Comparison and reproducibility of transthoracic bioimpedance and dual beam Doppler ultrasound measurement of cardiac function in healthy volunteers

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- 1 We compared the ease of use and reproducibility of two noninvasive methods, transthoracic electrical bioimpedance (TEB) (BoMed NCCOM3-R7) and non-imaging dual beam Doppler ultrasound (Quantascope — Vital Science), in cardiac output (CO) and stroke volume (SV) measurement in healthy volunteers at rest and during physiological stress, both short term and from day to day.
- 2 The TEB method was easier to use and not dependent on the operator. The TEB method was more reproducible both in the short term and from day to day. Both devices were able to detect CO and SV changes under physiological stress, but were less reproducible day to day during exercise.
- 3 At supine rest, the within subject coefficient of variation between time point for TEB was 4.6% for CO and 6.1% for SV, and 7.9% for CO and 7.4% for SV with Doppler.
- 4 The results from each device showed a linear correlation coefficient (r) of 0.69 for CO ($P < 0.0005$) and 0.64 for SV ($P < 0.0005$). The correlation coefficient improved to 0.76 ($P < 0.0005$) when only changes in CO and SV were considered. There was no systematic difference in the changes detected by the two methods, but the individual variation was wide.

Keywords transthoracic electrical bioimpedance Doppler reproducibility
volunteers cardiac output

Introduction

The noninvasive measurement of cardiac output (CO) has many possible applications in studies of drug effects. Because of the difficulties of measuring CO, surrogate measures such as systolic time intervals (Hassan *et al.*, 1983) or peak aortic blood velocity (Harry *et al.*, 1988) have been used instead. There are now available two devices which measure CO noninvasively using different principles; these are the Bomed NCCOM3-R7, which uses transthoracic electrical bioimpedance (TEB) (Sramek, 1981), and the Quantascope (Vital Science) which uses a nonimaging Doppler ultrasound method (Silke *et al.*, 1988).

The TEB method depends on the detection of changes in the electrical impedance across the thorax which occurs due to the movement of blood during each cardiac cycle. The theories underlying this technique and the equipment for its detection have developed over the years (Bernstein, 1986a), and the NCCOM3-R7 represents the most recent advances (Bernstein, 1989).

The Doppler device depends on the attenuation com-

pensated volume flow (ACVF) theory (Hottinger & Meindl, 1979) and requires the use of two parallel ultrasonic beams, one broad to insonate the whole diameter of the ascending aorta, and the other narrow, to insonate a small cross section of blood moving within the aorta. The Doppler indices derived from each are combined to avoid the need for imaging of the aorta and measurement of aortic root diameter, while measuring CO (Evans *et al.*, 1986).

Although advocated for patient management, neither has been widely accepted in clinical use because of variable correlation with what is taken to be the 'gold standard' of CO measurement in clinical medicine, the thermodilution technique (Kalkat *et al.*, 1988; Mattar *et al.*, 1986; Silke *et al.*, 1990; Wong *et al.*, 1988). Both methods seem satisfactory in studies with normal subjects (Jewkes *et al.*, 1989; Taylor & Silke, 1988), and hence their potential suitability for clinical pharmacological studies. There are few studies comparing the reproducibility and ease of use of the two methods. We

undertook a two-part study in normal subjects to investigate these. The first part of the study investigated the short term reproducibility of each method at supine rest and the second part investigated the day to day reproducibility of each method at rest and under physiological stress.

Methods

Subjects

Six healthy, non-smoking and drug free male volunteers (mean age 22 years, range 20 to 28) participated in the first part of the study and twenty-five healthy male volunteers (mean age 29 years, range 21 to 52) in the second part. The study was carried out with verbal informed consent from the volunteers and approval from the local ethical committee.

Cardiac function measurement

The NCCOM3-R7 is attached to the subject by eight spot electrodes on the root of the neck and lower chest. The height and weight of the subject are entered into the microprocessor, which then uses this data to interpret the electrical impedance signal and provide a reading of the CO with each cardiac cycle. The device automatically rejects poor quality signals. The NCCOM3-R7 was adjusted so that each set of data recorded was the average of 16 acceptable cardiac cycles ('slow mode').

