Chapter 3

An evaluation of cardiac output by five arterial pulse contour techniques during cardiac surgery

R.B.P. de Wilde¹, J.J. Schreuder², P.C.M. van den Berg¹ and J.R.C. Jansen¹

¹Department of Intensive Care, Leiden University Medical Center, Albinusdreef 2, P.O.B. 9600, 2300 RC, Leiden, the Netherlands. ²Department of Cardiac Surgery, San Raffaele Hospital, Milan, Italy

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Summary
The bias, precision and tracking ability of five different pulse contour methods were evaluated by simultaneous comparison of cardiac output values from the conventional thermodilution technique (COtd). The five different pulse contour methods included in this study were: Wesseling’s method (cZ); the Modelflow method; the LiDCO system; the PiCCO system and a recently developed Hemac method. We studied 24 cardiac surgery patients undergoing uncomplicated coronary artery bypass grafting. In each patient, the first series of COtd was used to calibrate the five pulse contour methods. In all, 199 series of measurements were accepted by all methods and included in the study. COtd ranged from 2.14 to 7.55 l.min⁻¹, with a mean of 4.81 l.min⁻¹. Bland-Altman analysis showed the following bias and limits of agreement: Wesseling’s cZ, 0.23 and -0.80 to 1.26 l.min⁻¹; Modelflow, 0.00 and -0.74 to 0.74 l.min⁻¹; LiDCO, -0.17 and -1.55 to 1.20 l.min⁻¹; PiCCO, 0.14 and -1.60 to 1.89 l.min⁻¹; and Hemac, 0.06 and -0.81 to 0.93 l.min⁻¹. Changes in cardiac output larger than 0.5 l.min⁻¹ (10%) were correctly followed by the Modelflow and the Hemac method in 96% of cases. In this group of subjects, without congestive heart failure, with normal heart rhythm and reasonable peripheral circulation, the best results in absolute values as well as in tracking changes in cardiac output were measured using the Modelflow and Hemac pulse contour methods, based on non-linear three-element Windkessel models.

Introduction
Monitoring of hemodynamic pressures and cardiac output are the keystones in general management of surgical and intensive care patients. A change in fluid management and use of catecholamines is often based on these findings. However, in recent years, the rationale behind and efficiency of hemodynamic monitoring to affect outcome has been questioned [1]. One of the reasons for the limited value of cardiac output monitoring is the non-continuous nature of most used methods, whereas in highly unstable patients continuous monitoring would be more appropriate. Among the methods to monitor cardiac output continuously an increasing amount of attention has been focused on pulse contour methods [2–19]. However, in a literature survey, we showed large differences between various pulse contour methods and the conventional bolus thermodilution method [20]. We evaluated the bias, precision and tracking ability of five different pulse contour techniques by simultaneous comparison of cardiac output values with that of the standard right heart bolus thermodilution technique (COtd). The five methods studied were Wesseling’s cZ method (COcz); the Modelflow method (COmf); LiDCO’s PulseCO method (COli); the PiCCO method (COpi); and a recently developed Hemac method integrated in a haemodynamic monitoring and blood pressure control unit (COhe).

Methods
Patients In a prospective study the bias, precision, limits of agreement and tracking ability of five different pulse contour cardiac output methods were compared with standard thermodilution cardiac output (COtd) under conditions of routine use during cardiac surgery. The study was conducted according to the principles of the Helsinki declaration. After approval from the local ethics committee, written informed consent for participation in the study was obtained from all patients. This consent was obtained the day before surgery. All patients had symptomatic coronary artery disease
without previous myocardial infarction. Patients with congestive heart failure (NYHA class IV), aortic aneurysm, extensive peripheral arterial occlusive disease, or concomitant heart valve disease, were not considered for this study. Patients with postoperative arrhythmia or the necessity for artificial pacing or heart assist devices were also not considered. No postoperative complications were monitored. Following premedication with lorazepam 5 mg two hours before surgery, a peripheral venous cannula, a radial artery cannula (20G) and a 7F pulmonary artery catheter were sited. Anaesthesia was induced and maintained with continuous infusion of propofol and sufentanil. Muscle relaxation was maintained with pancuronium bromide. The lungs were ventilated with a PEEP of 2–5 cmH\textsubscript{2}O, at a rate of 10–15 breaths.min\textsuperscript{-1}. Minute ventilation was adjusted to maintain arterial pCO\textsubscript{2} between 4.2 and 5.6 kPa. The patients were treated with vasodilators and/or inotropes according to local guidelines.

