Heart output by arterial pulse contour: reliability under hemodynamic derangements

Stefano Romagnoli*a,b, Salvatore Mario Romano*c, Sergio Bevilacqua*a,b, Francesco Ciappi*a,b, Chiara Lazzeri*c, Adriano Peris*a, Daniele Dinib, Sandro Gelsomina

*Department of Heart and Vessels, Experimental Surgery Unit, Careggi Hospital, Viale Morgagni 85, 50134 Florence, Italy
bdDepartment of Cardiac and Vascular Anesthesia and Post-Surgical Intensive Care Unit, Careggi Hospital, Viale Morgagni 85, 50134 Florence, Italy
cDepartment of Critical Care Medicine and Surgery, University of Florence, Careggi Hospital, Florence, Italy
dDepartment of Intensive Care Medicine, Careggi Hospital, Florence, Italy

Received 16 December 2008; received in revised form 18 February 2009; accepted 18 February 2009

Abstract

Pulse contour methods (PCM) for the measurements of cardiac output (CO) are gaining popularity in intensive care settings but their reliability during hemodynamic instability has been questioned. Pressure-recording-analytical-method (PRAM) is a newly developed uncalibrated hemodynamic monitor and its capability in measuring CO during hemodynamic instability is still under investigation. Dobutamine (2.5 and 5 μg/kg/min), vasoconstriction (arginine-vasopressin 4, 8 and 16 IU/h), hemorrhage (–10%, –20%, –35%, and –50% of the theoretical volemia), and volume resuscitation were induced in eight swine. CO by means of thermodilution (CO\textsubscript{ThD}), transesophageal echocardiography (CO\textsubscript{TEE}) and PRAM (CO\textsubscript{PRAM}) were contemporarily registered. R\textsuperscript{2}, bias, and percentage error were used to compare the methods. Comparison between CO\textsubscript{max} and CO\textsubscript{max} resulted in: R\textsuperscript{2} = 0.87; bias = –0.006 l/min; precision = ± 0.87 l/min; percentage error = 22.8%. Comparison between CO\textsubscript{max} and CO\textsubscript{max} resulted in: R\textsuperscript{2} = 0.85; bias = –0.007 l/min; precision = ± 0.86 l/min; percentage error = 22%. Sub-group analysis revealed disagreement between methods only during the last two steps of hemorrhage: CO\textsubscript{PRAM} vs. CO\textsubscript{max}: R\textsuperscript{2} = 0.67; bias = –0.37 l/min; precision = ± 1.04 l/min, limits of agreement = –1.39 to 0.66 l/min, and percentage error = 45%; CO\textsubscript{PRAM} vs. CO\textsubscript{max}: R\textsuperscript{2} = 0.38; bias = –0.4 l/min, precision = ± 1.42 l/min, limits of agreement = –0.99 to 1.79 l/min, and percentage error = 62%. PRAM resulted to be accurate in measuring CO during hemodynamic stability, tachycardia, and vasoconstriction. When volemia was reduced by > 35%, disagreement between methods was observed.

© 2009 Published by European Association for Cardio-Thoracic Surgery. All rights reserved.

Keywords: Most-Care™; Pressure-recording-analytical-method (PRAM); Cardiac output; Arterial pulse contour

1. Introduction

Invasive hemodynamic monitoring is a cornerstone of the care of critically ill patients, with the assessment of cardiac output (CO) as one of its main components, since it allows for goal-directed therapy and the titration of inotropes and vasoactive drugs [1].

Thermodilution (ThD) by means of the pulmonary artery catheter (PAC) is considered the clinical gold standard for measuring CO [1]. Nevertheless, the intrinsic invasiveness of PAC has contributed to limit its use in selected populations of patients and to the development of a number of less invasive technologies based on the analysis of a peripheral arterial waveform [1–3]. From the basic model developed by Wesseling et al. [4], several algorithms have been elaborated and measurement of stroke volume (SV) and CO have become part of daily practice [5]. Though such methods are considered ‘non-invasive’, they require an initial calibration using either transpulmonary or pulmonary artery thermodilution [5]. Calibration is necessary because of inter-individual differences in arterial physical properties, continuous changes in vascular tone and volume status in response to therapies and different clinical conditions [5]. Most-Care™ (powered by Pressure-recording-analytical-method-PRAM; Vytech Health™, Padova, Italy) is a low-invasive arterial pressure-based monitor which does not need any starting calibration or central venous catheterization. Although this technology is considered accurate in conditions of hemodynamic stability [6, 7], when profound changes in hemodynamics occur, its accuracy is still to be validated [8]. Since an important clinical issue for a CO measurement technique is the detection of acute hemodynamic changes in critical circulatory states, the aim of our study was to investigate, in a swine model, the reliability of Most-Care™ in conditions of hemodynamic instability in comparison with ThD and transesophageal echocardiography (TEE).