The ACVF Doppler requires the positioning of the ultrasonic probe in the suprasternal notch of the subject, and manoeuvring it to obtain the best Doppler signal from the ascending aorta. Since the experience of the operator determines the quality of results from the ACVF Doppler (Taylor & Silke, 1988), the same experienced operator (HWKN) performed all readings. Settings for beam depth and gain were optimised (maximal power return from both beams with minimal background noise) for each subject before the trial, and used unchanged throughout. The high pass filter was preset at a cut-off frequency of 600 Hz to minimize signals from vessel walls and heart valves.

Both devices measure several parameters, including heart rate (HR, beats min⁻¹). Only CO (l min⁻¹) and stroke volume (SV) (ml) were chosen for analysis.

HR was measured by a separate 12 leads ECG monitor (Cardiokinetics—Cambridge CM3000). It was recorded over 16 beats each time a set of TEB data was generated and used for analysis.

Study design

Short term reproducibility Each subject lay supine throughout the study. After 10 min rest, simultaneous measurement was made by each device at 5 min intervals for 30 min. CO measurement started at 30 s before each time point until two sets of TEB data and the mean of at least eight Doppler waves were collected for analysis.

Day to day reproducibility Each subject was studied twice, at the same time of day on two separate days.

Subjects were either fasting or had taken a light breakfast and had abstained from alcohol and caffeine for the previous 12 h. Simultaneous measurement of CO and SV was done with each device at sequential fixed time points during the following protocol which was intended to test the devices over a range of physiological cardiac output changes:

- at 5 and 10 min while resting supine (time points 1 and 2);
- at 2, 5 and 10 min while passively tilted at 70° (time points 3, 4 and 5);
- at 5 and 10 min while resting supine after returning to the horizontal (time points 6 and 7);
- after 5 min standing (time point 8);
- after 5 min sitting (time point 9);
- during the last 30 s of each 2 min exercise on an erect bicycle ergometer at a workload of 60 W (time point 10) and 150 W (time point 11) while the subject continued to pedal throughout the two stages of exercise;
- at 2 min intervals for 10 min after exercise, while seated (time points 12 to 16).

CO measurement started at 30 s before each time point until two sets of TEB data and the mean of at least six Doppler waves were collected. If more than two sets of TEB data were obtained during the 30 s, in particular during exercise, only the last two would be used for analysis. If data was unobtainable within the 30 s by either method, it would be regarded as missing for that method.

Statistical analysis

The short term reproducibility of CO and SV of each method was assessed by analysing the variance, expressed as the coefficient of variation (CV). For the TEB method, the variance within and between time points were calculated. The heart rate was similarly analysed. For the ACVF Doppler method, only the variance between time points was calculated.

The day to day reproducibility of CO and SV of each technique at each time point was compared by plotting the difference between the two days' readings against the mean of the readings according to the method suggested by Bland & Altman (1986). The coefficient of reproducibility (CR = 2 × s.d. of mean difference) was estimated where appropriate (when the mean difference is not significantly different from zero, $P < 0.05$). HR was similarly analysed. Similar analysis can be used to compare the agreement of data obtained by two equipments measuring the same parameter, provided that there is no systematic bias in the data, i.e. the mean difference is not significantly different from zero, $P < 0.05$. In this case, the mean difference $\pm 2 \times$ s.d. gives the limits of agreement (LA). However, if there is systematic bias, it would be inappropriate to estimate the CR or the LA. The CO and SV data measured by the two methods were also compared by linear regression analysis and the coefficient of correlation (r) estimated. Changes in CO by each method under various stages of physiological stress were analysed by paired t -test. Significance was set at 5% level. We also considered the changes in CO and SV between each time point from the

pre-tilt 10 min supine rest, through the whole period of tilting to post-tilt 5 min supine rest; and from 5 min at sitting position, through the two stages of exercise till 10 min post-exercise rest. The LA of the changes was then analysed, and their correlation by linear regression.

Results

Short term reproducibility

There was no loss of data. Table 1 showed that the within subject mean CV between time points was smaller with the TEB method (4.6% for CO and 6.1% for SV) than the ACVF Doppler method (7.9% and 7.4% respectively). With the TEB method, the mean CV within time points for CO and SV was even smaller, 2.5% and 3.8% respectively. The within subject heart rate was reproducible, with a mean CV of 3.9% within and 4.8% between time points.

Day to day reproducibility

TEB obtained 98.9% and Doppler obtained 95.5% of all possible haemodynamic data. During supine rest, both techniques recorded data satisfactorily in all subjects. Passive tilt was abandoned in two subjects because of dizziness on one day each. Other problems in collecting data included difficulty in obtaining satisfactory Doppler readings in upright postures in five subjects who had poorly defined suprasternal notches. During 60 W exercise, 10% of possible data were unobtainable by Doppler but none was lost by TEB, while during 150 W exercise, 22% and 10% were lost respectively, due to body movement.