**Study protocol**

During the study we used the arterial pressure signal, a respiratory signal from a ventilator or a capnogram, a COM-2 thermodilution cardiac output computer (Edwards, Irvine, CA, USA), and a computer to control a proprietary electromechanical pump for bolus injection.

After specific identifiable changes in the patient's circulatory state a series of measurements was performed. We aimed to carry out a measurement series, at the following times; 3 min after the induction of anaesthesia, immediately after sternotomy, after opening of the pericardium, just before and just after cardiopulmonary bypass, after sternal fixation, after the completion of surgery, and after changes in drug dose. Pulmonary artery thermodilution was carried out with a bolus injection of 10 ml iced dextrose 5% solution at 4–7 °C, as measured by the in-line injectate sensor. All thermodilution cardiac output measurements and pulse contour analyses were performed over the same time periods. The radial artery pressure was used as input for the five pulse contour methods. Figure 3.1 shows a schematic diagram of the connection of the five pulse contour methods to the radial artery pressure. As can be observed, one pressure line and one pressure transducer are used to create an electrical radial pressure signal that is used by all five methods. An electric signal input for the PiCCO device is created using a pressure transducer simulator (PC80200, Pulsion Medical Systems, Munich, Germany).

The PiCCO (Pulsion) device is calibrated by a thermodilution simulator that generates thermodilution curves from which cardiac output (CO\textsubscript{td}) is computed by the PiCCO device equal to the values found by the conventional pulmonary artery thermodilution method. Furthermore, we used the radial artery pressure instead of the preferred femoral artery pressure as input for the PiCCO device because a recent study [21] showed the interchangeability of both pressure sites.
To compare the cardiac output found by each of the five different methods with thermodilution cardiac output, the beat-to-beat values were first averaged over the beats recorded during a single thermodilution measurement. Next, the four averaged values of pulse contour cardiac output and four thermodilution cardiac output measurements were averaged to obtain one single pair of values for further analysis. All data were stored on computer disk for off-line analysis.

**Arterial pulse contour techniques**

The estimation of cardiac output via pulse contour analysis is an indirect method. Cardiac output is computed from a pressure pulsation based on a model of the circulation. The original concept of the pulse contour method for estimation of beat-to-beat stroke volume was first described by Otto Frank in 1899 as the classic Windkessel model [22]. Most pulse contour methods used today are derived from this model.

*Wesseling's cZ method* (BMEYE, Academic Medical Center, Amsterdam, the Netherlands) relates cardiac output to the area under the systolic portion of the arterial pressure wave (Asys). Dividing Asys by aortic impedance (Zao) provides a measure of stroke volume: $V_z = \frac{\text{Asys}}{\text{Zao}}$. In Wesseling's model the mean arterial pressure (Pmean) is used to correct the pressure dependent non-linear changes in cross

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**Figure 3.1** Schematic diagram of the setup in the five pulse contour methods with a single pressure transducer.
sectional area of the aorta. The heart rate (HR) is used to correct for pressure reflections from the periphery. The corrections for arterial pressure and heart rate are age (Age) dependent. A detailed description of this method can be found elsewhere [2, 6]. Briefly, the computation can be written as:

\[ V_{CZ} = V_Z[0.66 + 0.005 \times HR - 0.01 \times Age \times (0.014 \times Pmean - 0.8)] \]

\[ CO_{CZ} = cal \times HR \times V_{CZ} \]

where \( CO_{CZ} \) is Wesseling's pulse contour cardiac output. The calibration factor, \( cal = \frac{CO_{CZ}}{CO_{ref}} \), is determined at least once for each patient by comparing pulse contour cardiac output with an absolute cardiac output estimate determined by thermodilution (\( CO_{ref} \)).

