Less invasive determination of cardiac output from the arterial pressure by aortic diameter-calibrated pulse contour

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Background. Cardiac output by modelflow pulse contour method can be monitored quantitatively and continuously only after an initial calibration, to adapt the model to an individual patient. The modelflow method computes beat-to-beat cardiac output (COmf ) from the radial artery pressure, by simulating a three-element model of aortic impedance with post-mortem data from human aortas.

Methods. In our improved version of modelflow (COmfc) we adapted this model to a real time measure of the aortic cross-sectional area (CSA) of the descending aorta just above the diaphragm, measured by a new transoesophageal echo device (HemoSonic 100). COmf and COmfc were compared with thermodilution cardiac output (COtd) in 24 patients in the intensive care unit. Each thermodilution value was the mean of four measurements equally spread over the ventilatory cycle.

Results. Least squares regression of COtd vs COmf gave $y=1.09\times [95\% \text{ confidence interval (CI)} 0.96–1.22], R^2=0.15$, and of COtd vs COmfc resulted in $y=1.02\times [95\% \text{ CI } 0.96–1.08], R^2=0.69$. The limits of agreement of the un-calibrated COmf were $-3.53$ to $2.79$, bias=0.37 litre min$^{-1}$ and of the diameter-calibrated method COmfc, $-1.48$ to $1.32$, bias=$-0.08$ litre min$^{-1}$. The coefficient of variation for the difference between methods decreased from 28 (un-calibrated) to 12% after diameter-calibration.

Conclusions. After diameter-calibration, the improved modelflow pulse contour method reliably estimates cardiac output without the need of a calibration with thermodilution, leading to a less invasive cardiac output monitoring method.


Keywords: arterial pressure; arteries, aortic diameter; heart, cardiac output; measurement techniques, thermodilution; model, computer simulation

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Different authors have shown in patients, by comparing the modelflow estimates with thermodilution estimates, the ability of the modelflow (pulse contour) method to replace the thermodilution method to follow cardiac output changes.¹–³ A patient calibration of the modelflow method is, however, needed to obtain quantitative cardiac output with high accuracy. This calibration is usually carried out by thermodilution cardiac output.¹–³

The parameters of modelflow are based on aortic pressure, and post-mortem data of cross-sectional area (CSA) vs pressure of the aorta just above the diaphragm.⁴ A recently developed M-mode ultrasound method, (Hemosonic 100 ARROW, Reading, PA, USA) has the ability to measure the diameter of the descending aortic just above the diaphragm. In addition, the system also measures aortic blood flow velocity.⁵ This oesophageal ultrasound method is considered to be less invasive than thermodilution cardiac output measurement by a pulmonary artery catheter (PAC).

In this paper we would like to test the hypothesis that calibration of the modelflow method by the measure of the aortic diameter results in an improvement of the accuracy of the method such that a calibration by thermodilution is no longer needed.

¹Declaration of interest. ARROW Int. provided the equipment for this study. One of the authors (J.S.) is a consultant to this company.
## Methods

### Patients and materials

The study was approved by the hospital ethical committee and was conducted according to the principles stated in the Helsinki convention. Written informed consent from each patient was obtained the evening before surgery. The improved modelflow method was evaluated in the intensive care unit (ICU) in 24 patients following coronary artery bypass graft and/or valve replacement. Exclusion criteria were severe tricuspid heart valve insufficiency, aortic aneurysm, aortic valve pathologies, and known pharyngeal or oesophageal pathologies.

Anaesthesia during surgery was performed according to institutional standards, with invasive monitoring of arterial pressure, central venous pressure, pulmonary artery pressure, pulmonary capillary wedge pressure, and thermodilution cardiac output with a PAC (Edwards Intellire Cath, Irvine, CA, USA).