The mean HR, SV and CO measured by both techniques were reproducible (Figures 1, 2 and 3). Both methods showed the expected physiological changes. Doppler CO and SV were consistently lower than those of TEB.

The reproducibility of HR was acceptable from day to day at all time points (Table 2). Tables 3 and 4 show results for reproducibility of the CO and SV by the two techniques at various time points. The CR of CO were less for TEB than Doppler at most time points. Figures 4 and 5 showed examples of the plots of individual difference of two CO measurements made at the same time

Figure 1 Heart rate changes on each of two days in 25 volunteers. Error bars omitted for clarity. See text for protocol and detail of A to G. ○ Day 1, □ Day 2.

Figure 2 Stroke volume changes on each of two days in 25 volunteers. Error bars omitted for clarity. See text for protocol and detail of A to G. ○ TEB day 1, □ TEB day 2, △ Doppler day 1, ▽ Doppler day 2.

Table 1 The mean and within subject coefficient of variation in CO (l min^{-1}), SV (ml) and heart rate (beats min^{-1})

		<i>Coefficient of variation</i>		
		<i>Mean</i>	<i>Between time points</i>	<i>Within time point</i>
TEB	CO	8.6	4.6	2.5
	SV	144	6.1	3.8
Doppler	CO	6.6	7.9	NA
	SV	111	7.4	NA
Heart rate		62	4.8	3.9

NA = not available.

point on separate days against the mean for each method. At 150 W exercise, the mean individual difference in TEB CO from day to day shows systematic bias, hence the CR cannot be estimated. At 60 W exercise, the CR of TEB CO became larger in relation to the mean CO compared with resting values. This suggests that TEB CO is less reproducible from day to day at 60 W exercise and not reproducible at 150 W exercise. Although the mean individual difference in Doppler CO shows no bias from day to day at all time points, the CR was large in relation to the mean CO. This suggests that Doppler CO from day to day was less reproducible than TEB CO.

Similarly, the CR of SV was less for TEB than Doppler at rest, suggesting better reproducibility from day to day. However, during exercise, reproducibility was generally decreased, with large CR relative to mean SV,

Figure 3 Cardiac output changes on each of two days in 25 volunteers. Error bars omitted for clarity. See text for protocol and detail of A to G. $\circ$ TEB day 1, $\square$ TEB day 2, $\triangle$ Doppler day 1, ∇ Doppler day 2.

Table 2 Heart rate: group mean (s.d.), mean individual difference of (day 2 – day 1) (s.d.), and coefficient of reproducibility (CR) of heart rate (beats min^{-1}) at various time points

Time point	Mean (s.d.)	n	Mean difference (s.d.)	CR	P
Pre-tilt supine 5 min	66 (11)	25	-1.8 (6.6)	13.2	0.19
Tilt 5 min supine	82 (12)	25	1.2 (8.8)	17.6	0.51
Post-tilt supine 10 min	62 (9)	25	0.7 (6.4)	12.8	0.61
Stand 5 min	79 (12)	24	-0.46 (10.0)	20	0.82
Sit 5 min	73 (10)	25	-0.46 (10.0)	20	0.82
Exercise 60 W	94 (13)	25	0.9 (11.3)	22.6	0.70
Exercise 150 W	128 (16)	21	-2.6 (8.5)	17	0.17
Post-exercise 10 min	82 (12)	25	-2.3 (9.7)	19.4	0.25

n = number of subjects with data on both days; *P* = *P* value of mean difference from zero.

and reproducibility of TEB SV could not be tested at 60 W exercise due to significant bias of mean individual difference.

Linear regression analysis of the data over all time points on the two days showed significant linear correlation. The *r* value for CO was 0.69, and the regression

Figure 4 TEB CO (l min^{-1}) at 5 min supine rest: individual difference between 2 days against the mean. 2 s.d. = CR (see text and Table 3).

