Maurizio Cecconi Manu L. N. G. Malbrain

Cardiac output obtained by pulse pressure analysis: to calibrate or not to calibrate may not be the only question when used properly

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M. Cecconi (⊠) Critical Care Department, St George's Hospital, London SW17 0QT, UK e-mail: m.cecconi@nhs.net

M. L. N. G. Malbrain Department of Intensive Care and High Care Burn Unit, Ziekenhuis Netwerk Antwerpen, ZNA Stuivenberg, Lange Beeldekensstraat 267, 2060 Antwerp 6, Belgium

Cardiac output (CO) is the main determinant of oxygen delivery and physical examination, and vital signs alone often fail to reflect significant derangements in CO [1]. Because of the complexity of assessment of clinical variables in unstable patients, direct measurement of CO is advisable. Pulse pressure (PP) analysis, often referred to as pulse contour (PC) analysis, is the analysis used by technologies that estimate changes in stroke volume (SV) and CO from an arterial pressure waveform signal [2, 3]. The theory behind this approach dates back to the end of the nineteenth century when the German physiologist Otto Frank proposed the Windkessel (air chamber) model of cardiovascular physiology [4]. In a system with air and fluid, different air chambers were filled with air in order to simulate compliance, resistance and impedance of the cardiovascular system. This proved to be pivotal to our understanding of the importance of the relationship between flow and pressure. In the early twentieth century Erlanger and Hooker defined a relationship between stroke volume and arterial pressure, and crucially a correlation between SV and PP [5].

It was not until the development of modern computer technology that this theory could be put into practice and SV and CO tracked continuously on a beat to beat basis [6]. Since then the number of PP analysis devices has increased continuously over the years; some of these devices require an initial calibration; some are "self-calibrating" based on nomograms and anthropomorphic data [7, 8].

No matter which one of these technologies one wants to use, the understanding of the physiological principles behind it is the cornerstone for its proper use. Without this, monitors may be used inappropriately and patients put at risk.

So what are the important questions related to PP analysis? There are several and in this editorial we would like to focus mainly on four:

- 1. Are there any conditions in which PP analysis may suffer from intrinsic limitations?
- 2. What are the possible indications for PP analysis CO monitors?
- 3. How does calibration fit into this?
- 4. How to translate this into practice?

1. Pressure waves and flow waves are not the same thing. The algorithms behind PP analysis have to estimate flow from pressure. In those situations in which either the signal is poor (for instance severely underdamped or overdamped traces), or in which the relationship between pressure and flow is severely deranged, as in the case of severe aortic regurgitation or with counter-aortic balloon pumps, PP analysis will not provide reliable information [2].

2. PP analysis can be used to take a snapshot of the circulation or to look at how SV and CO change over time [9]. Reliability derives mainly from two principles: accuracy and trending ability. Understanding of accuracy (how close to the real absolute value a measurement is) and trending ability is very important in order to use the

full potential of these devices [10]. Both these principles are used routinely at the bedside. For instance, when assessing a patient in shock, knowing if the CO is 2.0 or 15 L/min may be important to confirm our diagnosis and plan and guide future management [11]. In this case we are looking at how accurate our estimation of CO is. When an accurate initial assessment has been performed (often with an intermittent dilution technique), it is often more crucial to know whether a clinical intervention is leading toward one direction or the other. As such, the absolute value of CO is less important than the trending ability of monitors to track changes continuously [9, 12]. This is important because, for instance, it is unlikely that in patients with a hyperdynamic circulation (cirrhosis, pancreatitis, burns) PP analysis will provide accurate readings, unless calibrated frequently; however, trending over short periods of time may still be useful. There are also situations in which PP analysis simply does not represent a solution, because of limitations both in terms of accuracy and trending ability [13, 14]. Clinicians must be aware of these and that significant hemodynamic changes will affect the reliability of the devices in terms of accuracy and/or trending ability, as demonstrated in the present study.

3. Most PP analysis devices are a combination of two systems: a PP analysis algorithm and a calibration system. The PP analysis algorithm is the core of the monitor that allows beat to beat changes in SV and CO to be tracked. The calibration is what is used by the monitor to scale the estimated value of CO to an absolute value. While most calibrations will also provide additional information for the PP algorithm (therefore affecting also the way changes are detected) [15], their contribution relates more to the absolute value of CO. When performing a calibration this has to be done properly: similarly to the zeroing of an arterial line, if the calibration process is not done properly it will add error, instead of increasing accuracy [16]. If done properly it can set or reset the continuous CO to an accurate value. This is important to keep in mind when assessing longer periods of trend, as most devices will show some drift over time or after significant changes in vascular impedance [17].

4. Most often PP analysis is used to assess the response to a fluid challenge. As such PP analysis can help us to solve therapeutic conflicts (defined as a situation where each of the possible therapeutic decisions carries some potential harm) [1, 18]. Therapeutic conflicts are the biggest challenge for protocolized hemodynamic management in critically ill patients. A therapeutic conflict is where our decisions can make the biggest difference. We have to recognize that CO measurement may be a lot less informative and accurate than we may want (or think). Continuity of CO measurement (and trending ability) offers vital insights that may be hidden in the analog signals of our monitors and may be more important than accuracy. "Physiological examination"—observing multiple parameters on the monitor in real time—should be considered to be (at least) as important as the classic "physical examination" [1, 19].

Most of the points we discussed have been explored in the study by Petzoldt et al. [20]. In this study they looked at the performance of calibrated and uncalibrated PC monitors in the context of severe valvular disease, comparing them to transoesophageal echocardiography. The calibrated SV (SV_{PCCAL}) was measured via the PiCCOTM (Pulsion Medical Systems, Munich, Germany); in this case the calibration technique used was the transpulmonary thermodilution (TPTD). The uncalibrated SV $(SV_{PCUNCAL})$ was measured via the third-generation Flotrac/VigileoTM monitor (Edwards Lifesciences, Irvine, CA, USA). The lowest limits of agreement in terms of percentage error (PE) were found for TPTD both in aortic stenosis (AS) and aortic insufficiency (AI). In AS, TPTD and SV_{PCCAL} performed with an acceptable PE (26.3 and 25.7 %, respectively) compared to SV_{PCUNCAL} (50.4 %). In AI, both SV_{PCCAL} and SV_{PCUNCAL} did not show acceptable PE (51.5 and 61.9 %, respectively), while TPTD maintained good PE even in this context (PE 26.2 %). Looking at the polar plot for trending capacity, all three methods showed an acceptable performance, proving that in terms of trending even devices with a poor level of accuracy can provide useful information.

In this elegant study the authors have provided further confirmation regarding PP analysis:

- When PP analysis is used in severe valvular disease, especially for AI, an accurate snapshot requires calibration (and recalibration).
- Calibration with TPTD performs well even during valvular disease.
- Trending is partially maintained even when accuracy is not at its best.
- Continuity may be more important than accuracy.
- Physiological examination should be considered to be (at least) as important as the classic physical examination.

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