The *Modelflow* method (BMEYE) simulates the classical three-element Windkessel model to estimate cardiac output (\( CO_{mf} \)). The model includes three principal components of opposition: characteristic impedance, which represents the opposition of the aorta to pulsatile inflow; Windkessel compliance, which represents the resistance of the aorta to volume increases; and peripheral resistance, which represents the opposition of the vascular beds to the drainage of blood. Systemic peripheral resistance depends on many factors, including circulatory filling, metabolism, sympathetic tone and presence of vaso-active drugs. Aortic compliance decreases substantially when arterial pressure increases. This non-linear behaviour of the aorta would be a major source of error if not taken into account. These non-linear relationships were studied in vitro by Langewouters et al. [23] and described as mathematical functions whose properties regress closely dependent on patient age and gender, and slightly dependent on height and weight. A patient's aortic cross-sectional area is, however, not accurately known and true values in individual patients may deviate about 30% from Langewouters' study population average. Thus the uncertainty in computed cardiac output is also 30%. Therefore, to derive absolute cardiac output, calibration against thermodilution is performed once for each patient [6, 9].

The *Hemac* pulse contour method is part of a hemodynamic monitoring and automated blood pressure control program, recently developed by two of the authors. Its pulse contour method is based on a three-element Windkessel model, similar to the *Modelflow* method. However, instead of relying on in vitro, non-linear relations between cross-sectional area of the aorta and arterial pressure described by Langewouters [23] we used in vivo measurements of patients to correct the Langewouters relations. Via this new pressure/volume relationship we computed for each heartbeat the Windkessel compliance and aortic characteristic impedance, based on mean arterial pressure of the heartbeat. Total peripheral resistance was used from the previous heartbeat. Blood flow is found by solving the differential equation of the three-element Windkessel model. Stroke volume is given by integrated the flow over the ejection time of the heartbeat. Multiplying the stroke volume by the heart rate gives the cardiac output. Next, a new value of peripheral resistance is found by dividing the mean pressure by the computed cardiac output. Calibration with thermodilution improves the absolute accuracy of the method.
The *PulseCO* cardiac output method (LiDCO, London, UK) provides stroke volume from the arterial pressure waveform using an autocorrelation algorithm. The algorithm is not dependent on waveform morphology, but, it calculates nominal stroke volume after a pressure to volume transformation using a curvilinear pressure/volume relationship. The nominal stroke volume is converted to actual stroke volume by calibration of the algorithm. Usually, the calibration is performed by an independent indicator dilution measurement, e.g. lithium dilution cardiac output from the LiDCO system [10–12]. To allow comparisons with other measuring methods, in this study, a standard bolus thermodilution cardiac output method was used for calibration.

The *PiCCO* system (Pulsion Medical Systems, Munich, Germany) utilises pulse contour analysis according to a modified version of Wesseling’s cZ algorithm [13, 16]. This pulse-contour algorithm analyses the actual shape of the pressure waveform in addition to the area under the systolic portion of the pressure wave. The software takes into account the individual aortic compliance and systemic vascular resistance based on the following considerations. During systole, more blood is ejected from the left ventricle into the aorta than actually leaves the aorta. During the subsequent diastole, the volume remaining in the aorta flows into the arterial network at a rate determined by the aortic compliance (C), systemic vascular resistance (R), and the blood pressure (Windkessel effect). The shape of the arterial pressure curve (exponential decay time = R × C) after the dicrotic notch is representative for this passive emptying of the aorta. The systemic vascular resistance, R, is determined by the quotient of mean arterial pressure (MAP) and cardiac output measured by the reference method (R = MAP/CO). As the decay time and R are known, the compliance, C, can be computed. The PiCCO algorithm is summarised in the following equation:

\[ \text{CO}_{\text{Pi}} = K \times HR \int \left( \frac{P(t)}{SVR} + C_{(p)} \right) \times \frac{dP}{dt} \, dt \]

where \( \text{CO}_{\text{Pi}} \) = cardiac output; \( K \) = calibration factor; \( HR \) = heart rate; \( P \) = arterial blood pressure; \( \int P(t) \, dt \), area under the systolic part of the pressure curve; \( SVR \) = systemic vascular resistance; \( C_{(p)} \) = pressure-dependent arterial compliance; and \( \frac{dP}{dt} \) describes the shape of the pressure wave.

