Oesophageal Doppler and calibrated pulse contour analysis are not interchangeable within a goal-directed haemodynamic algorithm in major gynaecological surgery†

A. Feldheiser1‡, O. Hunsicker1‡, H. Krebbel1, K. Weimann1, L. Kaufner1, K.-D. Wernecke2 and C. Spies1*

1 Department of Anaesthesiology and Intensive Care Medicine, Campus Charité Mitte and Campus Virchow-Klinikum, Charité-University Medicine Berlin, Augustenburger Platz 1, 13353 Berlin, Germany
2 Charité-University Medicine Berlin and SOSTANA GmbH Berlin, Wildensteiner Straße 27, 10318 Berlin, Germany
* Corresponding author. E-mail: claudia.spies@charite.de

Editor’s key points
- Stroke volume (SV) measurements are commonly used to guide goal-directed fluid therapy.
- In a previous study, the authors recorded SV before and after a fluid challenge.
- SV was measured with oesophageal Doppler ultrasonography and pulse contour analysis.
- In the current study, they assessed concordance between SV changes as assessed by the above techniques.

Background. Evidence for the benefit of an intraoperative use of a goal-directed haemodynamic management has grown. We compared the oesophageal Doppler monitor (ODM, CardioQ-ODMTM) with a calibrated pulse contour analysis (PCA, PiCCO2TM) with regard to assessment of stroke volume (SV) changes after volume administration within a goal-directed haemodynamic algorithm during non-cardiac surgery.

Methods. The data were obtained prospectively in patients with metastatic ovarian carcinoma undergoing cytoreductive surgery. During surgery, fluid challenges were performed as indicated by the goal-directed haemodynamic algorithm guided by the ODM. Monitors were compared regarding precision and trending. Clinical characteristics associated with trending were studied by extended regression analysis.

Results. A total of 762 fluid challenges were performed in 41 patients resulting in 1524 paired measurements. The precision of ODM and PCA was 5.7% and 6.0% (P = 0.80), respectively. Polar plot analysis revealed a poor trending between ODM and PCA with an angular bias of −7.1°, radial limits of agreement of −58.1° to 43.8°, and an angular concordance rate of 67.8%. Dose of norepinephrine (NE) (scaled 0.1 µg kg⁻¹ min⁻¹) [adjusted odds ratio (OR) 0.606 (95% confidence interval, CI: 0.404–0.910); P = 0.016] and changes in mean arterial pressure (MAP) to a fluid challenge (scaled 10%) [adjusted OR 0.733 (95% CI: 0.635–0.845); P < 0.001] were associated with trending between ODM and PCA, whereas there was no relation to type of i.v. solution.

Conclusions. Despite a similar precision, ODM and PCA were not interchangeable with regard to measuring SV changes within a goal-directed haemodynamic algorithm. A decrease in interchangeability coincided with increasing NE levels and greater changes of MAP to a fluid challenge.

Keywords: goal-directed therapy; haemodynamic monitoring; oesophageal Doppler; pulse contour analysis; trending

Accepted for publication: 26 April 2014

Mortality after non-cardiac surgery is still high.1 During anaesthesia and in intensive care, conventional haemodynamic parameters such as arterial pressure (AP), central venous pressure (CVP), and urine output (UO) combined with clinical experience are still most frequently used to guide the haemodynamic management.2 However, AP, CVP, UO, and clinical signs are poor parameters to both predict and confirm an increase in stroke volume (SV) or cardiac index after volume administration.3 4 In recent years, evidence has grown for the use of a goal-directed haemodynamic management guided by oesophageal Doppler monitor (ODM, CardioQ-ODMTM) to increase circulatory flow while avoiding a detrimental hypo- and notably hypervolaemic state.5–7 Within most of the published goal-directed haemodynamic

‡ Both authors contributed equally.
algorithms, the response to i.v. volume administration is assessed by changes of SV.\(^8\)\(^9\)

The PiCCO\(^{TM}\) system offers a calibrated pulse contour analysis (PCA) method, which is well validated in intensive care medicine and the perioperative setting of cardiac surgery.\(^10\)\(^–\)\(^16\) The PCA has also been used to guide intraoperative haemodynamic algorithms in non-cardiac surgery. These studies used static or dynamic variables to assess cardiac preload\(^15\)\(^\)\(^16\) or to evaluate volume responsiveness.\(^17\)\(^\)\(^18\) However, none of the studies has guided haemodynamic therapy by SV measured by PCA to confirm a beneficial volume administration.

