Validation of cardiac output monitoring based on uncalibrated pulse contour analysis vs transpulmonary thermodilution during off-pump coronary artery bypass grafting

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Editor’s key points

- Uncalibrated pulse contour analysis (UPCA) derived from the arterial pressure signal might provide beat-to-beat cardiac index (CI) monitoring.
- Determination of CI by UPCA demonstrated an acceptable degree of agreement with results of intermittent transpulmonary thermodilution.
- The ability of UPCA to follow trends in cardiac output was poor.

Background. Cardiac output monitoring, as a part of a goal-directed haemodynamic management, has been shown to improve perioperative outcome in high-risk patients undergoing major surgical interventions. However, thorough validation of cardiac output monitoring devices in different clinical conditions is warranted. The aim of our study was to compare the reliability of a novel system for cardiac index (CI) monitoring based on uncalibrated pulse contour analysis (UPCA) with transpulmonary thermodilution (TPTD) during off-pump coronary artery bypass grafting (OPCAB).

Methods. Twenty patients undergoing elective OPCAB were enrolled into the study. CI measured by means of UPCA (CIUPCA) was validated against CI determined with TPTD technique (CIPTD). Parallel measurements of CI were performed at nine stages during the surgery and after operation. We assessed the accuracy and the precision of individual values and the agreement of trends of changes in CI.

Results. Totally, 180 pairs of data were collected. There was a significant correlation between CIUPCA and CIPTD (r = 0.836, P < 0.01). According to a Bland–Altman analysis, the mean bias between the methods was −0.14 litre min⁻¹ m⁻² with limits of agreement of ± 0.82 litre min⁻¹ m⁻² and a percentage error of 31%. A polar plot trend analysis revealed acceptable angular bias (−0.54°), increased radial limits of agreement (± 52.7°), and decreased polar concordance rate (74%).

Conclusions. In OPCAB, UPCA provides accurate and precise CI measurements compared with TPTD. However, the ability of this method to follow trends in cardiac output is poor.

Clinical trial registration. NCT01773720 (ClinicalTrials.gov).

Keywords: cardiac output; haemodynamic monitoring

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Cardiac output monitoring, as a part of a goal-directed haemodynamic management, has been shown to improve perioperative outcome in high-risk patients undergoing major surgical interventions, including off-pump coronary artery bypass surgery (OPCAB).1–5 According to Vincent and colleagues,6 the ‘ideal’ haemodynamic monitoring system should provide assessment of relevant variables, accurate and reproducible measurements, and interpretable data. It should also be readily available, operator-independent, and easy to use, have a rapid response-time, cause no harm, be cost-effective, and provide information that might be used to guide therapy. However, a system fulfilling all these requirements is not available yet. In clinical practice, the selection of monitoring device is influenced by several factors including invasiveness, technical limitations, heart rhythm, validity, accuracy, and repeatability of measurements. Moreover, the level of operator’s experience and the availability of additional haemodynamic variables might be of significance.7

Cardiac index (CI) is one of the most important variables to monitor during cardiac surgery. Traditionally, CI is monitored by means of either pre-pulmonary or transpulmonary thermodilution (TPTD) techniques.8 Both methods have demonstrated an acceptable accuracy and have been included in different protocols of goal-directed therapies.2 3 9–14 At the same time, thermodilution techniques are not fully operator-independent and require repeated injections of the thermal indicator.15 16 Moreover, the pre-pulmonary thermodilution technique utilizes a pulmonary artery catheter, and its use is controversial due to a low benefit to risk ratio.17–19 Therefore, alternative less invasive techniques have been developed.7 20
Recently, a novel system for CI monitoring (Professional Arterial Flow Trending, ProAQT, Pulsion Medical Systems, Germany) based on uncalibrated pulse contour analysis (UPCA) became available for clinical practice. This technology allows the operator to use a special sensor with an existing arterial pressure catheter to provide a beat-to-beat CI monitoring. The system does not require external calibration but uses an operator-activated automatic initial CI determination, which is based on characteristics of the patient combined with details of the systemic arterial pressure curve, as assessed by sampling at 250 Hz. The subsequent calculations of CI are performed by continuous analysis of the waveform of the arterial pressure curve by using the established PICCO algorithm.

