Accuracy of beat-to-beat cardiac output monitoring by pulse contour analysis in hemodynamical unstable patients

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SUMMARY

Background: Continuous determination of cardiac output (CO) by transpulmonary thermodilution calibrated pulse-contour analysis is gaining clinical acceptance. However there is doubt, whether this method is reliable in hemodynamically unstable patients. We compared pulse-contour analysis to thermodilution in patients with profound changes of CO.

Material and methods: 24 patients were investigated. CO was measured by transthoracic thermodilution and pulse-contour analysis in intervals of 60 min during study periods of 8–44 h without recalibration of the pulse-contour computer. Results of 517 measurements were compared by regression, structural regression and Bland-Altman analyses.

Results: Mean change of CO was 40±27% (range 20–139%), range of systemic vascular resistance was 450 dyn·s/cm–5 – 2360 dyn·s/cm–5. Correlation of pulse-contour analysis CO to thermodilution CO was r=0.88 with p=0.0001, bias was 0.2 l/min with 1.2 l/min standard deviation. Mean CO by pulse-contour analysis did not differ significantly from CO by thermodilution during the study period. There were no influences of heart rate or arterial pressure on the difference between both methods.

Conclusion: CO measurement by arterial pulse-contour analysis is reliable even in patients with profound changes of CO or during hemodynamic instability.

BACKGROUND

Continuous determination of cardiac output (CO) by arterial pulse-contour analysis is a technology which was developed several years ago [1–5]. Although the basic principle of this technology is relatively simple and satisfying results have been shown in comparison to standard pulmonary artery (PA) thermodilution [6–8], the method has not been clinically accepted in the past. One argument against this technology was, that there was still the need for calibration of the pulse-contour algorithm by PA thermodilution.

Recently a device for pulse-contour-analysis was developed (PiCCO, Pulsion Medical Systems, Munich, Germany), which does not require PA thermodilution for calibration, but instead uses transpulmonary (TP) thermodilution. As for the latter only a central venous and arterial line is necessary, this new method is less invasive and easier to apply than standard PA thermodilution. Since good results have been demonstrated in peri- and postoperative intensive care [9–12], the method is now gaining more and more clinical acceptance.

However there are investigators and clinicians, who argue that that during profound changes of a patients hemodynamic situation pulse-contour analysis is unreliable [8,13,14]. Other investigators do not confirm this assumption [6,11,15,16]. Therefore, the question whether pulse-contour analysis
is reliable during hemodynamic instability or not, is not answered until now.

The aim of this study was to investigate the reliability of pulse-contour during hemodynamic instability. Hemodynamic instability was defined as a change of CO of at least ±20% within 3 hours. In patients who – during their course at the ICU – showed such changes, the continuous pulse-contour-based monitoring was compared to thermodilution-based monitoring of CO. As it has been shown that standard PA thermodilution can be replaced by TP thermodilution for means of CO measurement [11,17–23], the latter was chosen as the reference method for this investigation.

**MATERIAL AND METHODS**

**Patients**

During the development and clinical validation of the PiCCO system (Pulsion Medical Systems, Munich, Germany) in all investigated patients the postoperative course of CO was computed by different pulse-contour-algorithms and compared to simultaneous measurements of CO by TP thermodilution. Out of those, 24 patients were identified who during their study period showed changes of CO of more than ±20% within 3 hours and who therefore were included in this investigation. All hemodynamic changes occurred as the result of the native postoperative course or mandatory postoperative treatment by vasoactive drugs. We did not influence the hemodynamic situation by means of planned pharmacological interventions. The study was performed at a cardiac surgical intensive care unit of an university hospital and conducted according to the declaration of Helsinki in its revised version of Tokyo (1975), Venice (1983), Hong Kong (1989) and Somerset West (1996), and the rules of Good Clinical Practice. Informed consent was obtained from all patients prior to their investigation.

**Devices and measurements**

The PiCCO system for continuous determination of CO by arterial pulse-contour analysis consists of a bedside computer, an inline injectate sensor in the central venous line and a thermistor tipped arterial catheter connected to a pressure transducer which detects arterial pressure waveform and heart rate. After detection the pressure wave is digitalized and analyzed according to the underlying pulse-contour algorithm. The inline sensor and the arterial thermistor are used for a TP thermodilution measurement of cardiac output, which is required to calibrate the pulse-contour computer after onset of the system.