*The calibration and reference method*

Thermodilution cardiac output measurements were performed with a computer controlled injectate syringe, an iced injectate container (CO-SET, Edwards, Irvine, CA, USA), a motor driven injectate syringe, a thermodilution pulmonary artery catheter, and a COM-2 cardiac output computer (Edwards). The start of a ventilatory cycle was derived from the ventilator. At precisely timed delays, four bolus injections (i.e. after 25% or 50% or 75% or 100% of respiratory cycle) were automatically started [24–26]. The averaged value of four measurements, equally spread over the ventilatory cycle, was assumed to represent the mean cardiac output [24].

*Data analysis*

We excluded the first series of cardiac output values in each patient from further analysis because it was used to calibrate the five pulse contour methods, and thus resulted in zero difference between the thermodilution measurements and the method to be evaluated.
To evaluate the tracking capability of the pulse contour methods for each patient, a trend score was computed. The trend score in an individual patient is found by subtracting the calibration (first cardiac output value) from consecutive cardiac output measurements. A positive trend is observed if the changes in cardiac output were in the same direction, whereas a negative trend was scored with changes in opposite direction. Ideally, only positive scores should be present. Separate scores were counted for changes when thermodilution cardiac output values differed by at least a clinically relevant 0.5 l.min⁻¹.

Hemodynamic stability was verified by analysis of mean arterial pressure and heart rate during a thermodilution series. Stability was considered absent if mean arterial pressure and heart rate averaged per injection period deviated more than 5% from their series average [9]. A condition of severe, persistent arrhythmias during thermodilution passage was additionally considered as absence of stability. If stability was not present, the series was excluded from further analysis.

Statistics
We used Bland-Altman analysis with the difference in cardiac output between COtd and each of the five pulse contour techniques plotted against their mean [27]. The agreement between pulse contour and thermodilution cardiac output is computed as the bias (mean (SD)), with limits of agreement computed as bias (2 SD) when differences followed normal distributions [27]. Normality was tested with the Kolmogorov-Smirnov one-sample test. The coefficient of variation was computed as CV = (SD/mean) × 100%. The agreement in changes was computed using cross tabulation. Data averages are given as mean (SD). A $p$-value < 0.05 was considered statistically significant.

Results
In five female and nineteen male patients, we performed 248 series of four cardiac output measurements. Twenty-four measurements were rejected due to heart rhythm irregularities or hemodynamic instability during measurements (defined as a deviation in mean arterial pressure of more than 5% within the series). Furthermore, 25 series were rejected because one or more of the pulse contour methods included in our study detected an abnormal/error condition. In four measurements an error caused dysfunction of all methods indicated by damped wave form detected by the Modelflow method, in 12 measurements the LiDCO device indicated unstable data, the dicrotic notch was not properly detected by the PiCCO and Hemac in twelve patients and in six patients by the cZ method. Some series were rejected by more than one device. Thus, 199 series of measurements fell within the pre-set criteria and were accepted by all five pulse contour methods, and these were analysed.

The range of thermodilution cardiac output values was 2.14 to 7.55 l.min⁻¹, mean value 4.81 l.min⁻¹. The values of the five different pulse contour methods and of thermodilution are presented in Table 3.1. Bland-Altman analysis (Fig. 3.2 and Table 3.2) showed the agreement between thermodilution cardiac output and each of the five different pulse contour methods.
Table 3.1 Cardiac output by thermodilution and each of the five pulse contour methods.

<table>
<thead>
<tr>
<th>Method</th>
<th>Mean CO l.min(^{-1})</th>
<th>Range of CO max l.min(^{-1})</th>
<th>min l.min(^{-1})</th>
</tr>
</thead>
<tbody>
<tr>
<td>COtd</td>
<td>4.81</td>
<td>2.14</td>
<td>7.55</td>
</tr>
<tr>
<td>cZ</td>
<td>4.57</td>
<td>2.22</td>
<td>7.21</td>
</tr>
<tr>
<td>MF</td>
<td>4.80</td>
<td>2.52</td>
<td>7.13</td>
</tr>
<tr>
<td>LiDCO</td>
<td>4.97</td>
<td>2.53</td>
<td>8.90</td>
</tr>
<tr>
<td>PiCCO</td>
<td>4.66</td>
<td>2.07</td>
<td>9.67</td>
</tr>
<tr>
<td>Hemac</td>
<td>4.74</td>
<td>2.38</td>
<td>7.99</td>
</tr>
</tbody>
</table>

Results of 199 observations. CO, cardiac output; mean, mean value of all series of CO measurements; max, min, maximal and minimal value of CO respectively; COtd, cardiac output by thermodilution.

