Pulse contour analysis after normothermic cardiopulmonary bypass in cardiac surgery patients

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Abstract

Introduction Monitoring of the cardiac output by continuous arterial pulse contour (CO\textsubscript{PICCOpulse}) analysis is a clinically validated procedure proved to be an alternative to the pulmonary artery catheter thermodilution cardiac output (CO\textsubscript{PACtherm}) in cardiac surgical patients. There is ongoing debate, however, of whether the CO\textsubscript{PICCOpulse} is accurate after profound hemodynamic changes. The aim of this study was therefore to compare the CO\textsubscript{PICCOpulse} after cardiopulmonary bypass (CPB) with a simultaneous measurement of the CO\textsubscript{PACtherm}.

Methods After ethical approval and written informed consent, data of 45 patients were analyzed during this prospective study. During coronary artery bypass graft surgery, the aortic transpulmonary thermodilution cardiac output (CO\textsubscript{PICCOtherm}) and the CO\textsubscript{PACtherm} were determined in all patients. Prior to surgery, the CO\textsubscript{PICCOpulse} was calibrated by triple transpulmonary thermodilution measurement of the CO\textsubscript{PACtherm}. After termination of CPB, the CO\textsubscript{PICCOpulse} was documented. Both CO\textsubscript{PACtherm} and CO\textsubscript{PICCOtherm} were also simultaneously determined and documented.

Results Regression analysis between CO\textsubscript{PACtherm} and CO\textsubscript{PICCOtherm} prior to CPB showed a correlation coefficient of 0.95 ($P < 0.001$), and after CPB showed a correlation coefficient of 0.82 ($P < 0.001$). Bland-Altman analysis showed a mean bias and limits of agreement of 0.0 l/minute and -1.4 to +1.4 l/minute prior to CPB and of 0.3 l/minute and -1.9 to +2.5 l/minute after CPB, respectively. Regression analysis of CO\textsubscript{PICCOpulse} versus CO\textsubscript{PICCOtherm} and of CO\textsubscript{PICCOpulse} versus CO\textsubscript{PACtherm} after CPB showed a correlation coefficient of 0.67 ($P < 0.001$) and 0.63 ($P < 0.001$), respectively. Bland-Altman analysis showed a mean bias and limits of agreement of -1.1 l/minute and -1.9 to +4.1 l/minute versus -1.4 l/minute and -4.8 to +2.0 l/minute, respectively.

Conclusion We observed an excellent correlation of CO\textsubscript{PACtherm} and CO\textsubscript{PICCOtherm} prior to CPB. Pulse contour analysis did not yield reliable results with acceptable accuracy and limits of agreement under difficult conditions after weaning from CPB in cardiac surgical patients. The pulse contour analysis thus should be re-calibrated as soon as possible, to prevent false therapeutic consequences.
determine the CO by this method [7]. Several investigators found a good correlation between these two methods of CO determination [4-6,8]. The device mostly used also offers continuous CO determination by arterial pulse contour analysis. Stroke volume calculation and CO calculation by pulse contour analysis was developed years ago and underwent several methodological improvements of the algorithm [9,10]. Monitoring of the CO by continuous arterial pulse contour analysis (COPiCCOpulse) is a widely used and clinically validated procedure proved to be an alternative to the pulmonary artery catheter thermodilution CO (CO PACtherm) in cardiac surgical patients [4,11]. Pulse contour monitoring demonstrated accuracy comparable with that of pulmonary artery thermodilution using a clearly less invasive approach [5,11,12]. There is ongoing debate, however, of whether the COPiCCOpulse is accurate and reliable after profound changes of the hemodynamic situation, such as after cardiopulmonary bypass (CPB) [4,13].

The aim of this study was therefore to compare the bias and the limits of agreement (two standard deviations) of the COPiCCOpulse after CPB, with a simultaneous measurement of the COPACtherm as the gold standard of CO measurement.

### Materials and methods

#### Patients

Following ethical committee approval and written informed consent, 50 patients were considered eligible for this clinical trial from February to November 2004. The inclusion criteria were age >18 and <75 years, and elective coronary artery bypass graft surgery. The exclusion criteria were withdrawal of consent, valve pathologies, a left ventricular ejection fraction <40% and symptomatic peripheral artery stenosis.