However, this novel system has not been validated yet in different clinical settings. Therefore, our aim was to compare the reliability of uncalibrated CI monitoring based on analysis of the systemic arterial pressure waveform with TPTD in patients undergoing off-pump coronary artery bypass grafting.

Methods

Patients

The study was conducted in compliance with the Helsinki Declaration. The protocol and the informed consent form were approved by the Ethics Committee of the Northern State Medical University, Arkhangelsk, Russian Federation, and registered with ClinicalTrials (ref: NCT01773720). Written informed consent was obtained from every patient.

The study was performed at the Department of Anaesthesiology and Intensive Care Medicine of the Northern State Medical University and the City Hospital #1 of Arkhangelsk (Arkhangelsk, Russian Federation). From October 2011 to April 2012, 21 adult patients with coronary artery disease, ranked ASA II–III, and undergoing elective OPCAB were enrolled. Exclusion criteria were age <18 and >80 yr, preoperative ejection fraction <0.35, severe cardiac valve dysfunction, peripheral vascular disease confirmed by preoperative ultrasound, permanent form of atrial fibrillation, and simultaneous interventions (carotid endarterectomy, aneurysm repair, etc.).

The exclusion criteria were used to make the study population more homogenous, to prevent complications resulting from femoral artery puncture and catheterization, and to avoid misinterpretation of results of CI measurements due to arrhythmias. The study was discontinued in patients transferred to cardiopulmonary bypass during the intervention.

Anaesthesia and surgery

After establishing routine haemodynamic monitoring with ECG including ST segment analysis, non-invasive arterial pressure, and oxygen saturation obtained by pulse oximetry (LifeScope, Nihon Kohden, Japan), anaesthesia was induced with i.v. midazolam (Dormicum, F. Hoffmann-La Roche Ltd, Switzerland) 0.07 mg kg\(^{-1}\) h\(^{-1}\), i.v. Anaesthesia was maintained with sevoflurane 0.5–3.0 vol% and fentanyl 1–3 \(\mu\)g kg\(^{-1}\) h\(^{-1}\). Mechanical ventilation in the operating theatre was performed using a semi-closed anaesthetic circuit (Fabius, Dräger, Germany) with \(F_{O_2}\) 0.5, tidal volume 7–8 ml kg\(^{-1}\), respiratory rate 12–14 bpm, positive end-expiratory pressure 4 cm H\(_2\)O, and a fresh gas flow of 1 litre min\(^{-1}\).

Fluid therapy included an infusion of Ringer’s lactate at rates of 6–7 ml kg\(^{-1}\) h\(^{-1}\) before and during surgery and 2–3 ml kg\(^{-1}\) h\(^{-1}\) during the first 6 h after operation. If the patients presented with hypovolaemia (global end-diastolic index <680 ml m\(^{-2}\)), a 500 ml bolus of 6% hydroxyethyl starch 130/0.42 (6% Tetraspan, B.Braun, Germany) was infused over a period of 30 min aiming at global end-diastolic index within the range of 680–800 ml m\(^{-2}\). If needed, the bolus infusion was repeated once up to a total volume of 1000 ml. All the patients were operated by the same team of surgeons using an Acrobat SUV OM-9000S (Guidant, Santa Clara, CA, USA) device for stabilization of the heart during revascularization.