To date, most of the method comparison studies have focused on comparing agreement of absolute values of SV or cardiac output between haemodynamic monitors at specific predefined time points in critical care medicine as if they were tools for snapshot measurements.\(^19\) But the monitors have to track haemodynamic changes in flow variables\(^20\) to indicate and most notably confirm a beneficial volume administration as the therapeutic impact is more dependent on tracking changes than on device accuracy.\(^19\)

Therefore, the objective of this study was to investigate if ODM and PCA are interchangeable with respect to measuring SV changes within a goal-directed haemodynamic algorithm in major non-cardiac surgery.

We aimed (i) to compare the ODM and PCA in terms of intrinsic precision and the resulting least significant change (LSC); (ii) to investigate the agreement of SV changes (trending) between both monitors to i.v. fluid administration during an outcome-based goal-directed haemodynamic algorithm during the course of surgery; and (iii) to identify perioperative clinical characteristics being associated with trending between ODM and PCA.

**Methods**

This study is a subanalysis of a previously published randomized controlled trial comparing a balanced crystalloid with a balanced colloid within a goal-directed haemodynamic algorithm (BalaCriCo, ISRCTN 53154834).\(^21\) This subanalysis investigates the interchangeability of two haemodynamic monitors including data obtained from a PCA that were not reported in the previous publication of the main study. The entire data were obtained from the per-protocol group of the BalaCriCo trial resulting in a subset of 48 patients with metastatic ovarian carcinoma undergoing cytoreductive surgery. Ethical approval was given by the Ethical Committee (No. EK 12 581/08) and the competent German authority (Bundesinstitut für Arzneimittel und Medizinprodukte, No. 4034705) and was internationally subscribed (ISRCTN 53154834). The trial was conducted at Charité-University Medicine Berlin, Campus Virchow Klinikum, Berlin, Germany, and written informed consent was obtained from all patients.

**Clinical pathway**

Participants were treated within an interdisciplinary clinical pathway defined by standard operating procedures always accessible in the intranet of the University Hospital of the Charité as published previously.\(^21\) Briefly, the patients had a low thoracic epidural catheter placed which was infused with a bolus and a basal rate of ropivacaine and sufentanil during surgery. After induction of anaesthesia and oral intubation, all patients had a central venous line inserted. The distal lumen was connected to the PCA monitoring kit (PV8215, Pulsion Medical Systems, Munich, Germany). In addition, a thermistor-tipped arterial catheter (PVPK2015L20-A, Pulsion Medical Systems) was inserted via the femoral artery and was then connected to the pulse contour monitor (PiCCO\(^{TM}\), Pulsion Medical Systems). After placing a nasogastric tube, the oesophageal Doppler probe (DP12, Deltex Medical, Chichester, UK) was inserted nasally and connected to the oesophageal Doppler monitor (CardioQ-ODM\(^{TM}\); Deltex Medical). After zeroing of the arterial and central venous line to atmospheric pressure and checking for over- and underdamping by performing a fast flush test, calibration of the PCA was performed by a three-time transpulmonary thermodilution with 20 ml of ice-cold normal saline (<8°C). The obtained values were then averaged. Ensuring an ideal placement, the Doppler probe was carefully adjusted until a crisp Doppler sound was heard and a maximization of the velocity–time wave was seen on the ODM screen. During surgery, patients were ventilated using a pressure-controlled mode targeting to maintain normoventilation without any spontaneous breathing.

**Intraoperative haemodynamic management**

The haemodynamic management was performed according to an outcome-based goal-directed haemodynamic algorithm\(^9\) guided by the ODM.