After transfer of the patient to the ICU, the haemodynamic status was stabilized giving fluids and catecholamines as required. The lungs were ventilated with oxygen 40%, 12 bpm, and a positive airway pressure of 5 cm H2O. Tidal volume was adapted to bring the arterial Pco2 in the range of 40–45 mm Hg. The HemoSonic 100 probe was inserted into the oesophagus after haemodynamic and respiratory stability had been achieved. During this stage diameter-calibration of modelflow was performed. To prevent instability during this period, nursing activities and treatment of the patients were minimized. Measurement series with changes in arterial pressure or heart rate larger than 5% were rejected and repeated.

### Modelflow method

Increase in aortic pressure as a result of left ventricular contraction, causes inflow of blood into the arterial system. This inflow is, however, opposed and thus moderated by aortic and peripheral systemic properties such as arterial counter pressure and impedance.

The modelflow method simulates this behaviour according to a three-element Windkessel model of arterial input impedance.6,7 The three-element model, representing the three major properties of the aorta and arterial system, has three principal components: aortic characteristic impedance, which represents the opposition of the aorta to pulsatile inflow; Windkessel compliance, which represents the ability of the aorta and arterial system to elastically store the cardiac stroke output of the left ventricle; and peripheral resistance, which represents the opposition of the vascular beds to the drainage of blood.

The impedance and compliance of the model depend on pressure itself,3 and total systemic peripheral resistance depends on many factors including circulatory filling, metabolism, sympathetic tone, and vasoactive drugs.

The aortic Windkessel compliance decreases substantially when aortic pressure increases. This non-linear behaviour of the aortic wall would be a major source of error if not taken into account. The aortic characteristic impedance, in contrast to compliance, increases moderately when aortic pressure increases. These non-linear relationships were studied post-mortem by Langewouters and colleagues4 and described as mathematical functions of the patient’s age, gender, height, and weight. Individual inaccuracy in aortic diameter determination translate into an inaccuracy in the absolute level of cardiac output computed for an individual patient, but the ability to reliably track the changes in cardiac output remains intact.3 To overcome the individual inaccuracy in aortic diameter determination, a real time measurement of aortic diameter was introduced using an ultrasound echo system (M-mode, HemoSonic 100). According to Langewouters and colleagues,5 the thoracic aortic CSA can be predicted as a function of aortic pressure (Pa) by the following formula:

\[
CSA(P_a) = CSA_{max} \left[ 0.5 + \frac{1}{\pi} \arctan \left( \frac{P_a - P_0}{P_1} \right) \right]
\]

CSAmax is the maximal cross sectional area at a very high pressure, P0 defines the position of the inflection point. P1 defines the width between the point at one-half and three-quarter amplitude. The measured CSA of the descending aorta is computed from the measured aortic diameter. The patient-dependent arctangent relation between pressure and CSA is next linearly scaled through the measured CSA (Fig. 1).

Total systemic peripheral resistance is known only approximately from physiology. The uncertainty in this model parameter is removed as follows. For the first beat detected in the arterial pressure waveform a population average value for peripheral resistance is assumed in the model and mean arterial pressure and cardiac output is computed.
The ratio of pressure to cardiac output for this first beat defines a new resistance value used in the model for the next beat, and so forth. Within 5 beats after start, usually, model resistance stabilizes to the systemic peripheral resistance value. The model follows changes in systemic peripheral resistance that further occurs. This self-adaptation scheme is possible because systemic peripheral resistance changes are slow, with time constant typically near 10 s.

Radial arterial pressure was taken from the monitor in use in the ICU, and HemoSonic 100 diameter was sampled by a computer system at 100 Hz and used as input to the model, to compute an aortic flow waveform. The flow waveform was integrated during arterial systole to deliver stroke volume. Cardiac output was computed for each beat as the product of stroke volume and heart rate. A detailed description of the computation can be found in previous papers.3–13

**Measurement of aortic diameter**
Aortic diameter was obtained from the M-mode transducer of the oesophageal Hemosonic probe.5 During probe positioning, first, best ultrasound signal quality was adjusted by rotation of the probe using the acoustic and visual Doppler signal. Secondly, the M-mode transducer was rotated giving the largest distance between anterior and posterior wall, that is diameter, of the descending aorta. After operator validation and adjustment of the edge detection of the anterior and posterior wall of the aorta, the measurement of the diameter is then automatically and continuously followed by the instrument, and displayed on the screen. A chest X-ray was taken to check the position of the probe.