Measurements and data collection

After induction of anaesthesia, an 8.5 F four-lumen 20 cm central venous catheter was inserted into the internal jugular vein. The femoral artery was catheterized with a 5 F arterial thermodilution catheter (Pulsiocath PV2015L20, Pulsion). This catheter was connected to the PICCO \(_2\) monitor (Pulsion Medical Systems) for intermittent TPTD measurements and monitoring of CI (CI\(_{TPTD}\)), global end-diastolic volume index (GEDVI), extravascular lung water index (EVLWI), mean arterial pressure (MAP), systemic vascular resistance index (SVRI), and stroke volume variation (SVV). The thermodilution measurements were performed in triplicate with a cooled (\(<\)8 °C) 5% dextrose solution injected via the central venous catheter. The average of three measurements with \(<10\%\) variation was used for data analysis. In parallel, the same femoral thermocatheter catheter was connected to the ProAQT monitor for continuous measurements of CI based on UPCA (CI\(_{UPCA}\)).

The haemodynamic variables registered simultaneously with both monitors were recorded after induction of anaesthesia, after sternotomy, at the restraint of the heart surface using a stabilizing device, after restoration of blood flow via the coronary grafts, at the end of surgery, and at 2, 4, 6, and 24 h after operation. These perioperative time-points were selected for the TPTD measurements and repeated activations of automatic-based CI determination. Initially, the system requires that the patient-related data (age, sex, height, weight) are entered. At all stages, we flushed and zeroed the pressure line followed by activation of the inner algorithm assessing mathematically the arterial pressure waveform with 250 Hz sampling.

Statistical analysis

For data collection and analysis, we used SPSS software (version 14.0; SPSS Inc., Chicago, IL, USA), MedCalc software (version 12.3; MedCalc Software bvba, Belgium), and SigmaPlot software (version 11.0; Systat Software, Inc., USA). The data
distribution was assessed using the Shapiro–Wilk test. Data are presented as mean (standard deviation, SD) or median (25th–75th percentile). Repeated data were analysed using repeated-measures analysis of variance followed by a test of contrasts or the Friedman test followed by the Wilcoxon two-sample test, depending on the data distribution.

According to the distribution of data, Pearson’s $r$ or Spearman’s $\rho$ correlation coefficients were calculated to estimate the correlation between variables, as determined by TPTD and UPCA. To describe the agreement between $CITPTD$ and $Cl_{UPCA}$, a Bland–Altman analysis with assessment of the mean difference (bias) of two methods and limits of agreement ($\pm 1.96 \times SD$ of bias of the methods) was performed for all data pairs taken together (with correction for multiple measurements per subject) and for each stage of study separately. According to Critchley and Critchley, the percentage error (PE) was calculated as: $1.96 \times SD$ of the bias of the methods/mean CI of the two methods $\times 100\%$.

To investigate the ability of UPCA to track CI changes, the correlation coefficient between $CITPTD$ and $Cl_{UPCA}$ was determined for serial data in each patient. After the calculation of delta CI ($\Delta CI$) between two consecutive measurements for both methods ($\Delta CITPTD$ and $\Delta Cl_{UPCA}$, respectively) by subtracting the value of the preceding stage from that of the consequent stage, a half-circle polar plot was made. According to Critchley and colleagues, central zone data with the mean $\Delta CI < 10\%$ representing statistical noise component were excluded from further analysis. Based on polar data, angular bias, radial limits of agreement, and polar concordance rate were calculated. A trending ability was assumed as good if angular bias was within $\pm 5\%$, radial limits of agreement within $\pm 30\%$, and polar concordance rate at $30\%$ was 95% or higher.

For all the tests, a $P$-value of $< 0.05$ was considered as significant.

**Results**

Figure 1 displays a flow chart for enrolment of the patients. One patient required cardiopulmonary bypass because of haemodynamic instability and was excluded from further analysis. The main characteristics and biometric data of the patients are presented in Table 1. Seven patients required inotropic/vasopressor support with dobutamine or ephedrine at different stages of the study.

The perioperative changes in haemodynamic and volumetric variables are presented in Table 2. We observed a significant

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**Fig 1** Flow chart of patient enrolment.
increase in CI from the stage of restraint of the heart surface until 24 h after the surgery (Fig. 2). In parallel, SVRI decreased at the same stages. MAP increased significantly at 4 and 6 h after operation. Global end-diastolic volume and SVV increased transiently after OPCAB (P < 0.05), whereas EVLW did not change significantly.