Briefly, after induction of anaesthesia and establishing the haemodynamic monitoring, volume optimization was started. First, an initial fluid challenge of 200 ml of i.v. fluid was given over 5 min. If SV measured by ODM (SV\(_{ODM}\)) failed to increase by ≥10%, no further fluid challenge was given. If SV\(_{ODM}\) increased by ≥10%, additional fluid challenges with an i.v. bolus of 200 ml were given until no further increase in SV\(_{ODM}\) of ≥10% could be measured. After a period of 15 min or clinically relevant haemodynamic changes of mean arterial pressure (MAP) or heart rate (HR), SV\(_{ODM}\) was measured again and a decrease of >10% compared with SV\(_{ODM}\) after the last beneficial fluid challenge re-indicated an optimization trial.

Fluid challenges were performed during the entire course of surgery as indicated by the goal-directed haemodynamic algorithm. Fluid challenges were conducted either with a balanced crystalloid (Jonosteril\(^{®}\), Fresenius Kabi, Bad Homburg, Germany) or a balanced colloid solution (Voluven\(^{®}\), 6%, 130/0.4, Fresenius Kabi) as randomized for each particular patient. At the maximum dose of the study fluid (when 50 ml kg\(^{-1}\) body weight was reached), the fluid challenges were conducted by transfusion of fresh-frozen plasma (FFP). In addition, the haemodynamic algorithm indicated a bolus or continuous administration of norepinephrine (NE) if MAP decreased below 70 mm Hg (for preoperative normotensive patients). Positive inotropic drugs were given if cardiac index decreased below 2.5 litre min\(^{-1}\) m\(^{-2}\), while SV could not be raised further by
volume administration. In the case of an acute haemodynamic instability or massive bleeding and a decrease in corrected flow time (FTc) below 300 ms, the volume bolus of the fluid challenge was doubled to 400 ml until haemodynamic stability was reached again.

The goal-directed haemodynamic algorithm distinguished between volume and fluid therapy. While volume therapy was carried out by a goal-directed approach as described above, fluid therapy was performed by an intraoperative continuous and restrictive maintenance rate of a balanced crystalloid solution.

Data collection
All fluid challenges and measurements were performed and recorded by members of the study group well trained in handling the ODM and PCA.

The following haemodynamic variables were simultaneously obtained from both monitors before and 1–2 min after a fluid challenge: stroke volume (SV_{ODM}), SV index (SVI_{ODM}), cardiac index (CI_{ODM}), peak velocity (PV_{ODM}), flow time corrected (FTC_{ODM}), and systemic vascular resistance index (SVRI_{ODM}) by ODM; SV index (SVI_{PCA}) and pulse contour cardiac index (CI_{PCA}) by PCA; systolic AP, diastolic AP, and MAP, CVP, and HR.

SVI_{ODM} was computed by averaging five heart cycles, while SVI_{PCA} was calculated by averaging a period of 12 s. During volume administration and data collection, there were no changes in anaesthetic treatment, ventilator settings, dose of NE or inotropic drugs, and patient positioning. Before every optimization period, the Doppler probe was readjusted to ensure an ideal placement. Every 30 min, a three-time transpulmonary thermodilution of the PCA, zeroing of the arterial and central venous line, and a fast flush test were performed. Data were recorded manually and digitally and transferred to a digital database after operation.

Haemodynamic data were excluded from analysis for the following reasons: (i) missing data before or after a fluid challenge, (ii) doubled volume bolus of 400 ml, (iii) presence of any arrhythmia, or (iv) any damping of the arterial waveform. The entire haemodynamic data set of a particular patient was excluded from analysis if PCA could not be established at the beginning of surgery or patients had a known right ventricular failure, valvular heart disease, or intracardiac shunt.

Statistical analysis
According to the haemodynamic algorithm, a positive flow response to volume administration was defined as a volume-induced increase in SV of ≥10% (=responder) displayed by the ODM. A negative flow response (=non-responder) was defined as failing of SV to increase by ≥10%. Data were expressed as median (25%, 75% quartiles), mean (± SD), or as frequencies (%). The non-parametric exact Wilcoxon test for pairwise comparisons and the exact Mann–Whitney tests for independent groups were used.