2. Materials and methods

The study was approved by the Institutional Ethics Committee and animals were managed according to the principles of the ‘Guide for the Care and Use of Laboratory
Animals' and according to the Italian national guide for the care and use of laboratory animals (DL. 116/1992).

Eight healthy swine, mean weight 43.3 (11.9; 27–60 kg), were anesthetized with ketamine hydrochloride 1 h before surgery and after muscular paralysis, the trachea was intubated and mechanically ventilated. Anesthesia was delivered with sevoflurane (2–3%). Basic monitoring consisted of ECG (DII) and SpO2. The right femoral artery was cannulated with a standard 18-gauge catheter and connected with Most-Care™ (Ver. 8.04-A) via a pressure monitoring set. The resulting signal was processed for the determination of CO. The right internal jugular vein was cannulated with a standard 18-gauge catheter and connected with Most-Care™ (Ver. Prisma) (Vigilance Monitor, Baxter Edwards Critical Care, Irvine, CA, USA). Then, a TEE probe was positioned and connected to the echo machine (Vivid™; General Electric Medical System). An aortic long-axis view (Fig. 1) was obtained and the probe was fixed maintaining the angle between the aortic blood flow and the continuous wave Doppler beam between 0° and 20°.

2.1. Experimental protocol

The following hemodynamic conditions were induced in the following temporal order:

1. Baseline
2. Dobutamine
3. Baseline
4. Vasoconstriction
5. Baseline
6. Hemorrhage
7. Volume resuscitation

After the achievement of each hemodynamic state, the following parameters were measured: a) simultaneous measurements of CO by means of PAC (CO PAC), TEE (CO TEE), and Most-Care™ (CO MOST); b) heart rate (HR); c) mean arterial pressure (MAP); d) central venous pressure (CVP). Systemic vascular resistances (SVR) were then calculated.

Bolus pulmonary artery thermodilution was performed in triplicate. CO TEE was calculated with the velocity-time integral (VTI) of the blood flow, assessed along the ascending aorta (AA), and the radius of the vessel (r) according to the following formula [9]: $V T I_{AA} (cm) \times CSA_{AA} (cm^2) = SV (cm^3)$; $[CSA_{_AA} = \pi \times r^2$].

Fig. 1. Long-axis view of ascending aorta (left side); continuous wave Doppler (right side). AA, ascending aorta; VTI, velocity time integral.

The series of hemodynamic steps is shown in Fig. 2 where CO trend is depicted. Before starting the dobutamine phase, a baseline measurement was recorded (B1). The dobutamine phase was performed in two separate steps: 2.5 µg/kg/min (D1) and 5 µg/kg/min (D2). Dobutamine infusion was then stopped and after the HR returned within 10% of that measured in B1, C0s were newly performed during this re-established stable condition (B2). Then, three steps of vasoconstriction were induced with arginine-vasopressin (AVP) at the doses of 4 (AVP1), 8 (AVP2), and 16 (AVP3) IU/h. After the end of arginine-vasopressin infusion and normalization of the MAP, a new set of COs were measured (B3). Hemorrhage was obtained with a controlled bleeding obtaining four progressive steps of hypovolemia (H1-H4): H1: −10%, H2: −20%, H3: −35%, and H4: −50% of the theoretical volemia [10]. The last step, volume resuscitation (VR), consisted of the re-establishment of the initial circulating volume with an isovolemic infusion of hydroxyethyl starch 6%.