#### Perioperative management

Oral premedication was 0.1 mg/kg midazolam. In all patients a femoral artery was cannulated with a 4-Fr cannula (Pulsiocath; Pulsion Medical AG, Munich, Germany) prior to induction of anesthesia. A central venous catheter and a pulmonary artery catheter (Thermilution Catheter; Arrow, Reading, PA, USA) were inserted via the right internal jugular vein.

General anesthesia was induced with etomidate (0.2 mg/kg), 5 µg/kg fentanyl and 0.1 mg/kg pancuronium. Maintenance was with infusion of 5–10 µg/kg per hour fentanyl, boluses of

### Table 1

| Patient characteristics | Mean | Standard error of the mean |
|-------------------------|------|---------------------------|
| Age (years)             | 62   | 1                         |
| Height (m)              | 1.77 | 0.01                      |
| Body weight (kg)        | 91   | 2                         |
| Body mass index (kg/m²) | 29.1 | 0.6                       |
| Number of grafts (n)    | 3    | 0                         |
| Duration of anesthesia (minutes) | 314   | 7                         |
| Duration of surgery (minutes) | 201   | 6                         |
| Temperature prior to cardiopulmonary bypass (°C) | 35.2 | 0.1                       |
| Temperature after cardiopulmonary bypass (°C) | 36.1 | 0.1                       |
| Cardiopulmonary bypass time (minutes) | 71    | 3                         |
| Aortic clamping time (minutes) | 44    | 2                         |

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| Aortic clamping time (minutes) | 44    | 2                         |

### Table 2

| Hemodynamic data | Mean | Standard error of the mean |
|------------------|------|---------------------------|
| Heart rate prior to CPB (l/minute) | 69   | 3                         |
| Heart rate after CPB (l/minute) | 81*  | 2                         |
| Mean arterial pressure prior to CPB (mmHg) | 70   | 2                         |
| Mean arterial pressure after CPB (mmHg) | 73   | 2                         |
| Central venous pressure prior to CPB (mmHg) | 9    | 1                         |
| Central venous pressure after CPB (mmHg) | 11   | 1                         |
| Mean pulmonary arterial pressure prior to CPB (mmHg) | 21   | 1                         |
| Mean pulmonary arterial pressure after CPB (mmHg) | 20   | 1                         |
| Pulmonary wedge pressure prior to CPB (mmHg) | 11   | 1                         |
| Pulmonary wedge pressure after CPB (mmHg) | 12   | 1                         |
| Systemic vascular resistance prior to CPB (dyn/s per cm) | 861  | 53                        |
| Systemic vascular resistance after CPB (dyn/s per cm) | 727* | 47                        |
| Pulmonary vascular resistance prior to CPB (dyn/s per cm) | 115  | 10                        |
| Pulmonary vascular resistance after CPB (dyn/s per cm) | 93   | 8                         |
| COPACtherm prior to CPB (l/minute) | 6.2  | 0.4                       |
| COPACtherm after CPB (l/minute) | 7.9* | 0.3                       |
| COPiCCOtherm prior to CPB (l/minute) | 6.2  | 0.3                       |
| COPiCCOtherm after CPB (l/minute) | 7.6* | 0.3                       |
| COPiCCOpulse after CPB (l/minute) | 6.5  | 0.3                       |

CPB, cardiopulmonary bypass. COPACtherm, pulmonary artery catheter thermodilution cardiac output; COPiCCOtherm, aortic transpulmonary thermodilution cardiac output; COPiCCOpulse, continuous arterial pulse contour analysis cardiac output. *P < 0.05 compared with baseline.
0.1 mg/kg midazolam, 0.03 mg/kg pancuronium and 0.6–1% end-tidal isofluorane. All patients were ventilated with an oxygen–air mixture (inspiratory oxygen fraction, 0.5) to maintain an end-tidal partial pressure of carbon dioxide of 35–45 mmHg. The CPB technique was normothermic using intermittent antegrade warm blood cardioplegia as described by Calafiore and colleagues [14]. Transfusion management was performed according to our standard operating procedure [15]. The durations of anesthesia, surgery and aortic occlusion and the number of coronary artery bypass grafts were recorded.

**Determination of cardiac output**
Prior to CPB, the COPICCOtherm and the COPACtherm were determined immediately after sternotomy under stable hemodynamic conditions.