Figure 5 Doppler CO (l min^{-1}) at 5 min supine rest: individual difference between 2 days against the mean. 2 s.d. = CR (see text and Table 3).

equation was (TEB CO) = $3.76 + 0.82$ (Doppler CO), $P < 0.0005$. Similarly, the *r* value for SV was 0.64, with regression equation (TEB SV) = $49.5 + 0.76$ (Doppler SV), $P < 0.0005$. Linear regression analysis of the changes in CO (ΔCO) and SV (ΔSV) showed better correlation between the two methods. For CO, the regression equation was $\Delta(\text{TEB CO}) = 0.027 + 0.86 \Delta(\text{Doppler CO})$; $r = 0.76$, $P < 0.0005$. For SV, the regression equation was $\Delta(\text{TEB SV}) = 0.44 + 0.78 \Delta(\text{Doppler SV})$; $r = 0.76$, $P < 0.0005$.

Table 5 showed the magnitude of changes in CO detected by each method under various physiological stress on day 1. Similar changes were obtained on day 2. TEB detected larger changes during exercise while Doppler detected larger changes from supine to upright position. TEB did not detect significant change ($P = 0.52$) in CO from standing to sitting position while Doppler did ($P = 0.037$). This is because TEB SV showed less change in SV (mean difference = 7.7 ml, $P = 0.0036$) than Doppler (mean difference = 11.6 ml, $P = 0.0026$).

As Doppler CO and SV were consistently lower than those of TEB (Figures 2 and 3), there was obviously no agreement in the absolute values. However, analysis of the overall agreement of ΔCO and ΔSV by both techniques by the Bland & Altman method showed a mean difference ($\Delta(\text{Doppler CO}) - \Delta(\text{TEB CO})$) (s.d.) of only -0.03 (2.1) l min^{-1} , not significantly different from

Table 3 Cardiac output: group mean (s.d.), mean individual difference of (day 2 – day 1) (s.d.), and coefficient of reproducibility (CR) of CO (l min⁻¹) by TEB and Doppler at various time points

<i>Time point</i>	<i>Method</i>	<i>n</i>	<i>Mean (s.d.)</i>	<i>Mean difference (s.d.)</i>	<i>CR</i>	<i>P</i>
Pre-tilt supine 5 min	TEB	25	8.2 (1.9)	-0.1 (0.9)	1.8	0.59
	Doppler	25	6.5 (1.3)	-0.2 (1.4)	2.8	0.44
Tilt 5 min	TEB	25	6.3 (1.5)	0.1 (0.6)	1.2	0.42
	Doppler	24	3.4 (1.0)	0.2 (0.9)	1.8	0.19
Post-tilt supine 10 min	TEB	25	7.7 (2.0)	0.01 (0.8)	1.6	0.97
	Doppler	25	5.5 (1.2)	-0.2 (1.2)	2.4	0.56
Stand 5 min	TEB	24	6.1 (1.5)	-0.1 (0.7)	1.4	0.70
	Doppler	23	3.2 (1.1)	-0.1 (1.1)	2.2	0.81
Sit 5 min	TEB	25	6.2 (1.4)	-0.2 (0.6)	1.2	0.16
	Doppler	24	3.7 (1.1)	-0.2 (1.0)	2.0	0.50
Exercise 60 W	TEB	25	11.0 (2.7)	-0.5 (1.4)	2.8	0.10
	Doppler	22	7.8 (2.3)	-0.2 (1.8)	3.6	0.61
Exercise 150 W	TEB	21	16.1 (4.3)	-1.5 (2.7)		0.02*
	Doppler	21	11.5 (2.9)	-0.1 (2.4)	4.8	0.91
Post-exercise 10 min	TEB	25	6.6 (1.2)	0.1 (0.7)	1.4	0.58
	Doppler	24	4.0 (1.2)	0.1 (1.0)	2.0	0.58

n = number of subjects with data on both days; *P* = *P* value of mean difference from zero;

* = mean difference significantly different from zero.

Table 4 Stroke volume: group mean (s.d.), mean individual difference of (day 2 – day 1) (s.d.) and coefficient of reproducibility (CR) of SV (ml) by TEB and Doppler at various time points

