Lack of agreement between pulmonary arterial thermodilution cardiac output and the pressure recording analytical method in postoperative cardiac surgery patients‡

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Editor’s key points

- The pressure recording analytical method (PRAM) is a recent development of uncalibrated pulse-contour analysis-based methods for CO determination.
- 46 paired CO measurements of PRAM-and thermodilution-CO were obtained in 23 patients after cardiac surgery.
- Large differences between PRAM-CO and ThD-CO were found with percentage error of 87%.
- PRAM-CO cannot replace thermodilution-CO in cardiac surgery patients.

Background. Pulse-contour analysis method (PCM) cardiac output (CO) monitors are increasingly used for CO monitoring during anaesthesia and in the critically ill. Very recently, several systems have been introduced that do not need calibration; among them the pressure recording analytical method (PRAM). Sparse data comparing the accuracy of the PRAM-CO with conventional thermodilution CO (ThD-CO) in cardiac surgery patients are available.

Methods. In this prospective comparison study, paired CO measurements with a pulmonary artery catheter and a PRAM monitoring set were obtained 20–30 min apart (t1, t2) in 23 extubated patients on the first postoperative day after cardiac surgery. Data were analysed by the Bland–Altman method.

Results. A total of 46 paired CO measurements (23 for each interval) were collected. The Bland–Altman analysis showed a mean difference (bias) of 0.0 litre min⁻¹ and limits of agreement (1.96 SD) of 4.53 to −4.54 litre min⁻¹ [upper 95% confidence interval (CI), 3.26–5.80; lower 95% CI, −5.8 to −3.27]. The percentage error (1.96 SD/mean of the reference method) was 87%.

Conclusions. These results question the reliability of the PRAM technology for the determination of CO in postoperative cardiac surgery patients.

Keywords: cardiac surgery; haemodynamic monitoring; pressure recorded analytical method; pulmonary arterial thermodilution; pulse-contour analysis

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Establishing and maintaining adequate cardiac output (CO) and oxygen delivery is a pivotal part of perioperative haemodynamic management in patients undergoing cardiac surgery.1 Traditionally, CO monitoring in this field has been accomplished by the use of a pulmonary artery catheter (PAC) and pulmonary arterial thermodilution (PA-ThD), an approach that is still favoured by many clinicians.2

Arterial pulse-contour method (PCM) systems offer a promising alternative method for the determination of CO. Several of these monitoring systems are increasingly used during cardiac surgery.3–6 The pressure recording analytical method (PRAM) is a relatively new technology that does not require external calibration or adjustments for age, gender, or anthropometric variables (height and weight). The technique is based on the analysis of peripheral artery waveform morphology and has been extensively described elsewhere.7–8 It is of note that PRAM is recommended also for use in patients treated with an intra-aortic balloon pump (IABP),9,10 an unique feature in comparison with the other commercially available PCM technologies.

† These authors contributed equally to this work.
‡ This article is accompanied by Editorial II.
Experimental data show an acceptable agreement of PRAM-derived CO (PRAM-CO) in comparison with (ThD-CO) and suggest that PRAM is a useful alternative for CO monitoring. However, clinical comparative data about the accuracy of the PRAM system in comparison with standard technologies are still sparse.

The present study was designed to determine the reliability of PRAM-CO in comparison with ThD-CO in a heterogeneous group of patients after cardiac surgery.

**Methods**

**Patients**

After approval by the local ethical committee and preoperative written informed consent, 27 ASA consecutive physical status III patients (13 females/14 males) were enrolled. Four patients needing postoperative treatment with an IABP were excluded from further analysis.

Mean age, height, and weight were 67 (range 51–82) yr, 166 (154–181) cm, and 71 (56–115) kg, respectively. All patients had undergone cardiac surgery with cardiopulmonary bypass and moderate hypothermia. The surgical procedures were: coronary artery bypass grafting (CABG), n=12; CABG and aortic replacement, n=6; CABG and mitral valve reconstruction, n=2; CABG and mitral valve replacement, n=2; and CABG and aortic valve replacement and mitral valve reconstruction, n=5.

Patients were studied on the first postoperative day after cardiac surgery when treated in the intensive care unit (ICU). Patients were awake, calm, and spontaneously breathing during the measurements. CO was determined twice; the first measurement cycle was performed without supplemental oxygen, the second measurement cycle was performed after the optimization of oxygen delivery with 4 litre min$^{-1}$ supplemental oxygen via a face mask with the intention to eliminate interfering instabilities of the oxygen delivery/oxygen demand ratio.