No statistical difference could be detected between the normal distribution and the distributions of the differences of thermodilution and each of the five methods (the p value ranged from 0.08 to 0.86). The difference between thermodilution and Wesseling’s cZ, the PiCCO and the LiDCO methods showed a small bias. The Bland-Altman plot (Fig. 3.2) shows that the spread of values is different among the methods. This is confirmed by ANOVA, which showed significant (\(p < 0.001\) unequal homogeneity of the variances of the five methods.

The Modelflow and Hemac pulse contour methods have the smallest bias (0.00 and 0.06 l.min\(^{-1}\)) and the smallest range of the limits of agreement (-0.74 to 0.74, and -0.81 to 0.93 l.min\(^{-1}\)). Bias and limits of agreement for LiDCO were -0.17 and -1.55 to 1.20 l.min\(^{-1}\), respectively, and for PiCCO, 0.14 and -1.60 to 1.89 l.min\(^{-1}\), respectively.

Tracking cardiac output with serial measurements

The changes in cardiac output of each of the five pulse contour methods against changes in thermodilution cardiac output are shown in figure 3.3. The changes in cardiac output in all five pulse contour methods correlate significantly with the changes in cardiac output by thermodilution.

The agreement of positive and negative changes in COtd and CO in each of the five pulse contour methods are calculated using cross tabulation. We found the highest score for the Modelflow and Hemac methods, and a lower score for the LiDCO and PiCCO methods (Table 3.3). These scores improve if clinically irrelevant changes smaller than 0.5 l.min\(^{-1}\) (i.e. < 10% change) are not counted. Of the changes 96% were in agreement with each other for the Modelflow and Hemac methods.
Figure 3.2 Bland-Altman plot with cardiac output values in five pulse contour methods and cardiac output values by conventional thermodilution method. CO, cardiac output; COtd, CO by thermodilution; COcz, CO by Wesselings cZ method; COmf, CO by Modelflow; COLi, CO by the LiDCO system; COpi, CO by the PiCCO system; COhe, CO by the Hemac system. The solid line represents the bias and the dashed line the limits of agreement by 2 SD.
Table 3.2 Bland-Altman analysis of five pulse contour methods.

<table>
<thead>
<tr>
<th>method</th>
<th>Npat</th>
<th>Nobs</th>
<th>Difference with COtd</th>
<th>Limits of agreement</th>
<th>Calculated precision with COtd</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Bias</td>
<td>Precision</td>
<td>lower l.min⁻¹</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>l.min⁻¹</td>
<td>%</td>
<td>l.min⁻¹</td>
</tr>
<tr>
<td><strong>Current study</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>cZ</td>
<td>27</td>
<td>199</td>
<td>0.23</td>
<td>4.81</td>
<td>0.52</td>
</tr>
<tr>
<td>MF</td>
<td>27</td>
<td>199</td>
<td>0.00</td>
<td>0.03</td>
<td>0.37</td>
</tr>
<tr>
<td>LiDCO</td>
<td>27</td>
<td>199</td>
<td>-0.17</td>
<td>-3.60</td>
<td>0.69</td>
</tr>
<tr>
<td>PiCCO</td>
<td>27</td>
<td>199</td>
<td>0.14</td>
<td>3.00</td>
<td>0.87</td>
</tr>
<tr>
<td>Hemac</td>
<td>27</td>
<td>199</td>
<td>0.06</td>
<td>1.21</td>
<td>0.44</td>
</tr>
<tr>
<td><strong>Literature survey</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>cZ</td>
<td>193</td>
<td>675</td>
<td>0.07</td>
<td>1.33</td>
<td>0.64</td>
</tr>
<tr>
<td>MF</td>
<td>103</td>
<td>796</td>
<td>-0.03</td>
<td>-0.48</td>
<td>0.56</td>
</tr>
<tr>
<td>LiDCO</td>
<td>88</td>
<td>301</td>
<td>-0.02</td>
<td>-0.37</td>
<td>0.65</td>
</tr>
<tr>
<td>PiCCO</td>
<td>144</td>
<td>1021</td>
<td>-0.07</td>
<td>-1.26</td>
<td>1.01</td>
</tr>
<tr>
<td>Hemac</td>
<td>none</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Npat, number of patients; Nobs, number of observations; bias, mean difference between thermodilution cardiac output and each of the five pulse contour cardiac output; %, percentage of mean cardiac output; precision, is standard deviation (SD) of the bias; limits of agreement as bias ± 2SD; calculated precision assuming a precision of 5% or 10% of the thermodilution method.
Figure 3.3 Relationship between changes in cardiac output values in five pulse contour plotted against changes and changes in cardiac output values by conventional thermodilution method. For abbreviations see figure 3.2. The line of identical change is indicated (dashed line).
Table 3.3 Trend score of changes in cardiac output by thermodilution and by five pulse contour methods.