A total of 180 pairs of CI measurements were collected during the study. Nine outlying data pairs that we relate to measurement errors were excluded from further analysis. The overall median (25th–75th percentile) of CI$_{TPTD}$ was 2.68 (2.17–3.28) litre min$^{-1}$ m$^{-2}$, which did not differ significantly from the overall median (25th–75th percentile) of CI$_{UPCA}$, which was 2.50 (2.02–3.12) litre min$^{-1}$ m$^{-2}$. We found a significant correlation between CI$_{UPCA}$ and CI$_{TPTD}$ (Spearman’s $\rho = 0.836, P < 0.001$). For all the included data pairs, the mean bias between CI$_{UPCA}$ and CI$_{TPTD}$ was $-0.14$ litre min$^{-1}$ m$^{-2}$ with limits of agreement of $\pm 0.82$ litre min$^{-1}$ m$^{-2}$ and a PE of 31%, as presented in Figure 3. Table 3 demonstrates correlations, results of the Bland–Altman analysis, and PEs of the two methods of CI assessment at different stages of the study. There was a significant correlation between CI$_{UPCA}$ and CI$_{TPTD}$ at each stage with a slight underestimation of CI$_{UPCA}$ in comparison with CI$_{TPTD}$ and a PE of between 28% and 37%. The variation in bias of the two methods correlated with SVRI (Spearman’s $\rho = 0.3, P < 0.01$).

Significant correlations between the serial data pairs determined in each individual patient were shown in an analysis including all the patients. The median (25th–75th) value for the correlation was Pearson’s $r = 0.92$ (0.86–0.94). Figure 4 demonstrates a half-circle polar plot. The angular bias was $-0.54^\circ$ and radial limits of agreement were $\pm 52.7^\circ$. Based on the 30° radial limits, the polar concordance rate was 74%.

**Discussion**

Our study revealed that determination of CI by UPCA during off-pump coronary surgery demonstrated an acceptable

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**Table 1** Main characteristics of the patients (n = 20). Data presented as mean (SD), median (25th–75th percentile), or percentage. BMI, body mass index.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (range) (yr)</td>
<td>43 – 77</td>
</tr>
<tr>
<td>Gender, male/female (%)</td>
<td>75/25</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>169 (8)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>83 (12)</td>
</tr>
<tr>
<td>BMI (kg m$^{-2}$)</td>
<td>28.9 (4.8)</td>
</tr>
<tr>
<td>Preoperative ejection fraction</td>
<td>0.61 (0.07)</td>
</tr>
<tr>
<td>Number of grafts</td>
<td>3 (2–4)</td>
</tr>
<tr>
<td>Duration of surgery (min)</td>
<td>175 (33)</td>
</tr>
<tr>
<td>Total amount of intraoperative fluid infusion (ml)</td>
<td>2000 (1500–2000)</td>
</tr>
<tr>
<td>Requirement in colloids (%)</td>
<td>50</td>
</tr>
<tr>
<td>Requirement in inotropes/vasopressors (%)</td>
<td>35</td>
</tr>
<tr>
<td>Blood loss (ml)</td>
<td>300 (300–375)</td>
</tr>
</tbody>
</table>