No patients with cardiac arrhythmias were included in this study; all patients were either in sinus rhythm or paced by epicardial atrial pacing electrodes. Measurements were performed during stable haemodynamic conditions achieved by continuous infusions of 0.027–0.073 μg kg$^{-1}$ min$^{-1}$ noradrenaline, 1.9–5.7 μg kg$^{-1}$ min$^{-1}$ dobutamine, and 0.22–0.54 μg kg$^{-1}$ min$^{-1}$ milrinone.

Four patients were treated with an IABP.

**Measurement of CO by thermodilution**

All patients were routinely monitored by means of a radial artery catheter, a central venous line, and a PAC (CCombo 744HF75) for semi-continuous and bolus determination of CO connected to a Vigilance II$^\text{TM}$ monitor (Edwards Lifesciences, Irvine, CA, USA). ThD-CO was calculated as the mean of at least three separate measurements not deviating more than 20% obtained over 3 min by injection of 10 ml of 4°C NaCl 0.9% solution. The two determinations of CO were performed 12–16.5 h after surgery 20–30 min apart (t1 and t2, respectively, see above).

**Basic physical principles of PRAM**

In contrast to other methods for the determination of CO from the arterial pulse like the PICCO monitor and the LiDCO system, but comparable with the FlowTrac system, the PRAM is not only based on the analysis of the systolic area under the curve of the arterial pulse but also on the analysis of the complete systolic and diastolic pulse wave. The PRAM technique does not require external calibration or adjustments for age, gender, height, or weight. Changes in the arterial pulse wave during the complete cardiac cycle systolic pressure, dicrotic notch, diastolic pressure, and additional waves that may result from pulse wave reflection (termed: points of instability) are recorded with a sampling rate of 1000 min$^{-1}$ and analysed according to the physical principles of perturbation, an analytic approach to approximate a value that cannot be calculated precisely. The theoretical and physical principles of this method have been extensively described elsewhere.

**Measurement of CO by PRAM**

A PRAM-CO MostCare monitoring set (Vygon GmbH & Co. KG, Aachen, Germany) for continuous determination of CO was connected to the standard ICU haemodynamic monitor (Infinity, Dra¨ger, Lu¨beck, Germany) and the system was set up and started according to the instructions of the manufacturer. The average of three 1 min continuous registrations with 1 min intervals between each was taken as the representative result.

**Statistical analysis**

The sample size was adjusted to comparable comparison studies. No formal power analysis was performed. A total of 54 paired CO measurements (27 for each interval) were collected. Patients requiring temporary support by an IABP were excluded from the analysis, because of lack of power in this small group of four patients. This exclusion left 46 data pairs to be analysed.

Analyses were performed by MedCalc 11.0 for Windows. After analysis for normal distribution by the Kolmogorov–Smirnov test, data were analysed parametrically by Student’s t-test. Pearson’s correlation coefficient was used to compare PRAM-CO and ThD-CO. Further, the Bland–Altman statistics, as well as percentage errors (1.96 σ⁄mean of reference method) were calculated. A mean percentage error not exceeding 30% was defined to indicate clinical useful reliability of the PRAM-CO. Data are given as mean (sd); a P-value of < 0.05 indicates statistical significance.

**Results**

The CO range was 2.6–9.2 litre min$^{-1}$ for PA-ThD and 2.4–12 litre min$^{-1}$ for PRAM.

A comparison of the measurements at t1 and t2 with a t-test for paired samples revealed no significant differences between ThD-CO (P=0.305) and PRAM-CO (P=0.280) or other haemodynamic variables (Table 1). This finding
Lack of agreement between ThD-CO and PRAM-CO