**Thermodilution method**
To improve the accuracy of the thermodilution method, measurements were performed with an automated system under computer control,3–8–10 and included an injectate system (CO-SET, Edwards, Irvine, CA, USA), a proprietary, motor driven injectate syringe, a PAC (Edwards) and a cardiac output computer (COM2, Edwards).

Cardiac output was estimated four times, each measurement initiated in a different phase of the ventilatory cycle. Hence, each injection of 10 ml of glucose at room temperature was delayed from the start of the ventilatory period over either 0, 25, 50, or 75% of the duration of the ventilatory cycle. The start of the ventilatory cycle and the cycle time were detected from the tracheal pressure waveform. The four cardiac output measurements were averaged to obtain one single value for averaged cardiac output. For this technique to work optimally, the haemodynamic and ventilatory frequency must be stable during the series.11

**Data acquisition and analysis**
The best position of the ultrasound probe was checked shortly before the determination of mean cardiac output by performing one series of four thermodilution measurements. During this series of four measurements the position of the probe was not changed. As cardiac output in a patient can be quite variable it is important to acquire the data of each method simultaneously. Therefore, the data of arterial pressure, thermodilution cardiac output and aortic diameter was stored on computer disk, simultaneously. To obtain one single data pair per series, modelflow cardiac output (COmf and COmfc) and thermodilution cardiac output (COtd) are averaged over the same period of time. Haemodynamic stability was verified by analysis of mean arterial pressure and heart rate (not cardiac output) during a series. Stability was considered absent if mean arterial pressure and heart rate averaged per injection deviate more than 5% from their overall average during a series.3 Severe, persistent arrhythmias during passage of thermal indicator was additionally considered as absence of stability. If stability was not present, the series were repeated as one prerequisite for a precision comparison had not been fulfilled.

**Statistical analyses**
The main statistical tool is the Bland–Altman analysis with differences in data pairs plotted against their average.12 The agreement between modelflow and thermodilution cardiac output was computed as the bias [mean (SD)], with limits of agreement computed as bias ±2 SD when the distribution of differences was normal as tested with the Kolmogorov–Smirnov test. The coefficient of variation was computed as $\text{CV} = \sqrt{\text{SD/mean}} \times 100\%$. Data are given as mean (SD). Statistical significance was considered present if P<0.05.

**Results**
Twenty-four paired sets of data were obtained in 24 patients. Individual thermodilution cardiac output measurements indicated a certain scatter within some series of four measurements, but no measurement was rejected. In all patients we were able to obtain a measure of the diameter of the aorta with the HemoSonic 100. In one patient, with acromegaly, the measured diameter of 42.0 mm was used although it was not within the HemoSonic specified measurement range.

Table 1 summarizes the patient data and selected haemodynamic variables. These include thermodilution cardiac output and aortic diameter.

**Table 1** Patient characteristics and haemodynamic data. MAP, mean arterial pressure; PAP, mean pulmonary artery pressure; CVP, central venous pressure; HR, heart rate; COtd, thermodilution cardiac output; COmf–COtd, difference between un-calibrated model and thermodilution cardiac output; COmfc–COtd, difference between calibrated model and thermodilution cardiac output.

<table>
<thead>
<tr>
<th>Variable</th>
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<th>Range</th>
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<tr>
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</tr>
<tr>
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<td>4–17</td>
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<tr>
<td>HR</td>
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<tr>
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<td>3.11–8.82</td>
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<tr>
<td>COmf–COtd</td>
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<td>1.58</td>
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<tr>
<td>COmfc–COtd</td>
<td>litre min⁻¹</td>
<td>−0.08</td>
<td>0.70</td>
<td>−1.41–1.08</td>
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output and the differences between modelflow and thermodilution cardiac output before and after diameter-calibration. The mean calibration factor of all patients was 0.99 and not significantly different from 1.00, \( P > 0.05 \). The cardiac output bias of \( \frac{\text{CO}}{\text{CO}^0} \) before calibration decreased to \( \frac{\text{CO}}{\text{CO}^0} 0.08 \), both not significantly different from 0.00, \( P > 0.05 \). The SD of the difference of 1.58 litre min\(^{-1}\) is halved after calibration to 0.70 litre min\(^{-1}\).