All volume substitution was stopped during the measurements. The COPACtherm and the COPICCOtherm were measured by triple injection of 10 ml iced isotone sodium chloride solution into the central venous line of the PAC. The COPACtherm and the COPICCOtherm were calculated by commercially available monitors (CCO module, Solar 8000; Marquette Hellige, Freiburg, Germany; and PICCO CCO monitor; Pulsion Medical AG). In case of a deviation >10% of a measurement, five measurements were performed and the highest and lowest were rejected. The COPICC pulse measurement was automatically calibrated by the COPICCOtherm measurement. The COPACtherm and the COPICCOtherm measurements were carried out simultaneously.

The measurement after CPB was carried out 15 minutes after decanulation of the aorta. The prerequisite for this measurement was an optimized preload and stable hemodynamic condition with no damping of the arterial pressure line, which could be achieved in all patients. At this time the COPICC pulse was documented. Simultaneously, the COPACtherm and COPACtherm were determined by thermodilution measurement as already described.

**Statistical analysis**
All data are expressed as the mean and standard error of the mean. Statistical analysis was performed by linear regression analysis. The bias and limits of agreement (LOA) (two standard deviations) were assessed according to the method described by Bland and Altman [16]. All numerical calculations were carried out with SPSS for WINDOWS (release 11.5.1, ©1989–2002; SPSS Inc, Chicago, IL, USA).

**Results**
Anesthesia and surgery were uncomplicated in all patients analyzed during this study. Five patients had to be excluded due to their impossibility to achieve a valid COPACtherm or COPICCOtherm measurement. Therefore, 45 patients remained in the study for analysis. Basic patient characteristics are presented in Table 1. Hemodynamic data are presented in Table 2. The heart rate, COPACtherm and COPICCotherm increased significantly compared with the pre-CPB values. The systemic vascular resistance decreased significantly compared with the baseline measurement.

Prior to CPB, the regression analysis between the COPACtherm and COPICCotherm measurements showed an excellent correlation, with a correlation coefficient of 0.95 (P < 0.001). Bland–Altman analysis showed a mean bias and LOA of 0.0 l/minute and -1.4 to +1.4 l/minute. The regression analysis after CPB also showed a good correlation between the COPACtherm and the COPICCotherm with a correlation coefficient of 0.82 (P < 0.001). The Bland–Altman analysis after CPB showed a mean bias and a precision of 0.3 l/minute and -1.9 to +2.5 l/minute.

Comparison of COPICC pulse versus COPICCotherm and of COPAC pulse versus COPACtherm showed only a fair correlation after CPB, with a correlation coefficient of 0.67 (P < 0.001) and 0.63 (P < 0.001), respectively. Bland–Altman analysis showed a mean bias and LOA of -1.1 l/minute and -1.9 to +2.5 l/minute, respectively.
Discussion
The main finding of this study is that the CO measured by pulse contour analysis was considerably different compared with the CO\textsubscript{PCCOtherm} and the CO\textsubscript{PACtherm}. The CO\textsubscript{PCCOtherm} and CO\textsubscript{PACtherm} measurements correlated well before and after CPB, indicating that CO measurement by pulse contour analysis needs to be recalibrated after CPB to achieve valid results.

Pulse contour analysis CO has been shown previously to serve as a valid and cost-effective device for CO determination after calibration [17]. In our study we investigated the validity of continuous CO measurement by pulse contour analysis after CPB. The main advantage of CO\textsubscript{PCCOpulse} measurement after CPB would be the fast determination of CO. As soon as pulsatile flow is restored, the algorithm of the CO monitor automatically starts determination of the CO by continuous pulse contour analysis. Therefore, during a period when the anesthetist’s full attention is focused on vasoactive and volume therapy necessary for successful weaning from CPB, a fast and continuous approach such as continuous pulse contour analysis might be much more practical than time-consuming intermittent thermodilution techniques for determination of CO. However, these advantages would only apply if the obtained data are valid.