2.2. Statistical analysis

All the data were analyzed with Stats Direct (Ver.2.5.8, Cheshire, UK) and GraphPad (Ver.Prism 4.0; San Diego, USA). The Kolmogorov–Smirnov test was used to test all data for normality. Continuous data are expressed as the mean (∆D.S.). Hemodynamic variables at each time point were tested for significant differences by two-way ANOVA for repeated measures and Bonferroni’s correction was applied for the post-hoc analysis. The relationships among the three technique variables were investigated by linear regression analysis and Pearson’s correlation coefficient ($r^2$). Agreement between methods was assessed with a Bland–Altman plot [11] obtaining: bias (mean difference between methods), precision ($±2$ S.D. of bias), and limits of agreement (calculated as the bias $(1.96 \times S.D.)$). The percentage error was calculated according to Critchley and Critchley [12], and 30% was set as criterion for interchange-
Table 1
Pearson’s correlation coefficient and Bland–Altman analysis in all data and subgroups

<table>
<thead>
<tr>
<th>Measure</th>
<th>All data</th>
<th>B_r</th>
<th>D_r</th>
<th>AVP_r</th>
<th>H_r</th>
<th>H_r</th>
<th>H_r</th>
<th>VR</th>
</tr>
</thead>
<tbody>
<tr>
<td>( r^2 )</td>
<td>0.8759</td>
<td>0.8227</td>
<td>0.9650</td>
<td>0.8294</td>
<td>0.7264</td>
<td>0.8605</td>
<td>0.6688</td>
<td>0.9261</td>
</tr>
<tr>
<td>Bias (l/min)</td>
<td>-0.0067</td>
<td>-0.0292</td>
<td>0.0375</td>
<td>-0.15</td>
<td>0.0687</td>
<td>0.14</td>
<td>-0.37</td>
<td>0.2125</td>
</tr>
<tr>
<td>Precision (l/min)</td>
<td>±0.87</td>
<td>±0.76</td>
<td>±0.57</td>
<td>±0.72</td>
<td>±1.18</td>
<td>±0.68</td>
<td>±1.04</td>
<td>±0.82</td>
</tr>
<tr>
<td>LoA (l/min)</td>
<td>-0.86</td>
<td>-0.77</td>
<td>-0.52</td>
<td>-0.86</td>
<td>-1.08</td>
<td>-0.53</td>
<td>-1.39</td>
<td>-0.56</td>
</tr>
<tr>
<td>PE (%)</td>
<td>0.84</td>
<td>0.72</td>
<td>0.59</td>
<td>0.56</td>
<td>1.22</td>
<td>0.80</td>
<td>0.66</td>
<td>1.04</td>
</tr>
</tbody>
</table>

ThD, thermodilution; TEE, transesophageal echocardiography; PRAM, pressure recording analytical method; B_r, basal; D_r, dobutamine; AVP_r, arginine vasopressin; H_r, hemorrhage; VR, volume resuscitation; LoA, limits of agreement; PE, percentage error.

3. Results
Throughout the study, an overall of 312 CO measurements were performed. CO_THD ranged from 1.9 to 4.93 l/min, CO_TEE from 2.1 to 5.3 l/min, and CO_PRAM from 1.7 to 5 l/min.

Table 1 and Figs. 3 and 4, depict the statistical analysis: linear regression with Pearson’s correlation coefficient, Bland–Altman plot and data, percentage error calculation. The statistical analysis including all measurements showed optimal agreement between PRAM with both PAC (\( r^2 = 0.88 \), bias = -0.0067, percentage error = 22.8%) and TEE (\( r^2 = 0.85 \), bias = -0.007, percentage error = 22%). The selected analysis of the different hemodynamic phases showed good agreement in every phase other than during...
the hemorrhage where percentage error increased to 43.6% (PRAM-ThD) and 53.3% (PRAM-TEE).

The sub-analysis of hemorrhage showed that during the first and second step (H₁₂₃) a good agreement between methods was confirmed while during the last two steps (H₄₅₆) a worsening of agreement came out in both PRAM-ThD ($r^2=0.67$, bias = -0.37, and percentage error = 45%) and PRAM-TEE ($r^2=0.38$, bias = 0.4, and percentage error = 62%).

