Radial Artery Applanation Tonometry for Continuous Noninvasive Cardiac Output Measurement: A Comparison With Intermittent Pulmonary Artery Thermodilution in Patients After Cardiothoracic Surgery

Julia Y. Wagner, MD; Harun Sarwari; Gerhard Schön, MSc; Mathias Kubik, MD; Stefan Kluge, MD; Herrmann Reichenspurner, MD; Daniel A. Reuter, MD; Bernd Saugel, MD

Objectives: Radial artery applanation tonometry allows completely noninvasive continuous cardiac output estimation. The aim of the present study was to compare cardiac output measurements obtained with applanation tonometry (AT-CO) using the T-Line system (Tensys Medical, San Diego, CA) with cardiac output measured by intermittent pulmonary artery thermodilution using a pulmonary artery catheter (PAC-CO) with regard to accuracy, precision of agreement, and trending ability.

Design: A prospective method comparison study.

Setting: The study was conducted in a cardiosurgical ICU of a German university hospital.

Patients: We performed cardiac output measurements in 50 patients after cardiothoracic surgery.

Interventions: None.

Measurements and Main Results: Three independent sets of three consecutive thermodilution measurements (i.e., PAC-CO) each were performed per patient, and AT-CO was measured simultaneously. The average of the three thermodilution cardiac output measurements was compared with the average of the corresponding three AT-CO values resulting in 150 paired cardiac output measurements. In 13 patients, cardiac output–modifying maneuvers performed for clinical reasons additionally allowed to evaluate trending ability. For statistical analysis, we used Bland-Altman analysis, the percentage error, four-quadrant plot, and concordance analysis. Mean PAC-CO was 4.7 ± 1.2 L/min and mean AT-CO was 4.9 ± 1.1 L/min. The mean of differences was –0.2 L/min with 95% limits of agreement of –1.8 to + 1.4 L/min. The percentage error was 34%. The concordance rate was 95%.

Conclusions: Continuous cardiac output measurement using the noninvasive applanation tonometry technology is basically feasible in ICU patients after cardiothoracic surgery. The applanation tonometry technology provides cardiac output values with reasonable accuracy and precision of agreement compared with intermittent pulmonary artery thermodilution measurements in a clinical study setting and is able to reliably track cardiac output changes induced by cardiac output–modifying maneuvers. (Crit Care Med 2015; XX:00–00)

Key Words: cardiac output; critical care; hemodynamic monitoring; pulmonary artery catheter; T-Line
Cardiac output (CO) is an essential variable when it comes to adequately monitoring and optimizing a patient’s hemodynamics in the ICU and during intermediate-risk and high-risk surgical procedures (1, 2).

In the 1970s, the pulmonary artery catheter (PAC) developed by Harold Jeremy Swan and William Ganz became available for the invasive CO measurement by thermodilution (3, 4). Despite its decline approximately 30 years later triggered by studies demonstrating an unfavorable risk-benefit profile (5, 6), the PAC still proves to be of outstanding importance in distinct clinical situations (7) and is still considered as the clinical criterion standard method for measuring CO (8).

During the years after the decrease in routine PAC use, a number of alternatives for invasive, less-invasive, and noninvasive CO measurements have been introduced and evaluated (9–14).

One of the novel technologies that provides continuous completely noninvasive CO monitoring is the radial artery applanation tonometry (AT). One commercially available device using the AT technology for the assessment of hemodynamic variables is the T-Line system (Tensys Medical, San Diego, CA). The AT technology’s ability to measure blood pressure continuously and noninvasively has already been demonstrated (15–20). Furthermore, our group recently described and evaluated an algorithm for CO determination based on AT in a proof-of-concept analysis using impeccable arterial waveforms of ICU patients selected from a database (12).

In the present study, we investigate the accuracy, precision of agreement, and trending ability of the AT technology for the measurement of CO in comparison with pulmonary artery thermodilution as the clinical criterion standard method in postoperative cardiothoracic surgery patients.

MATERIALS AND METHODS

Patients, Inclusion/Exclusion Criteria, and Study Measurements

Our study was conducted in a cardiothoracic ICU of a German university hospital (University Medical Center Hamburg-Eppendorf, Hamburg, Germany). The ethics committee (Ethikkommission der Ärztekammer Hamburg) approved the study. We obtained written informed consent from all patients prior to study enrollment.

The study included patients aged at least 18 years, who underwent nonemergency cardiothoracic surgery, and had a PAC inserted for medical reasons according to the standard clinical protocol of the Department of Anesthesiology unrelated to the present study. Patients were not eligible for study inclusion if AT study measurements at the patient’s wrist were not possible because of anatomical abnormalities of the study limb. The PAC (INTRATHERMODIN 4lumen [7F, 110 cm]; intraspecial catheters GmbH, Rehlingen-Siersburg, Germany) was inserted preoperatively after routine anesthetic induction, and all PAC-obtained values were displayed on the vital signs monitor (Infinity Delta; Dräger AG, Lübeck, Germany).