<table>
<thead>
<tr>
<th>Method</th>
<th>Agreement %</th>
<th>Disagreement %</th>
</tr>
</thead>
<tbody>
<tr>
<td>All data n=199</td>
<td></td>
<td></td>
</tr>
<tr>
<td>cZ</td>
<td>77</td>
<td>23</td>
</tr>
<tr>
<td>MF</td>
<td>81</td>
<td>19</td>
</tr>
<tr>
<td>LiDCO</td>
<td>72</td>
<td>28</td>
</tr>
<tr>
<td>PiCCO</td>
<td>70</td>
<td>30</td>
</tr>
<tr>
<td>Hemac</td>
<td>81</td>
<td>19</td>
</tr>
<tr>
<td>Data exclusion of changes COtd from -0.5 to +0.5 L/min n=99</td>
<td></td>
<td></td>
</tr>
<tr>
<td>cZ</td>
<td>91</td>
<td>9</td>
</tr>
<tr>
<td>MF</td>
<td>96</td>
<td>4</td>
</tr>
<tr>
<td>LiDCO</td>
<td>88</td>
<td>12</td>
</tr>
<tr>
<td>PiCCO</td>
<td>84</td>
<td>16</td>
</tr>
<tr>
<td>Hemac</td>
<td>96</td>
<td>4</td>
</tr>
</tbody>
</table>

n, number of observations; agreement, sum of percentage of data points in the upper right quadrant and in the lower left quadrant of figure 3.3; disagreement, sum of percentage of data points in the upper left quadrant and in the lower right quadrant of figure 3.3.

Discussion

We evaluated the bias, precision and tracking ability of five different pulse contour techniques by simultaneous comparison of their cardiac output values with the cardiac output values measured by the conventional thermodilution technique. The mean difference in cardiac output between thermodilution and each of the five methods is low (range -0.17 to 0.33 l.min⁻¹). However, the limits of agreement differ considerably, with the best results being found for the Modelflow and Hemac methods. Besides this, the Modelflow and Hemac were the most reliable in tracking changes in cardiac output, compared with COtd.

Jansen and van den Berg recently published the results of a literature survey on continuous cardiac output monitoring [20], which reported the results of Wesseling’s cZ, Modelflow, LiDCO and the PiCCO method. No published results are available yet for the Hemac pulse contour method.

We found in our study better precision and limits of agreement for each of the pulse contour methods than those published, except for the LiDCO (Table 3.2). This was true for the PiCCO method where we used the radial artery pressure instead of the femoral artery pressure.

The data used in this study were filtered out by preset exclusion criteria and needed to be accepted by all five pulse contour methods. We could include 199 measurement series of outspoken quality in our evaluation. Having data accepted by all five pulse contour methods is clinically impractical, but we consider this strategy as the fairest for the purpose of our study. As this study was set up to investigate the bias, precision and tracking changes in cardiac output, comparison of cardiac output should not be impaired by inadequate arterial pressure recordings or by a poor reference method.

We used the averaged result of four thermodilution measurements under stable hemodynamic and ventilatory conditions to calibrate each of the five pulse contour methods once per patient. Thereafter, we used the same technique as reference
method. The injections for thermodilution cardiac output measurement were synchronised with the mechanical ventilation, and spread over the ventilatory cycle. In this way much closer estimates of real mean cardiac output can be obtained [24–26] because ventilatory effects on circulation are taken into account. In a previous study we showed that our thermodilution errors are probably limited to no more than 5% SD, whereas in clinical practice an SD of 10–20% is accepted. Application of this precise calibration and reference method may have positively influenced our results.