<i>Time point</i>	<i>Method</i>	<i>n</i>	<i>Mean (s.d.)</i>	<i>Mean difference (s.d.)</i>	<i>CR</i>	<i>P</i>
Pre-tilt supine 5 min	TEB	25	126 (33)	1.8 (14.3)	28.6	0.54
	Doppler	25	102 (18)	0.3 (21.5)	43	0.94
Tilt 5 min	TEB	25	77 (19)	-0.1 (9.9)	19.8	0.42
	Doppler	24	42 (12)	2.4 (11.4)	22.8	0.31
Post-tilt supine 10 min	TEB	25	125 (32)	-0.9 (14.9)	29.8	0.78
	Doppler	25	91 (15)	-3.2 (17.6)	35.2	0.38
Stand 5 min	TEB	24	79 (19)	0.3 (13.6)	27.2	0.92
	Doppler	23	44 (14)	2.1 (16.6)	33.2	0.55
Sit 5 min	TEB	25	86 (22)	-1.9 (10.7)	21.4	0.39
	Doppler	24	53 (14)	-0.7 (15.2)	30.4	0.83
Exercise 60 W	TEB	25	117 (28)	-6.5 (13.8)		0.03*
	Doppler	22	85 (20)	0.6 (17.2)	34.4	0.88
Exercise 150 W	TEB	21	125 (28)	-9.1 (23.6)	47.2	0.09
	Doppler	21	95 (23)	0.0 (20.3)	40.6	1.00
Post-exercise 10 min	TEB	25	82 (18)	3.1 (10.3)	20.6	0.14
	Doppler	24	51 (14)	0.9 (13.0)	26.0	0.75

n = number of subjects with data on both days; *P* = *P* value of mean difference from zero;

* = mean difference significantly different from zero.

Table 5 Changes in CO (l min^{-1}) detected by TEB and Doppler under various stages of physiological stress on day 1

	Method	n	Mean difference (s.d.)	P
Pre-tilt supine 10 min to tilt 2 min	TEB	25	-2.0 (1.4)	< 0.0005
	Doppler	25	-2.9 (1.5)	< 0.0005
Post-tilt supine 10 min to stand 5 min	TEB	25	-1.5 (1.6)	< 0.0005
	Doppler	24	-2.3 (1.2)	< 0.0005
Stand 5 min to sit 5 min	TEB	25	0.07 (0.6)	0.52
	Doppler	24	0.5 (1.2)	0.037
Sit 5 min to exercise 60 W	TEB	25	5.0 (2.1)	< 0.0005
	Doppler	23	4.2 (1.7)	< 0.0005
Exercise 60 W to exercise 150 W	TEB	24	5.4 (3.3)	< 0.0005
	Doppler	20	3.6 (2.2)	< 0.0005
Exercise 150 W to post-exercise 2 min	TEB	24	-6.7 (3.6)	< 0.0005
	Doppler	18	-6.5 (2.6)	< 0.0005

zero ($P = 0.78$). This suggested no systematic bias in the changes detected by the two techniques. However, there was wide individual variation as the LA (mean difference $\pm 2 \times \text{s.d.}$) were wide (4.17 to -4.23 l min^{-1}). Similarly, for SV the mean difference ($\Delta(\text{Doppler SV}) - \Delta(\text{TEB SV})$) (s.d.) was $-0.6 (22.2) \text{ ml}$ ($P = 0.54$) and the LA were 43.8 to -45 ml .

Discussion

We have compared the ease of use, short term resting reproducibility and day to day reproducibility under physiological stress of TEB and ACVF Doppler in CO and SV measurement in healthy volunteers. The agreement of cardiac output of both TEB and ACVF Doppler with that of the thermodilution method has been studied. TEB has been found to agree well (Appel *et al.*, 1986; Mattar *et al.*, 1986), particularly when the cardiac output was around the normal physiological range of 3.5 to 5.5 l min^{-1} (Jewkes *et al.*, 1989). TEB was less reliable when cardiac output was either very low ($< 2 \text{ l min}^{-1}$) (Bernstein, 1986b) or very high (about 8 l min^{-1}) (Kalkat *et al.*, 1988), or in certain disease states such as congestive cardiac failure, tachyarrhythmias, or severe sepsis, or in patients with cardiac valvular insufficiency, intra-cardiac shunts or severe hypertension. Other lesser problems causing unreliable results included motion artifacts or very greasy skin (Appel *et al.*, 1986; Bernstein, 1986b; Shoemaker *et al.*, 1988).

The ACVF Doppler technique has not been so well studied. Taylor & Silke (1988) compared Doppler and thermodilution in 21 patients undergoing routine cardiac catheterisation. There was good correlation and agreement between the two methods ($r = 0.96$, average difference was 0.14 l min^{-1} , s.d. of the difference was 0.3 l min^{-1}). The ACVF Doppler has also been found to be useful in studying haemodynamic responses to drugs in patients with angina pectoris at rest (Silke *et al.*, 1990). In general, the limitations and possible role of the ACVF Doppler in patient management have not yet been defined.