The study measurements were performed within the first postoperative hours after the patient’s transfer from the operating room to the cardiothoracic ICU. Independent of the study, all medical decisions regarding analgosedation and hemodynamic management during the postoperative period were at the discretion of the treating ICU physician. This included the need for IV opioids for analgesia and propofol for sedation and the timing of extubation. The patient’s hemodynamic state and fluid responsiveness were evaluated (e.g., using passive leg raising test) and optimized with IV fluids and catecholamines. Each diagnostic and therapeutic intervention was based on the ICU physicians’ medical decisions independent from the study measurements.

After arrival in the ICU, patients were connected to the AT study device (T-Line 400 monitor). A bracelet was placed on the patient’s wrist equipped with an electromechanical system and a sensor that moves over the radial artery in order to find the optimal applanation pressure as described before (21, 22). When the optimal signal is available, the T-Line monitor provides a continuous arterial waveform. In order to compensate for height differences between the study limb and the patient’s heart level, the level function of the T-Line system was applied. By using the level function one levels the T-Line monitor electronically by entering on the T-Line monitor’s touchscreen the vertical height of the study limb above or below the patient’s heart level.

After entering the patient’s biometric data (height, weight, age, and gender), the AT system’s monitor displays CO values derived from pulse contour analysis using a proprietary auto-calibrating algorithm.

The study measurements were performed at three different time points during the postoperative period. The intervals between the time points differed depending on the clinical routine events. At each time point, one pulmonary artery thermodilution measurement using the PAC consisted of five injections of 10-mL ice-cold sodium chloride. The five corresponding AT CO measurements (AT-CO) were recorded simultaneously. In order to avoid an impact due to discrepancies between the single pulmonary artery thermodilution measurements, the average of the three of five closest thermodilution CO measurements (PAC-CO) was used for comparison with the average of the corresponding three AT-CO values. Immediately after the patient monitor displayed the thermodilution-derived CO value, the corresponding CO value measured with AT was recorded using screen shots.

In a subgroup of the study patients, the ICU physician in charge decided that a passive leg raising maneuver or a volume challenge was indicated in order to assess volume responsiveness (23, 24) or another CO-influencing clinical intervention took place (propofol bolus, a change in the settings of the patient’s external pacemaker) during our study measurements. In these cases, we performed one set of study measurements prior to the clinical intervention (time point 1 or 2) and one shortly after the intervention (time point 2 or 3).

Statistical Analysis

For the patient characteristics, we calculated either absolute and relative numbers (percentages) or the median with the interquartile range (i.e., 25–75% percentile range).
For PAC-CO and AT-CO, the mean CO values ± sd were separately calculated. We computed the mean of the differences (= bias) between PAC-CO and AT-CO, the sd, and the 95% limits of agreement (= bias ± 1.96 × sd). The Bland-Altman method accounting for repeated measurements was performed (25). Furthermore, we computed the percentage error as described by Critchley and Critchley (26).

For the assessment of the AT technology’s trending ability, we created a four-quadrant plot and performed concordance analysis. Furthermore, we calculated a variance components model (mixed model) in order to know the amount of variation that can be explained by the different sources of variation: 1) variation due to patient, 2) variation due to different measurement time points, and 3) residual variation (i.e., variation due to the three single measurement values used to calculate the mean CO value at each of the three measurement time points per patient).

All statistical analyses were performed using Excel (Microsoft, Redmond, WA), IBM SPSS Statistics 21 (SPSS, Chicago, IL), and the statistical software package R Version 3.1.2 (R Core Team [2014]: R: A language and environment for statistical computing; R Foundation for Statistical Computing, Vienna, Austria; URL: http://www.R-project.org).

RESULTS

Patients

We enrolled 60 patients in the study. In seven patients, CO measurements in the postoperative period were not possible due to technical problems with the PAC (three patients) or AT (four patients). Furthermore, we secondarily excluded three patients without sinus rhythm from the study. Finally, 50 patients were available for the statistical analysis. Fourty-eight patients had undergone off-pump coronary artery bypass surgery, one patient additionally received carotid artery surgery, and one patient underwent lung transplantation.

The patients’ demographic and clinical characteristics are presented in Table 1.

CO Measurements

A total of 150 matched CO data points were available for the final statistical analysis.

