite the mean values showing good agreement, there were large individual variations in both the absolute values and the slopes. Table 2 shows the values for cardiac output, stroke volume and heart rate at rest and during exercise and shows that the increase in cardiac output during exercise was mainly due to the increase in heart rate.

The reproducibility of cardiac output assessed as ± 2 S.D. of differences between paired estimates by

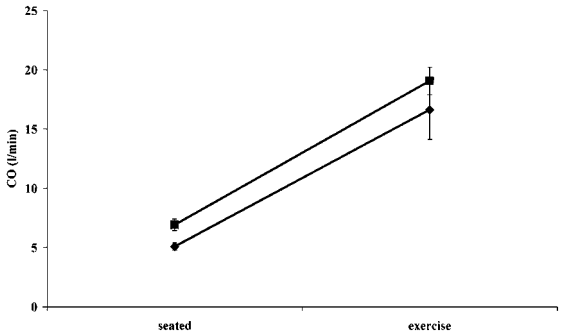

Figure 1 Cardiac output values at rest and during maximal exercise

Data are means ± S.E.M. ■, Portapres® data; ◆, rebreathing data. The values at rest (seated) were significantly ($P < 0.01$) different. Note the similar proportionate increases by both methods.

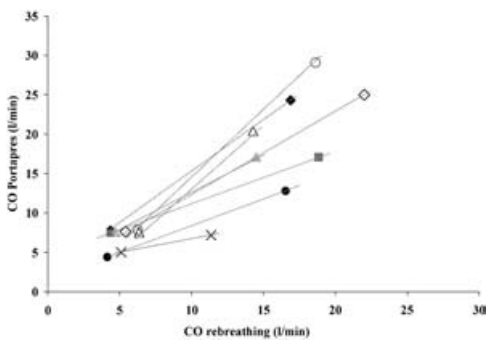

Figure 2 Comparison of estimates of cardiac output by Portapres® and rebreathing at rest and during maximal exercise

Individual subject data are shown. Note the variability of the slopes of the data from the individual subjects.

Portapres®, was ± 2.4 litres/min at rest and ± 2.6 litres/min during maximal exercise (Table 3). When expressed in relation to the means (coefficient of variation), the values become ± 35 % at rest, but only ± 14 % during exercise.

Comparison of Portapres® with rebreathing estimates during orthostatic stress

Again, Portapres® tended to overestimate cardiac output in comparison with rebreathing. The values during supine, head-up tilt and tilt + LBNP (lower body negative pressure) are shown in Figure 3. The supine estimates were significantly different (Welch test, $P < 0.05$). The small differences in the mean values hid quite large individual variations (Figure 4). This variability was indicated by the reproducibility values of ± 1.3, ± 1.26 and ± 1.2 litres/min during supine, head-up tilt and LBNP respectively (Table 3). When expressed

Table 2 Cardiac output, stroke volume and heart rate values during the various states

Values are means ± S.E.M. $^{**}P < 0.05$ and $^{**}P < 0.01$ when compared with rebreathing.

	Cardiac output (litres/min)		Stroke volume (ml)		
	Rebreathing	Portapres®	Rebreathing	Portapres®	Heart rate (beats/min)
Seated	5.1 ± 0.3	6.9 ± 0.5**	65.9 ± 5.6	85.0 ± 7.4**	79.1 ± 4.9
Exercise	16.6 ± 1.2	19.1 ± 2.5	110.8 ± 10.4	116.0 ± 15.1	153.1 ± 7.9
Supine	5.7 ± 0.2	7.0 ± 0.5*	81.5 ± 4.9	97.8 ± 6.7	71.0 ± 3.2
Tilt	5.3 ± 0.20	6.2 ± 0.48	72.0 ± 5.6	82.2 ± 5.2	75.2 ± 4.2
LBNP	4.7 ± 0.3	5.4 ± 0.5	55.6 ± 4.5	65.3 ± 7.5	86.9 ± 6.5

Table 3 Means and S.D. of differences between Portapres® and rebreathing estimates of cardiac output, and 2 S.D. of differences between paired estimates of cardiac output by Portapres®

$^{*}P < 0.05$, $^{**}P < 0.01$ for Portapres® − rebreathing.

	Cardiac output (litres/min)				
	Exercise study		Orthostatic stress		
	Sitting	Maximum exercise	Supine	Tilt	LBNP
Mean difference ± S.E.M.	1.8 ± 0.5**	2.4 ± 2.0	1.3 ± 0.6*	0.94 ± 0.53	0.7 ± 0.6
± 2 S.D. of paired differences	± 2.4	± 2.6	± 1.3	± 1.26	± 1.2

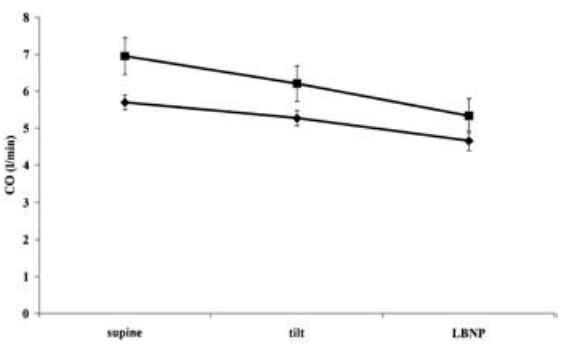

Figure 3 Cardiac outputs while supine, and during head-up tilt and tilt + LBNP

Values are means ± S.E.M. ■, Portapres® values; ◆, rebreathing values. Portapres® values were significantly higher ($P < 0.05$) during the supine phase, but values tended to converge during the orthostatic stress.