The results of the present study are clearly in contrast to other studies using PA-ThD, direct-oxygen Fick method, and Doppler echocardiography as a comparator, all coming to the conclusion that the PRAM technique is reliable for CO determinations during and after cardiac surgery and also during non-cardiac surgery. Romano and colleagues studied the reliability of PRAM in a small group of haemodynamically stable cardiac patients undergoing diagnostic right and left heart catheterization. In this study, the pressure signal was recorded from an aortic catheter and not from a radial line; an issue that may have important effects on the pulse contour. Comparably, two other studies by the same group found a good agreement between PRAM-CO and PA-ThD-CO during and after cardiac surgery. The number of patients was comparable with the size of the present study (n=32 and 28, respectively). Another study from Faltoni and colleagues comparing PRAM-CO with ThD-CO in eight cardiac surgery patients on IABP—available only as congress abstract—found good agreement between both methods, and the authors conclude that the PRAM technique may also be suitable for CO determination in patients treated with an IABP. Zangrillo and colleagues recently showed a significant correlation and clinically acceptable agreement with a percentage error of 30% between PRAM cardiac index (CI) and ThD-CI measurement in 32 haemodynamically unstable patients with IABP and/or high dose of inotropic drugs after cardiac surgery. However, in this study, measurements with artifacts caused by under- or overdamping of the arterial pressure curve were excluded without further definition of criteria on the signal quality. Good agreement between the PRAM technique and PA-ThD was found in a pig model, but the special anatomical conditions in the animal model used may have had a relevant impact on CO values.

The reason for the discrepancy between the previous work and our study is not clear. The sample size was comparable with previous studies and is of the typical size used for clinical comparison studies. The population described is representative of the typical patients treated after cardiac surgery in the ICU; most of them needing minor to moderate inotropic and vasopressor support. This is a typical condition where a non-invasive monitoring would be preferable to the invasive PAC. Further, all measurements were performed according to the instructions of the manufacturer.

Various factors may lead to erroneous ThD-CO measurements in patients after cardiac surgery, that is, acute temperature changes during rewarming in the immediate period after cardiopulmonary bypass and tricuspid regurgitation. Although the first aspect is not applicable in the presented study with patients more than 12 h after surgery, tricuspid regurgitation was ruled out by visual inspection of the central venous pressure curve and post-operative transoesophageal echocardiography.

### Table 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean t1</th>
<th>Mean t2</th>
<th>Paired samples t-test</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAP (mm Hg)</td>
<td>73.5</td>
<td>75.5</td>
<td>8.5</td>
<td>0.134</td>
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<tr>
<td>CVP (mm Hg)</td>
<td>12.0</td>
<td>11.9</td>
<td>5.6</td>
<td>0.808</td>
</tr>
<tr>
<td>PAP mean (mm Hg)</td>
<td>25.7</td>
<td>26.3</td>
<td>9.9</td>
<td>0.546</td>
</tr>
<tr>
<td>ThD-CO (litre min⁻¹)</td>
<td>5.2</td>
<td>5.2</td>
<td>0.9</td>
<td>0.573</td>
</tr>
<tr>
<td>PRAM-CO (litre min⁻¹)</td>
<td>5.1</td>
<td>5.4</td>
<td>2.3</td>
<td>0.144</td>
</tr>
<tr>
<td>SVO₂ (%)</td>
<td>64.8</td>
<td>72.6</td>
<td>5.3</td>
<td>0.002</td>
</tr>
<tr>
<td>SO₂ (%)</td>
<td>95.8</td>
<td>98.3</td>
<td>1.6</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

supported the combination of the measurements at the two time points in one analysis of a total of 46 data pairs.

The correlation between ThD-CO and PRAM-CO was r=0.313 (P=.049; 95% confidence interval (CI), 0.0–0.57), as shown in Figure 1.

The Bland–Altman analysis showed a mean difference (bias) of 0.0 (95% CI, −0.74 to 0.74) litre min⁻¹ and limits of agreement (1.96 SD) of −0.93 to 0.93 litre min⁻¹ (upper 95% CI, 3.26–5.80; lower 95% CI, −5.8 to −3.27) (Fig. 2). The percentage error (1.96 SD/mean of the reference method) was 87%.

The distribution of the data pairs in the scatter diagram (Fig. 1) suggested a growing deviation between the methods in the higher CO range. After stratification by the median of the reference method (median ThD-CO=5.1 litre min⁻¹), a second analysis for the ‘high’ and ‘low’ CO range was performed.

Patients with higher and lower CO did not differ in mean arterial pressure [ThD-CO ≥ 5.1 litre min⁻¹]: mean MAP=73.6 (SD 8.1) mm Hg, ThD-CO < 5.1 litre min⁻¹: mean MAP=76.1 (SD 9.4) mm Hg; P=0.353), the amount of norepinephrine, dobutamine, or milrinone.