Figure 2 shows un-calibrated and diameter-calibrated modelflow vs thermodilution cardiac output. In the scatter diagram, upper panel, the line of identity is given. Least square regression of \( \text{COtd vs COmf} \) gave \( y = 1.09 \times (95\% \text{ CI } 0.96–1.22) \), \( R^2 = 0.15 \) and of \( \text{COtd vs COmfc} \) gave \( y = 1.02 \times (95\% \text{ CI } 0.96–1.08) \), \( R^2 = 0.69 \). The Bland–Altman analyses showed the limits of agreement of the un-calibrated \( \frac{\text{CO}}{\text{CO}^0} \) (–3.53 to 2.79, bias = 0.37 litre min\(^{-1}\)) and of the diameter-calibrated method (–1.48 to 1.32, bias = –0.08 litre min\(^{-1}\)). Two extreme values can be observed in Figure 2 (3.15 and –4.45 litre min\(^{-1}\)), one in the male patient with acromegaly and an aorta diameter of 42.0 mm and the other in a small lady with an aortic diameter of 16.7 mm. After calibration of modelflow with the diameters measured by the HemoSonic system the differences became much smaller, 0.05 and –1.41 litre min\(^{-1}\), respectively.

**Discussion**

In a previous study we found the modelflow method can reliably track directional changes in thermodilution cardiac output larger than 0.5 litre min\(^{-1}\).\(^1\) Cardiac output can be monitored quantitatively and continuously with little error by the modelflow method only after an initial calibration to adapt the model to the individual patient. This study explored the feasibility to perform this initial calibration with a measurement of the aortic diameter in each patient. We found that the cardiac output values obtained with this adapted modelflow method agreed with the mean of four bolus-thermodilution measurements equally spread over the ventilatory cycle.

**HemoSonic**

A proper positioning of the M-mode echo probe is crucial. Therefore, to gain experience in using the HemoSonic 100, we underwent training, by the developers of this ultrasound device, followed by a learning population of six patients. Data of these patients were not included in this study. Despite such training, the aortic walls could not always be automatically identified unambiguously by the edge detecting of the HemoSonic 100. To overcome the problem we regularly needed to change the edge detection window.
manually. This was especially so in patients with aortic valve replacement. In these patients, the anterior wall was often seen at a larger distance from the probe due to oedema between the oesophagus and the aorta. In addition, the acoustical energy absorbed by the oedema results in a less pronounced edge of the posterior wall.

**Model calibration**

How the properties of the aorta depend on age, gender, pressure, and arteriosclerosis are well understood. We are, however, still left with the individual aortic diameter at maximal pressure, which may vary up to ±30% from the population average. Therefore, the absolute value of cardiac output cannot be computed with certainty. In contrast, changes in cardiac output can be detected with precision. If we calibrate (scale) the parameter of the maximal CSA of the aorta with the quotient between predicted CSA and measured CSA at the mean arterial pressure during the comparison, the agreement between model calculated cardiac output and measured thermodiilution cardiac output improved significantly. This was most explicitly demonstrated in the patient with acromegaly, where we found a model predicted diameter of 29.2 mm, and when measured with the echo probe, a diameter of 42.0 mm. After diameter-calibrating the modelflow (calibrated=CSA-measured/CSA-predicted=2.06), the computed cardiac output value increased from 2.90 to 6.01 litre min⁻¹ and the difference between thermodiilution and the model calculated cardiac output decreased from 3.15 to 0.05 litre min⁻¹. This patient-case illustrates the advantage of a direct measure of the aortic diameter with the HemoSonic 100, above a predicted diameter.