Preoperatively or immediately postoperatively upon arrival of the patients at the ICU, a 4F thermistor-tipped femoral arterial pulse-contour catheter (PV 2021L, Pulsion Medical Systems, Munich, Germany) was inserted and connected to the PiCCO system. The pulse-contour computer initially was calibrated by a triplicate TP thermodilution but not recalibrated during each patients study period. The indicator for TP thermodilution consisted of 10 ml iced dextrose 5% solution at a temperature of 4–7°C. To reduce the influence of variations of manual injection on the accuracy of the measurements to a minimum, the bolus injections were always carried out by the same person.

CO was measured as the mean of triplicate TP thermodilutions at intervals of 60 minutes, depending on the patients clinical situation. Simultaneously the arterial pulse wave was analyzed by the PiCCO system.

The basic algorithm for the determination of cardiac output from pulse-contour was developed by Wesseling and co-workers [3–5]. According to this algorithm, left ventricular stroke volume is computed by measuring the area under the systolic portion of the arterial pressure waveform and dividing this area by the aortic impedance. A subsequent multiplication with the heart rate yields pulse-contour cardiac output. To adjust for aortic impedance, which differs from patient to patient, a thermodilution measurement of cardiac output for the calibration of the system is required. Based on this original algorithm, the PiCCO-algorithm has been developed. In contrast to the Wesseling algorithm it does not only analyzing the area under the systolic portion of the pressure wave but also the shape of the pressure waveform. Furthermore the software takes into account the individual aortic compliance and systemic vascular resistances based on the following consideration: During systole more blood is ejected into the aorta than is actually leaving the aorta. During the subsequent diastole the volume stored in the aorta is flowing into the arterial network at a rate given by the aortic compliance; the systemic vascular resistance and the blood pressure (Windkessel-effect); the shape of the arterial pressure curve after the dicrotic notch is representing this passive emptying of the aorta. The individual compliance is determined by using TP ther-
modilution cardiac output as a reference method to obtain the blood flow while simultaneously measuring the blood pressure.

Similar to the Wesseling algorithm, there is still the need for a patient specific calibration factor, which is also determined by the TP thermodilution cardiac output measurement. The algorithm is shown in detail in Figure 1.

**Statistical analysis**

CO was computed by pulse contour analysis based on software version 4.1. (COpc) and compared to CO based on triplicate TP thermodilution (COtd) by means of multiple regression and Bland-Altman analyses. As the pulse-contour based values (due to the realtime character) might have changed within a triplicate thermodilution period, the mean of the values immediately before and after each set of thermodilutions were the values used for statistical evaluation. The stability of the initial calibration was evaluated by analyzing change in bias over time using Friedman’s two way analysis of variance, followed by Wilcoxon’s matched-pair test, making due allowance for multiple testing. Multiple regression was performed to assess the influence of heart rate and mean arterial pressure on the difference in CO derived from pulse contour analysis vs. TP thermodilution. All statistical analyses were computed by SPSS for Windows (Version 10.0.1999, SPSS Inc, Chicago).

**RESULTS**

In 24 patients a change of CO measured by TP thermodilution of more than 20% compared to the initial value was found, representing a total of 517 CO measurements with a mean of 22 measurements during study periods from 8 to 44 hours in each single patient.

The mean change of CO was 40±27%, in 4 patients changes of CO were higher than 50%, in one patient change of CO was higher than 100%. Mean systemic vascular resistance (SVR) ranged between 772±242 dyn·s/cm–5 and 1197±417 dyn·s/cm–5. The lowest SVR was 450 dyn·s/cm–5, the highest 2360 dyn·s/cm–5, in 5 patients the change in SVR was higher than 500 dyn·s/cm–5. As already mentioned, all changes occurred as the result of the native postoperative course or mandatory postoperative treatment by vasoactive drugs. A detailed description of the patients, the underlying diseases, applied vasoactive drugs and hemodynamic variances are shown in table 1.
The results of the comparison of COpc to COtd are presented in Figures 2a and 2b. The regression analysis resulted in a correlation coefficient of 0.88 at a significance level of p=0.0001. In the corresponding Bland-Altman analysis the bias was −0.02 l/min with a single standard deviation of 1.2 l/min.