Precision is an intrinsic system property and subsequently defined as the variability of the obtained values due to intrinsic random errors of measurements of the device and not as inter-patient variability of the bias as commonly used with the Bland–Altman analysis. Intrinsic precision is of major importance as it determines the LSC which is the change of SV that needs to be measured by a device to indicate a real change by the patient which is not caused by random error of the device. The coefficient of variation (CV=±SD/mean) and the precision (P=2×CV) of the ODM and PCA were calculated from four independent measurements per patient during a haemodynamic stable period after induction of anaesthesia and establishing the haemodynamic monitors. The LSC was calculated as $P \times \sqrt{2}$.

Aiming to investigate the interchangeability of ODM and PCA with respect to measuring SV changes to a fluid challenge, we analysed trending, which was subsequently defined as the agreement of SV changes between both devices to a fluid challenge. Trending between ODM and PCA was assessed by concordance analysis based on direction of change analysis from a four-quadrant plot and by polar statistics using polar plot methodology. In the four-quadrant plot, the concordance rate was calculated as the percentage of the number of paired ΔSVI values with the same directional change in relation to the total number of ΔSVI values. Acceptable concordance was set at >90–95%. Constructing polar plots, the polar angle was derived from the angle of the ΔSVI vector of both devices with the line of identity and the radius was derived from the mean change in SVI of ODM and PCA. Trending between the two methods is shown by the angle from the polar axis and the magnitude of the change in SVI by the distance from the origin. Determining the polar statistics, negative changes were converted to positive changes by rotating through 180° allowing to calculate the mean polar angle (or angular bias) and the radial limits of agreement (RLOAs, radial sector that contains 95% of the data points) with an upper (R-ULOA) and lower (R-LLOA) limit. Acceptable trending was defined as an angular bias less than ±5° and RLOAs lying within radial limits of ±30° around the angular bias (boundary limits). The angular concordance rate was calculated as percentage of data points lying within ±30° limits. The exact $χ^2$ test was used to compare angular concordance rates between fluid challenges performed with different types of i.v. solution. In the four-quadrant and polar plot analysis, central zone data (exclusion zone) were excluded due to intrinsic random error of the measurement of the ODM and PCA. The exclusion zone size was calculated according to a new approach by Monge Garcia and colleagues as $\sqrt{(LSC_{ODM})^2+(LSC_{PCA})^2}$ implying the combined LSC of ODM and PCA.

To study clinical factors being associated with trending between ODM and PCA, multivariate generalized estimating equations (GEE) using a binary logistic model (with adjustment for multiple measurements per patient) was performed. According to the results of polar plot analysis, data points lying within a range of ±30° were defined as fluid challenges with acceptable trending between ODM and PCA. Similar to polar plot analysis, the combined LSC was used to exclude...
Results

Patient characteristic and intraoperative data of the study patients are shown in Table 1. A total of 992 fluid challenges were performed in 48 patients. The data sets of seven patients (n=135 fluid challenges) were excluded from analysis, as PCA was not established. There were no patients with known right ventricular failure, valvular heart disease, or intracardiac shunt. Another 95 fluid challenges were excluded due to missing values (n=56), volume bolus of 400 ml (n=31), or damping of the arterial waveform (n=8).

Finally, 762 fluid challenges (1524 paired measurements for each monitor) were analysed in 41 patients; of whom, two patients (n=108 fluid challenges) had no thoracic epidural established. In total, 236 fluid challenges were performed with balanced crystalloid, 299 with balanced colloid, and 227 with FFP.

According to measurements of the ODM, 390 fluid challenges resulted in an increase of SV ≥10% (responder) and in 372 fluid challenges, SV failed to increase by ≥10% (non-responder). In the responder group, all haemodynamic variables changed significantly during volume administration, whereas among non-responders, there was no clinical relevant change in any haemodynamic variable. Comparing flow variables such as SV index or cardiac index between the ODM and PCA showed a significant and clinical highly relevant difference in the responder group. In the non-responder group, SV index did not differ, whereas cardiac index showed a significant difference between ODM and PCA, which was not clinically considerable (Table 2).