**Table 2** Changes in hemodynamic and volumetric variables during surgery and after operation. Data are presented as mean (SD) or median (25th–75th percentile) with P < 0.05 compared with ‘induction to anaesthesia’ stage. SVRI, systemic vascular resistance index; MAP, mean arterial pressure; GEDVI, global end-diastolic volume index; EVLWI, extravascular lung water index; SVV, stroke volume variation.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Induction of anaesthesia</th>
<th>After sternotomy</th>
<th>After reperfusion</th>
<th>Restoration of blood flow</th>
<th>End of surgery</th>
<th>2 h</th>
<th>4 h</th>
<th>6 h</th>
<th>24 h</th>
</tr>
</thead>
<tbody>
<tr>
<td>SVRI (dyns cm$^{-5}$ m$^{-2}$)</td>
<td>2619 (636)</td>
<td>1955 (639)</td>
<td>1915 (596)</td>
<td>1962 (401)*</td>
<td>1935 (592)*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MAP (mm Hg)</td>
<td>73 (10)</td>
<td>71 (18)</td>
<td>74 (14)</td>
<td>75 (19)</td>
<td>78 (13)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GEDVI (ml m$^{-2}$)</td>
<td>753 (103)</td>
<td>751 (103)</td>
<td>751 (103)</td>
<td>751 (103)</td>
<td>751 (103)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>EVLWI (ml kg$^{-1}$)</td>
<td>7 (5–9)</td>
<td>8 (5–9)</td>
<td>10 (5–9)</td>
<td>8 (5–10)</td>
<td>8 (5–10)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SVV (%)</td>
<td>7 (5–10)</td>
<td>7 (5–10)</td>
<td>7 (5–10)</td>
<td>7 (5–10)</td>
<td>7 (5–10)</td>
<td></td>
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</tbody>
</table>

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degree of agreement with the results of intermittent TPTD. However, the ability of the system to follow trends in cardiac output was poor.

Currently, several uncalibrated cardiac output monitoring devices utilizing different algorithms of pulse contour analysis have been developed. In comparison with calibrated analogues, the main advantage of the uncalibrated system lies in its simplicity of use. However, concomitantly, lack of external calibration reduces accuracy and stability of the system, especially in situations of rapid changes in vascular resistance.

The majority of studies validating UPCA-based devices against thermodilution techniques demonstrate a low-to-moderate agreement between the methods. We found that UPCA slightly underestimated the CI as determined by TPTD with a mean bias of –0.14 litre min⁻¹ m⁻² and limits of agreement of ±0.82 litre min⁻¹ m⁻². In addition, the variations in bias (Table 3) correlated significantly with SVRI. Similar effects have been described by investigators who evaluated different ‘less invasive’ monitoring techniques and might be explained by changes in vascular resistance and compliance influencing the analysis of the arterial waveform. At the same time, we noticed a weak correlation between CI and SVRI, possibly indicating that the ProAQT system is resistant to changes in the mechanical characteristics of the systemic arterial bed.

Assessing a new method for CI monitoring, it is of great importance to choose an accurate and precise reference method, per se. According to Critchley and Critchley, by using the thermodilution technique as a reference method, one should accept the assumption that an inherent accuracy for thermodilution cardiac output is ±20% and a similar accuracy of the test method, yielding a combined limit of agreement of ±28%, which is rounded up to 30% for simplicity. This PE is now widely accepted. In the present study, we demonstrate an overall PE of 31%, which is close to the reference value. However, the values of PE at different stages of the study ranged from 28% to 37%; thus, exceeding the acceptable value after induction of anaesthesia and at 2 and 24 h after operation. Such variations in precision might be due to imperfection of the current algorithm of pulse contour

Fig 2 Changes in CIs measured by UPCA and TPTD during the surgery and after operation. CIUPCA, cardiac index measured using uncalibrated pulse contour analysis; CIFTPTD, cardiac index measured using transpulmonary thermodilution. *P < 0.05 compared with induction of anaesthesia stage.

Fig 3 Bland–Altman plot for CI determined with UPCA and TPTD. Each marker represents a separate observation pair and each type of marker represents an individual patient. CIUPCA, cardiac index measured using uncalibrated pulse contour analysis; CIFTPTD, cardiac index measured using transpulmonary thermodilution; SD, standard deviation.
Interestingly, a recent meta-analysis conducted by Peyton and Chong31 questioned the reliability of the PE suggested by Critchley and Critchley. Based on the analysis of 47 studies comparing different minimally invasive techniques with thermodilution, the authors suggested a more liberal criterion for limits of agreement of 45%, which may represent a more realistic expectation of acceptable precision in clinical practice.