The course of mean CO by different methods over time is shown in Figure 3. At no point of time a statistical significant difference between the mean of both methods was found. Multiple regression analysis did also not show any influence of heart rate or arterial systemic pressure on the differences between pulse-contour analysis thermodilution.

As in the mean of all results, striking differences between both methods in single patients might have been lost, we additionally plotted the course of CO in every single patient. As an example, in Figures 4a and 4b the two patients with the highest percentile change of CO (139%, patient #13 and 94%, patient #6) and in figures 5a and 5b the two patients with the broadest range of SVR during their measurement period (1290 dyn.s/cm⁻⁵, patient #16 and 1170 dyn.s/cm⁻⁵, patient #6) are shown.

**DISCUSSION**

Theoretically, hemodynamic monitoring of intensive care patients by the use of this new pulse contour-technology is near the ideal concept. It is easy applicable, as there is only the need for a arterial and a central venous line, after onset it is continuously available without the need for regularly interventions by the personnel and it is cost effective as the required disposables and material are not more expensive than the present standard method of PA thermodilution.

<table>
<thead>
<tr>
<th>No.</th>
<th>Age (yrs)</th>
<th>Sex</th>
<th>Diagnosis</th>
<th>Vasoactive drugs</th>
<th>Measurements (#)</th>
<th>Range of SVR (dyn.s.cm⁻⁵)</th>
<th>Range of CO (l/min)</th>
<th>Max. CO deviation (%)</th>
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<td>450–940</td>
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<td>f</td>
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<td>Dop, Nit</td>
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<td>3.8–5.1</td>
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<td>Dop, Epi, Nit</td>
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<td>Dop, Dob</td>
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<td>f</td>
<td>AVR + CABG</td>
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<td>17</td>
<td>780–1040</td>
<td>7.0–9.4</td>
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</tr>
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</table>

**Table 1. Patient characteristics.**

(CABG – coronary artery bypass grafting; MVR – mitral valve replacement; MOF – multi organ failure; ARDS – acute respiratory distress syndrome; SSHCK – septic shock; LHI – left heart insufficiency; LE – lung embol; AVR – aortic valve replacement; Epi – epinephrine; Enx – enoximone; Dop – dopamine; Nit – nitroglycerine; Nor. norepinephrine; Dob – dobutamine)
Concerning the mere measurement of cardiac output, the pulmonary artery catheter method [24,25] has been well investigated and shown good results in the past and has deserved the confidence, that many physicians have in it. However the PA catheter has also been criticized in the past due to it’s invasiveness, complications and clinical misleading preload parameters [26,27]. The search for a new method for hemodynamic monitoring is therefore justified and the described pulse-contour technology may be in fact a new, ideal alternative.

However to be not only theoretically but actually an alternative for monitoring cardiac output one major qualification has to be fulfilled: The accuracy of measuring cardiac output by pulse-contour analysis must be comparable to that of PA thermodilution.

Several investigations already have shown that cardiac output measurement by pulse-contour analysis is in fact comparable to the standard method in different clinical settings and under different circumstances [7,9,11,16]. Although the results of all

Figure 3. Course of cardiac output over time measured by transpulmonary thermodilution and pulse-contour analysis (COtd – cardiac output determined by transpulmonary thermodilution, COpc – cardiac output determined by pulse-contour analysis)

Figure 4. A. Course of cardiac output over time measured by transpulmonary thermodilution and pulse-contour analysis in the patient with the highest percentile change of cardiac output during the study period; B. Course of cardiac output over time measured by transpulmonary thermodilution and pulse-contour analysis in the patient with the second highest percentile change of cardiac output during the study period, (COtd – cardiac output determined by transpulmonary thermodilution, COpc – cardiac output determined by pulse-contour analysis)
these studies were satisfying, no study design was
suited to invalidate the argument, that pulse-conto-
ur analysis is not reliable during profound changes
of CO. As in this study we only concentrated on
patients who did show profound changes of CO
we may – at least in part – give the first answer.

Our results show, that pulse-contour-analysis is re-
liable during profound CO changes when using the
new algorithm. We investigated a broad range of
cardiac output (2.7–14.1 l/min) and peripheral re-
sistance changes (450–2360 dyn/s/cm²) and found
reproducible results and satisfying accuracy in the
comparison with thermodilution cardiac output.
From this point of view, we can state that pulse-
contour-analysis is reliable even in the hemodyna-
mic unstable patient.