The CV of the ODM and PCA was 2.9 (2.0)% and 3.0 (2.0)% resulting in a precision (P) of 5.7% and 6.0% (P=0.80), respectively. The LSC of the ODM and PCA was 8.1% and 8.5%, respectively. Change of SV displayed by the monitors after the first i.v. fluid challenge at the beginning of surgery differed significantly between ODM and PCA. ODM showed a major change in SV compared with PCA (15.1% vs 2.4%, P=0.003, Fig. 1). According to measurements of the ODM, 64% of the patients had an increase in SVI ≥10% to initial fluid challenge.
Table 2: Hemodynamic variables of 41 patients before and after a fluid challenge. Data are shown as median (25%; 75% quartiles). P-values were calculated using the exact Wilcoxon test for comparison before and after a volume administration and exact Mann–Whitney test for comparison of DSVI and DCI between monitors within the responder and non-responder group. HR, heart rate; SAP, systolic arterial pressure; DAP, diastolic arterial pressure; MAP, mean arterial pressure; CVP, central venous pressure; FTc, flow time corrected; PV, peak velocity; SVRI, systemic vascular resistance index; SV, stroke volume; SVI, stroke volume index; CI, cardiac index.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Responder (SVI ≥ 10%) (n=31)</th>
<th>Non-responder (SVI &lt; 10%) (n=10)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before</td>
<td>After</td>
<td>Change (9%)</td>
<td>Before</td>
</tr>
<tr>
<td>HR (beats min⁻¹)</td>
<td>76 (66.89)</td>
<td>76 (66.89)</td>
<td>0</td>
</tr>
<tr>
<td>SAP (mm Hg)</td>
<td>112 (100;125)</td>
<td>121 (110;133)</td>
<td>6.7 (0.001*)</td>
</tr>
<tr>
<td>DAP (mm Hg)</td>
<td>70 (61; 80)</td>
<td>76 (66; 86)</td>
<td>6.7 (0.001*)</td>
</tr>
<tr>
<td>MAP (mm Hg)</td>
<td>60 (52; 72)</td>
<td>64 (55; 77)</td>
<td>5.8 (0.001*)</td>
</tr>
<tr>
<td>CVP (mm Hg)</td>
<td>10 (6; 13)</td>
<td>10 (6; 14)</td>
<td>8.3 (0.001*)</td>
</tr>
<tr>
<td>FTcODM (ms)</td>
<td>335 (298;365)</td>
<td>366 (337;396)</td>
<td>8.6 (0.001*)</td>
</tr>
<tr>
<td>PVODM (cm s⁻¹)</td>
<td>73.4 (59.8; 92.5)</td>
<td>81.4 (64.8;103)</td>
<td>7.2 (1.9; 14.5)</td>
</tr>
<tr>
<td>SVRIODM (dyn s cm⁻²)</td>
<td>22.7 (4.1)</td>
<td>1535 (1199;1918)</td>
<td>41.2 (0.001*)</td>
</tr>
<tr>
<td>SVIODM (ml m⁻²)</td>
<td>36 (29; 42)</td>
<td>39 (32; 46)</td>
<td>8.7 (0.001*)</td>
</tr>
<tr>
<td>SAPv (m²)</td>
<td>1746 (1408; 2196)</td>
<td>1582 (1245; 1999)</td>
<td>0</td>
</tr>
<tr>
<td>SVIPCA (ml m⁻²)</td>
<td>3.1 (2.5; 3.6)</td>
<td>3.6 (3.0; 4.4)</td>
<td>18.4 (11.1; 29.0)</td>
</tr>
<tr>
<td>CIODM (litre min m⁻²)</td>
<td>3.6 (2.9; 4.5)</td>
<td>3.5 (2.8; 4.4)</td>
<td>0</td>
</tr>
<tr>
<td>CIPCA (litre min m⁻²)</td>
<td>2.6 (2.2; 3.2)</td>
<td>2.8 (2.3; 3.4)</td>
<td>7.0 (0.16; 2)</td>
</tr>
<tr>
<td>SV (ml m⁻²)</td>
<td>3.1 (2.5; 3.6)</td>
<td>3.6 (3.0; 4.4)</td>
<td>18.4 (11.1; 29.0)</td>
</tr>
<tr>
<td>SVI (ml m⁻²)</td>
<td>3.1 (2.5; 3.6)</td>
<td>3.6 (3.0; 4.4)</td>
<td>18.4 (11.1; 29.0)</td>
</tr>
</tbody>
</table>