During the study, we observed changes in haemodynamics typical for OPCAB.3 32 CI measured with both methods increased throughout the study starting from the stage of restraint of the heart surface. In parallel, we observed a decrease in SVRI. These results comply with the results of other investigators and our own previous findings and can be explained by a gradual attenuation of myocardial depression after induction of anaesthesia with propofol. Moreover, the improvement of cardiac function may be a result of increased myocardial contractility after coronary revascularization, termination of surgical manipulations on the heart, and recovery from anaesthesia.2 3 33 We also noticed a significant increase in MAP at 4 and 6 h after operation that might be due to recovery from anaesthesia. On the other hand, GEDVI, EVLWI, and SVV remained relatively stable throughout the study as a result of volumetric-based haemodynamic optimization.

Unfortunately, in spite of a high degree of correlation between the serial data pairs demonstrating a rough tracking...
ability of the new device in individual patients, UPCA displayed a reduced possibility to follow the changes in CI with more detailed analysis. On the one hand, angular bias was within \( \pm 5^\circ \), indicating that the calibration of both methods was in agreement.\(^{26}\) At the same time, radial limits of agreement exceeded \( \pm 30^\circ \) boundary, demonstrating poor trending ability of the UPCA system.\(^{26}\) In addition, the decreased ability of the device to follow the changes in CI is confirmed by a low polar concordance rate (74%). We speculate that the combination of acceptable accuracy of measuring absolute CI values and poor trending ability might be partly random.

On the other hand, since the UPCA system has a marginal accuracy, bias between the methods can be increased after CI trend calculations resulting in reduced trending ability of UPCA.

The study has several limitations. First of all, we used a method based on the thermodilution principle for the determination of cardiac output. Assuming a precision error of 13–22% for both pre-pulmonary and transpulmonary techniques, thermodilution is not an absolutely precise reference method, although it is still considered the gold standard for validation.\(^{33, 34}\) However, in clinical settings, it is more cumbersome to apply high-precision reference methods such as, for instance, trans-aortic Doppler flowmetry, which requires direct access to the ascending aorta. In the present study, we used the same femoral artery catheter for assessment of CI with both the UPCA and the TPTD technique. Therefore, the reliability of monitoring CI by using a radial artery, which is considered a less invasive technique, should be determined in future studies. There are no previous reports regarding the use and accuracy of the uncalibrated pulse-contour analysis for measurements of CI during OPCAB, thus we did not perform a power analysis justifying the selected sample size. Since we were not able to provide equal conditions for all patients during the surgery (e.g. identical body position, equal duration of separate stages, etc.), we did not test the tracking ability of the ProAQT during specific therapeutic interventions including volume expansions. When considering our findings, it should be borne in mind that we assessed the novel technique in patients undergoing OPCAB, a specific clinical setting with a relatively limited range of variations in cardiac output. Thus, further studies are required to determine the reliability of UPCA under different haemodynamic conditions.

We conclude that in OPCAB patients, CI determined by UPCA showed an acceptable accuracy and degree of error, when compared with the thermodilution technique. However, the uncalibrated arterial waveform analysis demonstrated poor trending ability. Therefore, certain limitations must be taken into account when using the new technique for monitoring CI in off-pump coronary surgery.

**Authors’ contributions**

A.A.S., V.V.K., and M.Y.K. designed study protocol; A.A.S., A.H., and V.V.K. recruited patients and performed data collection; A.A.S. performed statistical analysis; A.A.S., L.J.B., and M.Y.K. participated in manuscript preparation; all the authors reviewed and approved the manuscript.

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**Declaration of interest**

M.Y.K. is a member of the medical advisory board of Pulsion Medical Systems.

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**References**

34 Stetz CW, Miller RG, Kelly GE, Raffin TA. Reliability of the thermodilution method in the determination of cardiac output in clinical practice. Am Rev Respir Dis 1982; 126: 1001–4

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