As not all of the investigated patients had a PA ca-
theter in place during their complete study period
we choose the TP thermodilution technique imple-
mented in the PiCCO system as the reference me-
thod for CO measurement. TP thermodilution has
shown to be identical to PA thermodilution in the
past [11,17–23], the comparison of TP thermodilu-
tion to CO measurement by the reference method
of Fick did also show good results [28]. In fact, in
studies in which both thermodilution methods we-
re compared to pulse-contour analysis, the results
were comparable for all three methods [9,12,15].
Thus, using TP thermodilution instead of PA ther-
modilution is justified for this study.

Another focus of this study was the performance of
the pulse-contour-device in the daily clinical prac-
tice. We therefore did not induce the changes of
hemodynamics in the investigated patients by me-
ans of pharmacologic interventions but we did ob-
serve the ‘natural clinical course’. Of course it mi-
ight have been possible to induce even more pro-
nounced alterations of the hemodynamic condi-
tions, however especially in cardiac surgical
intensive care this might be harmful to the patients.
Furthermore, induced changes possibly may wrongly
influence the measurement results.

The presence of arrhythmias during the measure-
ments may also have a distinct influence on a com-
parison of the two methods. According to the basic
principle, pulse-contour-analysis computes CO by
multiplying separately measured stroke volumes
with the present heart frequency; thermodilution
measures CO independent of single stroke vol-
umes by computing flow per time. As during arhy-
thmia stroke volume and heart frequency change
constantly, the resulting CO will also change con-
stantly. This however can be levelled out during
the time frame of thermodilution (especially during
the longer TP thermodilution period) but not by
beat-to-beat pulse-contour-analysis. That means,
that pulse-contour CO may differ clearly from a va-
ue computed at the end of a thermodilution pe-
riod and it can not be decided which CO is the
true CO in exactly that moment. At this time, the
pulse-contour method may even be more accurate
than thermodilution, however to answer this qu-
estion a different investigation i.e. comparison of
pulse-contour-analysis with electromagnetic or ul-
trasonic flow meters is necessary. Being aware of
this problem we did not differentiate according to
presence or type of arrhythmia in our patients.

Another aspect concerning accuracy is the time go-
ne by since the initial calibration of the pulse-con-
tour algorithm. We found no significant differences
of COpc to COtd during the study period. As the
differences did also not increase towards the end
of the measurement period, the time between cali-
bration and measurement seems to be uncritical
concerning accuracy. The results however were
obtained under study conditions and care was ta-
k to flush and check and if necessary recalibrate
the pressure transducers on a regular basis. Alth-
ough we do not want to completely exclude the in-
fluence of time on the accuracy of the pulse-con-
tour method, it should be mentioned that in daily
clinical routine some ‘unreliabilities’ of the pulse-
contour device may be more due to neglecting
pressure transducers and pressure lines than to the
method itself.

Of course we do not suggest to neglect recalibra-
tion for long periods of time, although in the pre-
sent study recalibration was not performed during
a time frame between 8 and 44 hours. We recom-
dend a recalibration at least every 8 hours or if
substantial changes of a patient’s condition occur.
To our opinion, recalibration at regular intervals is
not a disadvantage but the expression of a reasona-
ble way of dealing with technical devices.

To date, the use of pulse-contour analysis is limited
to femoral arterial, brachial or axillary arterial ac-
cess. As radial artery pressure measurement is
known to be unreliable under certain conditions
[29] at the moment we do not recommend to use
radial arteries for pulse-contour analysis. Especially
in severely ill patients with high catecholamine
support as is this study population many physicians
switch from radial to a more central arterial access
for reliable blood pressure measurement anyway. Nevertheless the possibility of using the easy to place radial arterial access for pulse-contour analysis needs to be achieved to have the in the above mentioned ideal monitoring concept available.

**CONCLUSION**

It can be concluded that pulse-contour-analysis is a good, since less invasive, alternative to pulmonary artery catheterization for the measurement of cardiac output even during hemodynamic instability. As for preload management less invasive parameters of better predictive value [11] are available too, we agree with others [22], that the use of PA catheters can be limited to patients in whom knowledge of right ventricular afterload is essential.

**REFERENCES:**

23. Von Spiegel T: Cardiac output evaluation by means of transthoracic cardiac thermodilution. An alternative to the pulmonary artery catheter? Anaesthesist, 1996; 45: 1045-50