Legend: ODM = dynamic monitors at the beginning of surgery during haemodynamic stable conditions. Data are shown as median (25%; 75% quartiles). P-values were calculated using the exact Wilcoxon test for comparison before and after a volume administration and exact Mann–Whitney test for comparison of DSVI and DCI between monitors within the responder and non-responder group. HR, heart rate; SAP, systolic arterial pressure; DAP, diastolic arterial pressure; MAP, mean arterial pressure; CVP, central venous pressure; FTc, flow time corrected; PV, peak velocity; SVRI, systemic vascular resistance index; SV, stroke volume; SVI, stroke volume index; CI, cardiac index; PCA, post-analytical correction algorithm for Zephyr monitors (Fig. 3B–D).
Discussion

Our findings address important issues on the interchangeability of ODM and PCA within a clinical context. The main findings of the study are (i) that ODM and PCA showed a comparable high intrinsic precision and acceptable LSC, suggesting that both haemodynamic monitors should potentially indicate a real change if measured SV increased $\geq 10\%$; (ii) that trending, defined as agreement of SV changes to a fluid challenge between both devices during the course of surgery, was poor; and (iii) that a higher NE dosage and a lower body temperature at the time of the fluid challenge and a major change of MAP to a fluid challenge were associated with a decreased interchangeability between ODM and PCA with respect to measure SV changes, whereas there was no relation to type of i.v. solution and other clinical characteristics.

An intraoperative goal-directed haemodynamic management aiming at optimizing flow has been shown to be beneficial in today’s anaesthesiological care covering major surgery. Guiding a goal-directed algorithm based on optimizing flow parameters, precision and the resulting LSC of the device seem to be substantial qualities to be able to assess if tracked changes in SV or cardiac index are real changes by the patient which are not caused by random error. ODM and PCA showed a comparable high precision (5.7% and 6.0%) resulting in an acceptable LSC (8.1% and 8.5%). These results are consistent with recent studies showing a precision of the ODM of 4.7% in critical care patients and 6.4% in patients undergoing major colorectal surgery. A lower precision of 8.5% of the ODM was reported by another study in abdominal surgery, while precision was assessed during the course of surgery, making it more difficult to ensure stable haemodynamic conditions. The precision of the PCA measured in our study was inferior to values provided by the manufacturer, which are based on laboratory testing [CV $\leq 2\%$, resulting in a precision of $\leq 4\%$]. Hence, according to our findings, both haemodynamic monitors should potentially indicate a real change if measured SV increased $\geq 10\%$, which is the most commonly defined threshold for a beneficial fluid challenge within most of the published goal-directed haemodynamic algorithms.

Comparing SV changes after the initial fluid challenge in each patient during stable haemodynamic conditions after induction of anaesthesia ODM showed a larger change than PCA. Most strikingly, according to measurements of the PCA, only one out of three patients had an initial beneficial fluid challenge compared with the ODM. Assessing the agreement of SV changes (trending) between both devices, polar plot analysis was performed in addition to concordance analysis by the four-quadrant plot, which ignores the magnitude of the underlying change of SV and the degree of agreement. According to a new approach by Monge Garcia and colleagues, only
fluid challenges with real changes of SV that are not caused by random error of measurements of the ODM and PCA were taken into account for these analyses. Both concordance by four-quadrant plot and polar statistics revealed that trending of SV during the fluid challenges between monitors was poor. Hence, extended logistic regression was used to identify perioperative clinical characteristics being associated with trending between ODM and PCA. Since the main study was a randomized controlled trial, the patients were randomly assigned to receive fluid challenges with either a balanced crystalloid or a balanced colloid solution or FFP after reaching the maximum dose of the study solution. Owing to the randomization and the fact that there are no previous data on the comparison of both study solutions with respect to trending between ODM and any PCA, we included the type of study solution into the regression analysis to adjust all other covariates. As shown by polar analysis and confirmed by regression analysis, we found that there was no difference between fluid challenges with balanced crystalloid, balanced colloid, or FFP with respect to trending. However, a greater change of MAP to a fluid challenge was associated with a worse trending between the two haemodynamic monitors. Clinically, ODM and PCA were less interchangeable with respect to SV changes if a patient responded with a greater...