Thirteen of the 50 study patients were available for evaluating the AT technology’s ability to track changes in CO because a CO-influencing clinical intervention took place during our study measurements, and the CO values measured by the criterion standard method (PAC) subsequently increased or decreased. In eight patients, a passive leg raising maneuver was performed, three patients received a propofol bolus injection during the period of our study measurements, one patient received a fluid challenge (500 mL fluid bolus), and in one patient the settings of the external pacer were changed.

The mean PAC-CO was 4.7 ± 1.2 L/min and the mean AT-CO was 4.9 ± 1.1 L/min. The Bland-Altman analysis revealed a bias of −0.2 L/min with an SD of ± 0.8 L/min and upper and lower limits of agreement of −1.8 and + 1.4 L/min, respectively (Fig. 1). The percentage error was 34%.

### Table 1. Patient and Clinical Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Data for 50 Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>74 (66–78)</td>
</tr>
<tr>
<td>Sex, male, n (%)</td>
<td>38 (76)</td>
</tr>
<tr>
<td>Height, m</td>
<td>1.75 (1.66–1.76)</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>84 (74–94)</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>28.0 (25.2–32.1)</td>
</tr>
<tr>
<td>Type of surgery</td>
<td></td>
</tr>
<tr>
<td>Off-pump coronary artery bypass,</td>
<td></td>
</tr>
<tr>
<td>n (%)</td>
<td>48 (96)</td>
</tr>
<tr>
<td>Off-pump coronary artery bypass +</td>
<td></td>
</tr>
<tr>
<td>carotid artery surgery, n (%)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Lung transplantation, n (%)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>Clinical characteristics on the day of study inclusion</td>
<td></td>
</tr>
<tr>
<td>Simplified Acute Physiology Score, points</td>
<td>32 (26–35)</td>
</tr>
<tr>
<td>Therapeutic Intervention Scoring System, points</td>
<td>22 (18–22)</td>
</tr>
<tr>
<td>Mechanical ventilation, n (%)</td>
<td>46 (92)</td>
</tr>
<tr>
<td>Noradrenaline therapy, n (%)</td>
<td>21 (42)</td>
</tr>
<tr>
<td>Noradrenaline dose, μg/min</td>
<td>4 (2–6)</td>
</tr>
<tr>
<td>Mean arterial pressure, mm Hg</td>
<td>74 (66–79)</td>
</tr>
<tr>
<td>Systolic arterial pressure, mm Hg</td>
<td>116 (102–123)</td>
</tr>
<tr>
<td>Diastolic arterial pressure, mm Hg</td>
<td>54 (49–61)</td>
</tr>
<tr>
<td>Central venous pressure, mm Hg</td>
<td>9 (8–11)</td>
</tr>
<tr>
<td>Mean pulmonary artery pressure, mm Hg</td>
<td>24 (19–28)</td>
</tr>
<tr>
<td>Systolic pulmonary artery pressure, mm Hg</td>
<td>33 (29–37)</td>
</tr>
<tr>
<td>Diastolic pulmonary artery pressure, mm Hg</td>
<td>16 (12–22)</td>
</tr>
<tr>
<td>Pulmonary artery occlusion pressure, mm Hg</td>
<td>13 (12–17)</td>
</tr>
<tr>
<td>Systemic vascular resistance, dyn·s/cm²</td>
<td>1,073 (838–1,400)</td>
</tr>
</tbody>
</table>

Data are presented as the median and interquartile ranges (25–75% percentile) or as absolute frequencies with percentages.

By calculating the variance components model (mixed model) in order to know the amount of variation that can be explained by the different sources of variation, we received the following results for the variable PAC-CO: 1.27 for the variation due to patient, 0.08 for the variation due to different measurement time points, and 0.09 for residual variation. The corresponding percentage distribution was 88%, 6%, and 6%, respectively. Thus, approximately 88% of the total variance of the variable PAC-CO can be attributed to the individual
The ability of the AT technology to track changes in CO is shown in the four-quadrant plot (Fig. 2). The concordance analysis resulted in a concordance rate of 95%, indicating acceptable trending ability (27).

The percentage error of 34% was slightly higher than the generally accepted cutoff value for acceptable precision of agreement of 28.3% (frequently rounded up to 30%) proposed by Critchley and Critchley (26). However, as nicely demonstrated by Peyton and Chong (33), it is questionable to unconditionally and generally apply this cutoff value (that requires a precision of method for both the reference technology and the studied technology of at least 20%) to clinical CO method comparison studies. In this context, definite recommendations for the definition of clinical acceptable agreement between two CO monitoring technologies are still a matter of debate (29). Peyton and Chong (33) demonstrated that less-invasive technologies—including pulse contour analysis based on an invasively assessed arterial pressure wave signal—usually fail to fulfill the percentage error threshold of 30%. What they are proposing instead is a percentage error in agreement with thermodilution of ± 45% as a more realistic achievable precision of agreement in a clinical setting (33).