4. Discussion

A number of minimally invasive monitoring devices based on pulse contour method (PCM) are commercially available. The most widely used are as follows: the PiCCOplus (Pulsion Medical Systems), PulseCO (LiDCO Ltd), and Flo Trac/Vigileo (Edwards LifeScience) systems [5, 15]. There are several differences between these systems, mainly regarding the method of initial calibration. The PiCCO system uses a transpulmonary thermodilution method, whereas LiDCO uses a lithium calibration technique. Resistance, compliance, and impedance are physical properties of the arterial system that have be taken into account for the SV calculation. Hence, when changes in vascular compliance occur, a recalibration could be necessary to avoid incorrect measures of CO. Flo Trac/Vigileo, in contrast to the previous systems, uses the patient’s demographic and physical characteristics (age, height, gender, and weight) to estimate SV. Stroke volume is calculated using arterial wave (S.D. of the pressure wave over a 20-s interval), using a constant $K$ derived from the patient’s specific vascular compliance based on patient’s characteristics. The PiCCO and LiDCO systems are validated against reference methods in different clinical conditions; Flo Trac/Vigileo is still under investigation since validation studies have produced conflicting results which may be due in part to different algorithms of SV estimation.

Most-Care with PRAM system is the only system that does not require external calibration or preloaded data. Since studies exploring the reliability of Most-Care in conditions of hemodynamic instability are still lacking, we performed this experimental study in order to evaluate its reliability under hemodynamic derangements.

During hemodynamic stability and all phases of both dobutamine infusion and vasoconstriction, Most-Care proved to be reliable in measuring CO when compared with both ThD and TEE, suggesting that its algorithm works with a high degree of precision in both conditions of tachycardia and increased tone of the vascular system. Otherwise, during hemorrhage, a consistent level of disagreement between methods was pointed out, with a percentage error exceeding the value of 30% suggested by Critchley and Critchley as limit for clinical acceptance for a new method [13]. Nevertheless the analysis of sub-groups of hemorrhage ($H_{₁₂₃}$ and $H_{₄₅₆}$) demonstrated that only when volemia decreases > 35% Most-Care and reference methods for CO measurement disagree. Such observations suggest that a deep reduction in SV may affect the accuracy of Most-Care.

This is the first study that evaluates an uncalibrated system for CO measurement based on PCM comparing it with both ThD and TEE. The decision to design the study to include an ultrasound technique, in addition to the widely adopted ThD, arises from two factors: firstly, to exclude heart diseases that are suspected to affect the arterial pulse contour by influencing the arterial pressure waveform (i.e. aortic valve stenosis or insufficiency); secondly, to overcome limits of ThD. Notorious, variability in the ThD method occurs because of differences in injection technique, fluctuation in blood temperature, and cyclical variations in CO with mechanical ventilation [14]. Moreover, TEE is considered an effective method for CO measuring and it is widely used in clinical daily practice in intensive care. We hope to achieve a higher level of accuracy in the different clinical conditions of hemodynamic instability by using both ThD and TEE as methods for comparison.

Some lack of agreement among methods of measurement is inevitable [13] but the amount by which methods disagree is important and, furthermore, what are the conditions in which variance becomes clinically unacceptable. Our study showed that Most-Care was less accurate during the lower-SV phases. It is worth noting that measurement of CO is particularly useful for clinicians when changes in arterial tone occur (i.e. septic states, post CPB-SIRS-like states, vasoconstrictive therapies for arterial pressure maintenance, etc.). In such conditions an over- or under-estimation of CO could be particularly harmful, since it could lead to errors in therapeutic strategies. In our study, Most-Care was not influenced by modifications in vascular tone probably because, unlike from other PCM [15], it does not use preloaded values but real-time calculates the degree of arterial impedance.

A low-invasive hemodynamic monitor may be a useful alternative to standard methods in a large population of patients as in settings in which an invasive and/or aggressive monitoring arrangement is not justified or disproportionate but the patients are at risk of developing hemodynamic instability (e.g. percutaneous interventions). However, clinicians should keep in mind the specific pitfalls and limitations that can affect the accuracy of such methods in order to avoid the risk of misinterpretation of numbers that can be similarly useful or harmful.