In the group with median ThD-CO <5.1 litre min⁻¹, the correlation was r=0.548 (P=0.022; 95% CI, 0.1–0.81) (Fig. 3A). In the Bland–Altman analysis, the bias was −0.90 litre min⁻¹ (95% CI, −1.86 to 0.05) and limits of agreement were −2.37 litre min⁻¹ (upper 95% CI, 1.43–4.75; lower 95% CI, −6.56 to −3.24). The percentage error was 93% (Fig. 4A).

In the group with median ThD-CO ≥5.1 litre min⁻¹, the correlation was r=0.233 (P=0.283; 95% CI, −0.2 to 0.6) (Fig. 3A). In the Bland–Altman analysis, the bias was 0.29 litre min⁻¹ (95% CI, −0.68 to 1.25) and limits of agreement were 5.08 to −4.49 litre min⁻¹ (upper 95% CI, 3.40–6.74; lower 95% CI, −6.16 to −2.82). The percentage error was 78% (Fig. 4A).
Additionally, the timing, injectate temperature, and the number of averaged bolus thermodilution measurements may influence the precision of PA-ThD-CO determination. However, all measurements were randomly distributed throughout the respiratory cycle, cold saline was used as an injectate solution, and thus, it is unlikely that differences between our and previous studies may be explained by imprecision of the reference method.

A possible explanation may be that all measurements were determined from radial and therefore peripheral arterial lines. It is well known that the pulse wave in the radial artery differs from the central aortic and the femoral arterial pulse wave, an effect that has been shown to alter the reliability of other PCM-CO monitors and may at least in part explain some discrepancies of the presented to previous works. In the present study, in a subgroup of patients with high CO, we found no

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**Fig 1** Correlation between ThD-CO and PRAM-CO. ThD-CO, thermodilution cardiac output; PRAM-CO, pressure recorded analytical method.

**Fig 2** The Bland–Altman analysis comparing ThD-CO with PRAM-CO. ThD-CO, thermodilution cardiac output; PRAM-CO, pressure recorded analytical method.
significant correlation between PRAM-CO and ThD-CO. As the
groups did not differ in the amount of inotropic agents or
vasopressors received, this lack of reliability in the subgroup
cannot be attributed to a change in arterial compliance due
to excessive vasopressor doses.

A methodological limitation is the application of the
Bland–Altman analysis for two repeated measures. However, this approach is appropriate for exploration of
data; therefore, the presented results have to be regarded
as descriptive rather than confirmatory.

In conclusion, the aforementioned factors do not suffi-
ciently explain the profound lack of agreement between
ThD-CO and PRAM-CO, with even no significant correlation
between the two methods in the range of higher CO. In
search for a minimally invasive tool for the low-to-medium
risk cardiac surgery patient, we chose a situation with more
or less stable haemodynamic conditions for the present
study. The immediately postoperative situation would have
involved various confounding factors as rapidly changing
arterial pressures due to changes in peripheral vascular
resistance, influence of rewarming, and agitation in awaken-
ing. Measurements in this period would have needed a much
greater sample size to allow reliable conclusions. However,
the lack of interchangeability of the ThD-CO and PRAM-CO

Fig 3 Correlation between ThD-CO and PRAM-CO after stratification by median thermodilution cardiac output. (a) ThD-CO<5.1 litre min⁻¹. (b) ThD-CO≥5.1 litre min⁻¹. ThD-CO, thermodilution cardiac output; PRAM-CO, pressure recorded analytical method.
even under stable conditions does not encourage further studies in more complex haemodynamic situations. On the basis of our data, we cannot make statements on reliability of the PRAM-CO under mechanical circulatory support. Further investigation is needed validating the use of PRAM-CO in patients with IABP support and other devices. Keeping in mind the limitation of the presented study, that is, the small sample size, our findings suggest that the underlying algorithm in the PRAM technology does not sufficiently reproduce the CO measured with ThD in haemodynamically stable patients after cardiac surgery. Consequently, at least until further modifications of the algorithm are available, the routine use of the PRAM technology for the determination of CO in cardiac surgery patients cannot be recommended. Ideally, future investigations should determine in a larger group of patients whether using a more central artery for recording the arterial pressure curve might improve the accuracy of the PRAM method.

**Conflict of interest**

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