Fig 3  Polar plots assessing trending of SV changes during a fluid challenge between ODM and PCA regarding all fluid challenges performed (A) and fluid challenges with different types of study fluid: balanced crystalloid (B); balanced colloid (C); and FFP (D). Radial ULOA, radial upper limit of agreement (bias + 1.96 SD); Radial LLOA, radial lower limit of agreement (bias – 1.96 SD). The exclusion zone size was calculated implying the combined LSC of ODM and PCA. The shaded area (defined by RLOAs and boundary limits) visualizes the magnitude of non-agreement between ODM and PCA. The angular concordance rate between fluid challenges performed with balanced crystalloid, balanced colloid, and FFP was not significantly different (NS; P=0.592).
change of MAP to a fluid challenge. This finding is supported by a recent study in critical care patients revealing that the agreement of absolute values of SV between ODM and different algorithms of pulse pressure analyses after a fluid challenge was substantially related to changes of MAP where changes of MAP 7.4% predicted a clinically relevant discrepancy with a reasonable sensitivity and specificity. Recently, it was supposed that the change of arterial load to a fluid challenge which implies changes of AP may be a substantial determinant to the discrepancy of measurements between ODM and many pulse pressure analyses after an intervention. However, analysing trending by polar plot analysis, variables such as effective arterial elastance cannot be studied due to statistical redundancy. Additionally, a higher NE dose at the time of the fluid challenge was found to be associated with a worse trending between ODM and PCA. The cardiac output response to changes of NE has been shown to be complex, with patients presenting with an increase or a decrease in CO depending on changes of vascular characteristics on the arterial and venous side of the circulation. In this context, NE-induced alterations on the arterial side seem to be the major determinant. Furthermore, a lower body temperature was related to a worse trending between ODM and PCA. Eventually, according to GEE analysis, the lack of agreement arises from central and peripheral resistance related issues such as MAP, NE use, and being cold and it would seem from a rational view that a system that measures flow directly from the aorta would be much more likely to measure SV changes accurately than one that measures flow indirectly from a pressure wave where we have information that the reliability of different pulse contour analyses has been questioned in increased vasopressor dosage. However, we do not intend to state that the worse trending is attributed to an impaired reliability of PCA or ODM or both, but from a clinical point of view, we can state that haemodynamic optimization especially during increased NE levels within a goal-directed haemodynamic algorithm with the oesophageal Doppler is not the same as with the calibrated PCA and vice versa. Furthermore, our results showed that age, BMI, pre-existing arterial hypertension, duration of surgery, and anaesthetics were not related to trending. Recently, concerns have been raised, if measurements of the ODM are reliable with respect to anaesthetics. According to our results, we can claim that clinically the use of volatile anaesthetics or propofol for maintenance of anaesthesia was not related to trending between ODM and PCA. Most strikingly, the continuous use of a thoracic epidural was not associated with a better or worse trending. The influence of a lumbar epidural to ODM readings has been postulated, and the association of a thoracic epidural with ODM measurements has been recently discussed extensively. In our study, only