In order to evaluate a novel noninvasive CO measurement technology’s accuracy and precision of agreement, the comparison with an invasive clinical standard criterion method is necessary (34). However, with regard to an adequate clinical risk-benefit ratio, a PAC, for example, is reserved to high-risk surgical or critically ill patients. As a consequence, a novel noninvasive CO measurement technology like the AT must be evaluated in a patient population that often does not represent its ideal target patient group (34). However, the goal is not necessarily to replace invasive CO monitoring by using noninvasive CO monitoring devices (e.g., the AT technology). Instead, the objective should be to find clinical settings in which patients...
might benefit from continuous noninvasive CO monitoring (e.g., intermediate-risk surgery, high-dependency unit) (34). Conversely, in clinical situations in which an invasive catheter’s removal is indicated, but continuous CO monitoring would still be valuable, a noninvasive technology might provide a reasonable alternative. So when thinking about the clinical use of a noninvasive CO technology, it is important to differentiate between the patient groups studied in clinical validation studies depending on the presence of an invasive catheter and the real final target patient group.

Another completely noninvasive method for measuring CO is the volume clamp method (35) using an inflatable finger cuff (36). Validation studies evaluating this technology in comparison with pulmonary artery or transpulmonary thermodilution revealed similar results compared with the AT technology’s CO measurement performance in our study (13, 36).

During study measurements, we noticed two limitations of the AT technology that need to be mentioned. First, it takes a certain time, up to several minutes, from the application of the device until the sensor has detected the optimal applanation pressure and displays an arterial waveform and thus CO values. Nonetheless, bearing in mind that the placement of an invasive arterial catheter might be challenging in certain patient groups and therefore time consuming in daily clinical practice as well, this can be seen as a relative disadvantage of the noninvasive AT technology. Second, the AT technology is very sensitive to movement artifacts. For example, slight movements of a patient during the postoperative recovery period or a medical professional bumping against the study limb lead to a period of “motion recovery” during which CO values are not available. This limitation emphasizes the current importance of adequately choosing the optimal target patient group and also for the further improvement of the technology’s measurement performance, for example, by reducing the bracelet size (34).

Our proof-of-concept analysis evaluating the AT technology’s CO algorithm for the first time (12) revealed a higher accuracy and precision of agreement with a low percentage error of 23% compared with the results of the present study. This finding is explained by the analysis of only selected impeccable waveforms of an ICU patient database in contrast to CO measurements obtained during clinical routine in an unselected group of postoperative cardiothoracic surgery patients. In this prospective study, we were now able to demonstrate the feasibility of the AT technology’s CO measurements in a clinical setting. In addition, we were also able to show the AT technology’s ability to reliably track changes in CO by performing CO-modifying maneuvers. As one limitation of our study, we have to mention that CO-modifying interventions in order to evaluate the AT technology’s trendability were performed in only a limited number of the study patients and thus in a probably heterogeneous patient group. Nevertheless, the fact that the AT technology reliably tracked changes in CO is a very important finding because it might be a particular benefit of a continuous noninvasive CO measurement technology to display changes in CO to the treating physician at the earliest possible stage. An intermittent CO measurement method like the pulmonary artery thermodilution used in our study implies a higher possibility of a delay in displaying such CO changes. Furthermore, it has been argued that in certain clinical scenarios, the tracking of CO changes might even be of more relevance than the CO monitor’s ability to provide CO values with high accuracy and precision of agreement (37). Of course, in critically ill patients treated in an ICU and during high-risk surgical procedures, artery cannulation is usually performed not only for continuous blood pressure measurements but also for arterial blood gas analyses. Furthermore, the presence of an arterial catheter allows minimally invasive radial artery waveform-based pulse contour analysis (38, 39). However, these technologies still bear the arterial catheter–associated risks, and their measurement performance is controversially discussed (10, 40). Such considerations again show clearly how important it is to select appropriate application areas for a noninvasive continuous CO measurement technology.

**CONCLUSIONS**

Our study demonstrates that CO measurements using the noninvasive AT technology are basically feasible in postoperative cardiothoracic surgery patients in an ICU setting. The AT technology provides CO values with reasonable accuracy and precision of agreement compared with intermittent pulmonary artery thermodilution measurements in a clinical study setting and is able to reliably track CO changes induced by CO-modifying maneuvers.

**REFERENCES**

34. Wagner JY, Saugel B: When should we adopt continuous noninvasive hemodynamic monitoring technologies into clinical routine? *J Clin Monit Comput* 2015; 29:1–3