Because aortic pressure is usually not available clinically, radial artery or femoral artery pressure is used instead. Although the radial and femoral pressure waves are distorted with respect to aortic pressure, the pulse contour methods should accept these pressures. Measurement of cardiac output using Wesseling’s cZ and Modelflow methods is not affected by whether the arterial pressure is measured in the aorta or in the radial artery [6]. Our study shows that cardiac output estimates from radial pressure can be accurate. In a recently published study [21] we showed the interchangeability of femoral artery pressure and radial artery pressure measurements as the input for the PiCCO system (Bland-Altman analysis showed a bias of -0.01 l.min⁻¹, and limits of agreement from -0.62 to 0.60 l.min⁻¹). Therefore, it seemed justified to use the radial pressure as input for the PiCCO system as we did in our comparison.

Critchley and Critchley [28] stated that if a new method is to replace an older, established method, the new method should have errors not greater than the older method. Therefore, knowledge and a careful application of the older method as a reliable reference method are essential for a good evaluation of a new technique. Otherwise, the difference between the evaluated method and the reference method could be determined mainly by the reference method.

Clinically, the conventional thermodilution method has been accepted as the ‘gold standard’. However, single estimates of cardiac output show substantial scatter (with a precision of 15%) [24, 26, 29, 30]. To improve the precision, the results of multiple measurements have to be averaged. A triplicate, randomly injected series of thermodilution measurements has an error of approximately 10% [24, 29, 30]. The averaged result of four thermodilution measurements at moments equally spread over the ventilatory cycle has an error of less than 5% [24].

The precision of the new method can be computed if the precision of the reference (ref) and the precision of the comparison (dif) are known using Pythagoras’ law: new = √(dif² − ref²) [28]. The averaged precision of each of the five pulse contour methods was calculated from the averaged differences between each of the five pulse contour methods and the conventional bolus thermodilution method, assuming two levels of precision for the thermodilution, i.e. 10% and 5% (Table 3.2).

None of the five pulse contour methods can replace the thermodilution technique with four measurements equally spread over the ventilatory cycle, even after calibration by a precise thermodilution technique. However, the Modelflow method (5% vs 6%) and the Hemac method (5% vs 7%) come close (Table 3.2). Most of the pulse contour methods can replace the thermodilution technique with three measurements randomly applied.

All pulse contour methods included in our study require calibration for each patient using a method such as thermodilution. After calibration, the purpose of the pulse contour methods is to track clinical changes in cardiac output accurately. To analyse the tracking capabilities of the five pulse contour method by Bland-Altman analysis seems insufficient. Therefore, we plotted the changes in cardiac output by the five methods against thermodilution cardiac output (Fig. 3.3). Furthermore, in an attempt
to quantify the tracking quality of the five methods, we compared the number of changes of the same direction in cardiac output found by thermodilution with those found by each of the five methods (Table 3.3). If we consider changes smaller than 10% (i.e. a change of 0.5 l.min\(^{-1}\) on a mean CO of 5.0 l.min\(^{-1}\)) as clinical irrelevant, then 96% of the changes were correctly followed by the Modelflow and Hemac method. Therefore, these two methods are able to follow changes in cardiac output accurately.

**Conclusion**

All pulse contour techniques need a reliable invasive calibration. After calibration, most methods may replace the thermodilution method with a precision of 10% (i.e. the averaged result of three randomly performed measurements). The Modelflow and Hemac techniques could replace the thermodilution estimates based on the averaged result of four measurements done equally, spread over the ventilatory cycle. The slightly lower precision of the continuous pulse contour cardiac output techniques may, in clinical settings, be outweighed by the advantages of being automatic and continuous. Under research conditions the use of the conventional thermodilution method with four measurements equally spread over the ventilatory cycle remains the method of choice. Due to the character of the examined study population, it must be emphasised that the findings of this study are still restricted to patients without congestive heart failure, with normal heart rhythm and reasonable peripheral circulation.

*Potential conflict of interest*

None of the authors has any commercial interest either in the devices or in the manufacture of the devices named in this study.
References