**Error analysis**

Critchley and Critchley¹³ stated that if a new method is to replace an older, established method, the new method should have not greater errors than the older method. Thermodiilution is the reference cardiac output in almost all studies, as in the present one. A standard single thermodiilution estimate of cardiac output has a coefficient of variation, further called error, of 15–20%.¹¹ A triplicate, randomly injected thermodiilution has an error of 10% as the result of averaging.¹¹ The model mean error after diameter-calibration for the difference between methods is near zero (Table 1). Thus, only the scatter errors of thermodiilution and modelflow remain. They are statistically independent because the methods are based on different physical principles. The error that we found between the calibrated model and thermodiilution is approximately 12% (Table 1). Our reference cardiac output only has a 5% error.⁹,¹⁰ Therefore, we may conclude that our calibrated model cardiac output has an error of √(12²–5²)=11%. This is not as good as a triplicate phase spread thermodiilution (11 vs 5%),¹¹ but it is close to the most commonly performed mean of a triplicate random thermodiilution method (10 vs 11%), and thus might replace it.¹

**Position of the model method**

In recent years, several studies based on different pulse contour models have attempted to provide reliable continuous cardiac output from the systemic arterial pressure. The method, proposed by Romano and Pistolesi,¹⁴ based on real time extraction of the model parameters was tested in 22 patients. The error for the difference between cardiac output by their pulse contour method and thermodilution is approximately 13%. Linton and Linton¹⁵ found an error of approximately 12% for the difference between their pulse contour method and thermodilution cardiac output, that is after calibration with one series of thermodilution cardiac output. Another pulse contour method based on the Windkessel model, however, with no dependency of model parameters on gender and age, has been build into the PiCCO device (Pulsion Medical Systems, Germany). Conflicting results were reported by various authors¹⁶–¹⁸ using this simplified Windkessel model. Rauch and colleagues¹⁷ demonstrated, after one initial calibration of the PiCCO system with a series of transpulmonary thermodiilution measurements, that pulse contour cardiac output differs from thermodiilution cardiac output by approximately 20% whereas others reported found values of 16¹⁸ and 10%.¹⁶ In a former study¹ we used the averaged result of one series of four thermodiilution measurements equally spread over the ventilatory cycle to calibrate modelflow and found a probability error of 7% for modelflow. Furthermore, it has been shown that one calibration of the modelflow method was adequate for more than 48 h of monitoring in ICU patients.²

In this study we calibrated modelflow cardiac output by a measure of aortic diameter once per patient. Similar to calibration of modelflow by thermodilution,² we expect that one calibration is adequate for more than 48 h of cardiac output monitoring. If we compare the results of our study to that of other pulse contour methods such as mentioned above, we found a similar error of comparison (12%). However, modelflow calibrated by thermodiilution measurements equally spread over the ventilatory cycle outperforms the other pulse contour methods. Therefore, if a patient is already equipped with a thermodiilution catheter, we consider calibration by thermodiilution preferable above diameter-calibration. In addition, diameter-calibration of modelflow requires a trained operator to position the ultrasound probe whereas our thermodiilution method runs under computer control and no extra training is needed.

**Invasiveness**

The pressure that determines cardiac output is proximal aortic pressure, which is not routinely available. Although the model simulated blood flow shape from the radial artery pressure differs considerably from the one simulated from the pressure measured in the proximal aorta, the computed
stroke volume was found to be not different. In our ICU, almost all patients have a radial artery pressure monitoring system. Notwithstanding the calibration of our new method by measuring the aortic diameter with the transoesophageal M mode ultrasound system, our new method can be considered as less invasive than other methods using indicator dilution methods to calibrate.

Conclusions

Previously, we showed the ability of modelflow to continuously monitor changes in cardiac output. After diameter-calibration, the improved modelflow pulse contour method reliably estimates cardiac output without the need of a calibration with thermodilution, leading to a less invasive cardiac output monitoring method.

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