Nevertheless, the two techniques clearly have potential advantages in studies in normal subjects, because of their ease of application and noninvasive nature. Neither has been compared with invasive methods in normals, and so no reliance can be placed on the absolute values obtained by either technique. However, in clinical pharmacological studies, reliable measurement of alteration in haemodynamic parameters is more important than absolute values.

In our short term reproducibility study, the mean CV in CO and SV between time points at rest obtained by the TEB method (4.6% and 6.1% respectively), were similar to those of Jewkes *et al.* (1989) (5.1% and 4.7% respectively). Northridge *et al.* (1990) found an even smaller CV in CO between time points (2.7%) in post myocardial infarction patients. This is similar to our mean CV in CO within time point (2.5%). In contrast, the mean CV in CO and SV between time points at rest obtained by ACVF Doppler (7.9% and 7.4% respectively) were larger than those obtained by Silke *et al.* (1988) (4.8% and 3.8% respectively). This may be partly due to the smaller number of recordings obtained for each individual (hence larger s.d.) and partly due to the smaller mean CO and SV in our study (6.6 l min^{-1} and 111 ml compared with 7.3 l min^{-1} and 125 ml respectively). Both of these factors will increase the CV (Bland, 1987). The other possibility may be variation introduced by the operator. We minimised this by having only one experienced investigator (HWKN) operate the ACVF Doppler.

Our finding that the ACVF Doppler has greater short term variability is consistent with one previous comparative study of the two devices (Acton *et al.*, 1989). In that study, eight healthy volunteers were infused with dobutamine to increase cardiac output at rest. The authors concluded that the greater overall variability with the ACVF Doppler method may reflect technical difficulties in ensuring complete insonation of the ascending aorta with the wide beam of the ACVF Doppler. Interestingly, in contrast to that study, we obtained consistently lower CO and SV readings with the ACVF Doppler than the TEB method. The reason for this difference was not clear.

In the day to day reproducibility study, we assessed the HR independently by an ECG monitor. The HR was reproducible at all time points. The difference in CO shown by both methods during an exercise was most likely due to difference in SV rather than HR because we ensured that the HR recorded by each method did not differ from that displayed on the ECG monitor by more than 5 beats min^{-1} . Although we showed that the mean individual difference from day to day of TEB CO at 150 W exercise and TEB SV at 60 W exercise was significant at 5% level, this may have well occurred by chance (Wallenstein *et al.*, 1980). The fact that we did multiple comparisons (16 time points) for each individual for each parameter (HR, SV and CO) would have increased the probability of showing a 'significant' difference at 5% level. Alternatively, if we lowered the significant level to 1%, then none of the parameters would show significant difference from day to day at any time point.

We found that in some individuals, particularly those with an anatomically short neck, and poorly defined suprasternal notch, the Doppler signal was so poor that it was almost impossible to obtain readings during upright posture, particularly during exercise, because of inevitable body movement especially at high work loads. This may partly explain the finding that Doppler detected larger fall in CO during upright posture but smaller during exercise (Table 5). The TEB fared little better with motion artefact causing the rejection by the device of a high proportion of impedance waveforms. Cox *et al.* (1989) estimated the sampling rate to be 81.5% at rest (sitting) and 48.5% during 'peak' erect

ergometric exercise. However, in that abstract, it was not clear how the sampling rate was calculated and the exercise protocol was different from ours. Nonetheless, this limitation by exercise exists for most means of measuring cardiac output.

Despite this limitation, our results show that both methods were able to demonstrate changes in SV and CO caused by physiological stress. The group mean values had excellent reproducibility from day to day by both methods (Figures 1, 2 and 3). The CR for TEB was less than that of Doppler at all time points except during exercise, implying better reproducibility for TEB (Tables 3 and 4) (as did our short term reproducibility study and the study of Acton *et al.*, 1989). However, as the CR at these non-exercise time points were greater than 1 l min^{-1} , direct comparison of absolute CO by these methods between days must be interpreted with caution in clinical pharmacological studies.

In conclusion, this study showed that TEB NCCOM3-R7 was easier to use, and both short term and day to day reproducibility were better than ACVF Doppler. Both techniques were able to detect physiological changes in CO and SV in healthy volunteers. The changes detected by both techniques correlate but do not agree. Both methods were suitable to measure individual changes in CO and SV under passive physiological stress but less suitable during exercise. We propose to study their suitability to investigate drugs induced changes in these parameters.

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