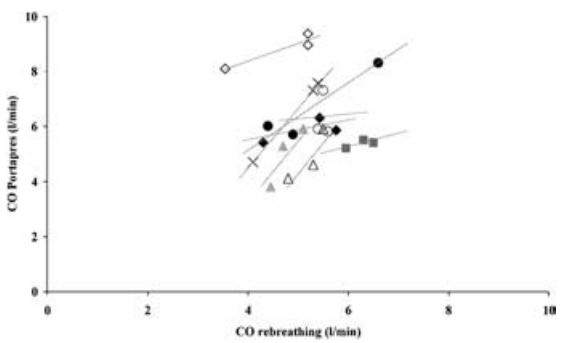

Figure 4 Comparison of estimates of cardiac output by Portapres® and rebreathing in each subject while supine and during orthostatic stress

Note the large variability in both the absolute differences between the estimates and the slopes of the relationships.

as percentages, these values became ± 19 %, ± 22 % and ± 18 % respectively. The mean data of cardiac outputs, stroke volumes and heart rates are given in Table 2.

DISCUSSION

The present study was undertaken to examine whether Portapres®, using the Modelflow® pulse wave analysis programme, was able to provide estimates of cardiac output which were suitable for use in exercise studies, where large increases in output were anticipated, and during orthostatic stress, where smaller decreases would be likely to occur.

We determined the systematic error of the Portapres® method by comparing the values with those obtained using a rebreathing method. Most previous assessments of the method, however, have used cardiac catheterization with thermodilution as the reference method [12–15,22]. Thermodilution is generally regarded as the 'gold standard'; however, it is really an unsatisfactory reference. Apart from its highly invasive nature, results generally are quite variable with errors of approx. ± 15 % [16]. Most non-invasive methods are actually little worse than this. We have shown previously [18] that rebreathing to equilibrate CO_2 between mixed venous blood and alveolar gas provides estimates of cardiac output that

do not differ significantly from those obtained by thermodilution and that they have a similar variability. We, therefore, felt justified, with these healthy volunteers, in using CO_2 rebreathing as the reference, rather than an invasive thermodilution technique.

Essentially, the results from both parts of the present study imply that Portapres® does not reliably estimate absolute values of cardiac output. This finding is in agreement with previous reports [12–15,22]. van Lieshout and Karemaker [23] emphasize that the Modelflow® method must be calibrated against a standard before it can be relied upon to provide absolute values. The question then arises as to how reliable the method is for following changes in cardiac output. Wesseling and co-workers performed a number of studies [13,14,22] in which they compared Portapres® estimates with those obtained by thermodilution under various conditions. In the absence of calibration, as in our present study, Modelflow® tended to overestimate cardiac output. Following calibration, this bias was removed and no significant differences were seen between subsequent estimates by the two methods. Comparisons were made in patients undergoing coronary artery surgery [14], patients in septic shock [13] and healthy subjects undergoing orthostatic stress [22]. It should be noted, however, that following calibration, even though the bias was eliminated, thereby ensuring that there would be no significant mean difference, there were quite large individual differences, of the order of ± 1 litre/min or more. These differences would, of course, include the errors of the thermodilution estimates.

We felt that, in the absence of a reproducible reference method, the only satisfactory way of assessing the reproducibility of Portapres® values was to make pairs of estimates under steady-state conditions when it could reasonably be assumed that the actual values would be near-constant. Having assessed the reproducibility of the method in this way, we can then only use it with confidence to evaluate changes that lie beyond these limits. We found ± 2 S.D. values of the paired estimates to range from ± 1.2 litres/min during the orthostatic stress to ± 2.6 litres/min during maximal exercise. This means that, although it may be possible to detect smaller changes in populations, individual values would need to change by more than these amounts to achieve statistical significance. The results of the exercise study indicate that the magnitude of the errors was similar both at rest and during maximal exercise. Therefore, in relation to the actual cardiac output, the error at rest is ± 35 %, but during exercise it reduces to only ± 14 %. During the orthostatic stress, the error was ± 1.2 litres/min, which may seem small but represents 22 % of the mean. Of particular importance is the fact that orthostatic stress decreased cardiac output by an average of 1.6 litres/min from the supine value, and this is not much more than the reproducibility of the estimate itself.

The Modelflow® method determines stroke volume rather than cardiac output directly. Exercise causes a large increase in heart rate, but stroke volume showed a relatively small increase. During orthostatic stress, heart rate increased but stroke volume decreased. Interestingly, during both exercise and LBNP, Portapres® estimates were 15 % higher than those from rebreathing. Portapres®, therefore, seemed to be able to respond equally to increases and decreases in stroke volume, irrespective of the change in heart rate.

We conclude from the present study that, although Portapres® is suitable for following small changes in cardiac output in large populations, for individual responses to be measured reliably, the changes need to be large, as in moderate to severe exercise.

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