### Association of trending with pre- and intraoperative characteristics

**Preoperative characteristics:**
- Age (yr)
- Pre-existing arterial hypertension

**Intraoperative characteristics:**
- Type of i.v. solution:
  - Balanced crystalloid (reference)
  - Balanced colloid
  - Fresh frozen plasma
  - Thoracic epidural
  - Total i.v. anaesthesia
  - Temperature (s.c. 0.1°C)
  - Remifentanil (s.c. 0.1 µg kg⁻¹ min⁻¹)
  - Norepinephrine (s.c. 0.1 µg kg⁻¹ min⁻¹)
- MAP before fluid challenge (mm Hg)
- ΔMAP during fluid challenge (s.c.10%)

![Forest plot visualizing the association of pre- and intraoperative characteristics with trending between ODM and PCA by presenting ORs obtained from multivariate logistic GEE. ORs are drawn on a logarithmic scale and are adjusted for all other covariates. Regarding the clinical interpretation, ORs of temperature, remifentanil, NE, and changes of MAP were scaled for changes of 0.1°C, 0.1 µg kg⁻¹ min⁻¹, and 10%. The covariate duration of surgery was not associated with trending (P=0.15) and was not shown due to the better illustration of all other covariates.](https://academic.oup.com/bja/article-abstract/113/5/822/2920117)
two patients without an epidural went for analysis, but these two patients had an extensive duration of surgery resulting in a total of 105 analysed fluid challenges. Owing to our findings, our study indicates carefully that in our study population, trending between ODM and PCA was not related with the continuous use of a thoracic epidural, but this fact has to be addressed more precisely by further studies.

Our study has some limitations. First, the ODM values are dependent on the quality of the signal, which is mainly influenced by an ideal placement of the Doppler probe. The intraoperative data were obtained by more than one investigator involving the risk of an interobserver variability which could have influenced data collection of the ODM values.\(^{40}\) However, it has been shown that training could improve the quality of signal and ensure reliability of measurement of the ODM.\(^{41}\) As the members of the study group were well trained in handling the ODM, the interobserver variability is assumed to be minimized.

Secondly, our study only included female patients. However, it is unlikely that sex has an influence on the results.

In conclusion, as yet, it is not possible to state that one monitor might be wrong and another is better. However, despite a similar precision, ODM and PCA were not interchangeable with regard to measuring SV changes within a goal-directed haemodynamic algorithm in our study population. It can be stated out of our data that haemodynamic optimization within a goal-directed haemodynamic algorithm during surgery with the oesophageal Doppler is not the same as with the calibrated PCA and vice versa.

**Authors’ contributions**


**Acknowledgements**

The authors would like to thank the BalaCriCo study group members for their support in conducting the study, Ansgar Jones, MD, and Olga Müller, MD, for participating recruiting patients and Mandy Koch, MD, Jean-Philipp Zallet, MD, Heike Sieglitz, MD, Kathrin Solzbach, MD, Julienne Köhler, MD, and David Lohre, MD, for the data acquisition.

**Declaration of interest**

None declared.

**Funding**

This research was an investigator-initiated study. It was supported by an unrestricted grant from Fresenius Kabi, Bad Homburg, Germany. The implementation of the ODM technology in the department was supported by Deltex Medical by an unrestricted grant unrelated to this study. The funders had no input into, or control over, study design, data collection, analysis, and interpretation of data; in the writing of the report; or in the decision to submit the paper for publication.

**References**

20 Linton NW, Linton RA. Is comparison of changes in cardiac output, assessed by different methods, better than only comparing cardiac output to the reference method? Br J Anaesth 2002; 89: 336–7; author reply 7–9
22 Roche AM, Miller TE. Goal-directed or goal-misdirected—how should we interpret the literature? Crit Care 2010; 14: 129
24 Critchley LA, Yang XX, Lee A. Assessment of trending ability of cardiac output monitors to measure trends in cardiac output. Europ J Anaesthesiol 2011; 28: 536–46
27 Bjorne H. Reply from the authors. Br J Anaesth 2013; 110: 661–2
33 Maas JJ, Pinsky MR, de Wilde RB, de Jonge E, Jansen JR. Cardiac output response to norepinephrine in postoperative cardiac surgery patients: interpretation with venous return and cardiac function curves. Crit Care Med 2013; 41: 143–50

Handling editor: A. R. Absalom