The initial calibration of the CO\textsubscript{PCCOpulse} measurement was performed by aortic transpulmonary CO determination prior to CPB. We found an excellent correlation between the CO\textsubscript{PCCOtherm} and the CO\textsubscript{PACtherm} measurements. This correlation has been described by previous investigators [12]. After CPB the correlation remained good, but Bland-Altman analysis revealed a trend for the CO\textsubscript{PCCOtherm} to slightly underestimate the CO, with increased LOA compared with the measurements prior to CPB. As we do not know the ‘true’ CO, it is speculative which CO measurement estimates more precisely the ‘true’ CO. An explanation for the greater scatter between the two CO measurements after CPB compared with the measurements prior to CPB might be an influx of cold blood. This cold blood might be derived from compartments, which might be hypoperfused during CPB and reperfused in the period after CPB as suggested by previous investigators [4,18]. Even though we performed normothermic CPB management, patients tended to display a slight decrease of their
body temperature, worsening the signal-to-noise ratio of the thermal indicator used for determination of the CO by these methods. Better results in this setting might be achieved using an indicator independent from thermal signals. Given the increased LOA of the CO_{PiCCOtherm} measurement, therefore, the calibration of the pulse contour analysis with a thermal indicator might be less than ideal in this period and should be repeated early after surgery.

After CPB, the pulse contour CO showed marked differences compared with the CO_{PiCCOtherm} and CO_{PACtherm} measurements. The CO_{PiCCOpulse} measurement systematically underestimated the CO determined by the other two methods. This has been described previously [4]. In our investigation the CO and the heart rate increased significantly after CPB. We also observed a significant decrease in systemic vascular resistance after CPB. Differences between pulse contour CO and thermodilution CO measurements in patients with significant changes of the systemic vascular resistance [13] have already been established in previous investigations. Further studies are therefore needed, addressing also the performance of newly developed pulse contour devices that do not include an independent technique for calibration under difficult clinical settings, such as after CPB.

The fact that we failed to determine the CO by a method independent of thermal signals such as echocardiographic or lithium dilution measurement of the CO to validate the thermodilution measurement [19,20] is a shortcoming of our study. Bearing in mind, however, that we did find an excellent correlation prior to CPB and a good correlation after CPB for the two thermodilution measurements, we believe that the thermodilution methods represent a reliable estimation of the ‘true’ CO in clinical practice. In case of severe hemodynamic instability after CPB, indicated by the CO_{PiCCOpulse}, CO_{PiCCOtherm}, CO_{PACtherm}, or other clinical parameters, echocardiography should be used to guide therapy as suggested previously [21]. It has been established formerly that pulse contour analysis CO is a valid and cost-effective device for CO determination after calibration. Another limitation is that the design of our study does not allow for an ultimate demonstration of a causal relationship between CPB and lack of agreement. However, a number of studies show that pulse contour analysis is valid for at least some hours if there are no severe changes in hemodynamics. The mean time between sternotomy and the start of CPB is about 60 minutes. We therefore think it is reasonable to assume that CPB is mainly responsible for the inaccuracy of the post-CPB pulse contour analysis observed in our study.

Conclusion
In conclusion, we observed an excellent correlation of CO_{PiCCOtherm} and CO_{PACtherm} measurement prior to CPB. Our study could not prove pulse contour analysis with a modified Wesseling algorithm used in this study to be a method yielding reliable results with excellent accuracy and limits of agreement under difficult conditions after CPB in cardiac surgical patients. Hence, due to the broad distribution and the underestimation of the CO after CPB, the use of the uncalibrated continuous pulse contour cardiac output cannot be recommended after weaning from CPB. A re-calibration in this setting is essential.

Key messages
- We observed an excellent correlation of CO_{PiCCOtherm} and CO_{PACtherm} measurement prior to CPB.
- Our study could not prove pulse contour analysis with a modified Wesseling algorithm to be a method yielding reliable results under difficult conditions after CPB in cardiac surgical patients.
- Due to the broad distribution and the underestimation of the CO after CPB, the use of the uncalibrated continuous pulse contour cardiac output cannot be recommended after weaning from CPB.

Competing interests
The authors declare that they have no competing interests.

Authors’ contributions
MS and CvH prepared the manuscript, carried out the cardiac output measurements, conceived of the study and performed the statistical analysis. AF, JG and VvD helped with the recruitment of the patients and the drafting of the manuscript. SD and WFK participated in the study design and helped with the recruitment of patients. CS drafted the manuscript, helped with the study design and coordination. All authors read and approved the final manuscript.

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