4.1. Most-Care – device characteristics

PRAM is based on the principle that, in any given vessel, volume changes occur mainly because of radial expansion in response to variations in pressure [6]. This process involves the dynamic interplay among several physical parameters including the force of left ventricular ejection, arterial impedance counteracting the pulsatile blood inflow, arterial compliance, and peripheral, small vessel resistance. These variables are closely interdependent and simultaneously evaluated by PRAM [6]. Thus, any kind of flow that is perceived at the peripheral arterial level, whether pulsatile and continuous, can be evaluated. According to pulse contour methodology [4] changes in the area (A) under the pulsatile systolic portion of the pressure waveform reflect changes in SV. In PRAM, differently from other PCM, A is computed taking into account both pulsatile
and continuous contributions of the physical forces underlying the relationship between pressure curve morphology and blood flow. The whole concept behind PRAM represents the practical application of a theoretical model totally developed a priori and, differently from other PCM [5, 15] PRAM does not requires prior calibration based on independent measurements of flow end/or pre-calculated parameters. The ratio between pulsatile and continuous A and SV is represented by a factor, system impedance Z(t), determined by the physical characteristics of the circulatory system of the subject under study. By applying PRAM, it is possible for each subject to compute Z(t) directly from the analysis of the pressure recording signal, without predicted data derived from unrelated in-vitro measurements nor calibrating factors derived by independent measurements of CO [6].

Another important characteristic of the PRAM methodology is the frequency sampling at 1000 Hz differently from the other PCM that usually use a sampling rate of 100 Hz. Since the Most-Care™ uses an algorithm of calculation closely dependent on a highly detailed arterial wave morphology that is analyzed by point by point, each intrinsic (aortic dissection, arterial compression, atherosclerotic plaques near the tip of the catheter, etc.) or extrinsic (bubble air, resonance phenomenon of the artery-catheter-tubing-transducer line, etc.) disturbances may influence the system leading to incorrect hemodynamic results. A careful observation of the arterial wave morphology represents the first and primary contribution that the physician has to take into account when an arterial-based hemodynamic monitoring is used.

References


eComment: Non-invasive ultrasonic cardiac output monitoring in the surgical operating room

Author: Karsten Knobloch, Hannover Medical School, Plastic, Hand and Reconstructive Surgery, Hannover, Germany
doi:10.1510/icvts.2008.200451

I read with great interest the recent experimental report by Dr. Romagnoli and co-workers evaluating a pressure-recording analytical method (PRAM, Most-Care) as an uncalibrated hemodynamic monitor in various hemodynamic states in anaesthetized swine [1]. In contrast to the PiCCO, the LiDCO or the Flo Trac (Vigileo) systems, which are to be calibrated, the Most-Care system is the only invasive pulse contour system that is thought not to require external calibration or preloaded data. However, both calibrated and non-calibrated pulse contour analysis do require an arterial line, thus it is invasive to a certain degree. Therefore, the claim to be non-invasive using pulse contour analysis is not valid.

The authors stated: ‘It is worth noting that measurement of CO is particularly useful for clinicians when changes in arterial tone occur (i.e. septic states, post CPB-SIRS-like states, vasoconstrictive therapies for arterial pressure maintenance, etc.).’ I would disagree with this statement, since hemodynamic information is important in various states. In the operating theatre, optimizing fluid resuscitation has been proved to improve clinical outcome. As such, complete non-invasive ultrasonic cardiac output monitoring (USCOM) has been found accurate during living transplantation [2].

Notably, as far as invasiveness is concerned, completely non-invasive external ultrasonic cardiac output monitoring has been tested clinically in various patient groups. USCOM compared with pulmonary artery catheters was found acceptable and capable in comparing different shock types in ICU patients [3]. In cardiac surgery patients, USCOM could determine non-invasive beat-to-beat cardiac output in postcardiac surgery patients without the possible complications associated with invasive right heart catheterization. The USCOM cardiac output and stroke volume showed a very good agreement with invasive Swan-Ganz measures and correlated with central venous saturation percentage. Recently, USCOM has been used in cardiac output monitoring even in an orthotopic total artificial heart clinically (CardioWest) [5].

References


