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Noninvasive continuous cardiac output monitoring in perioperative and intensive care medicine

B. Saugel[1†*], M. Cecconi[2†], J. Y. Wagner[1] and D. A. Reuter[1]

[1] Department of Anesthesiology, Center of Anesthesiology and Intensive Care Medicine, University Medical Center Hamburg-Eppendorf, Martinistrasse 52, Hamburg 20246, Germany
[2] Anaesthesia and Intensive Care, St George's Hospital and Medical School, London SW17 0QT, UK

* Corresponding author. E-mail: bernd.saugel@gmx.de

Editor's key points

- The authors review the burgeoning array of non-invasive cardiac output monitors.
- They note the varied limitations of the devices and note the need for appropriate description of device performance.
- The need for uniformity in defining clinically acceptable performance is highlighted.

Summary. The determination of blood flow, i.e. cardiac output, is an integral part of haemodynamic monitoring. This is a review on noninvasive continuous cardiac output monitoring in perioperative and intensive care medicine. We present the underlying principles and validation data of the following technologies: thoracic electrical bioimpedance, thoracic bioreactance, vascular unloading technique, pulse wave transit time, and radial artery applanation tonometry. According to clinical studies, these technologies are capable of providing cardiac output readings noninvasively and continuously. They, therefore, might prove to be innovative tools for the assessment of advanced haemodynamic variables at the bedside. However, for most technologies there are conflicting data regarding the measurement performance in comparison with reference methods for cardiac output assessment. In addition, each of the reviewed technology has its own limitations regarding applicability in the clinical setting. In validation studies comparing cardiac output measurements using these noninvasive technologies in comparison with a criterion standard method, it is crucial to correctly apply statistical methods for the assessment of a technology's accuracy, precision, and trending capability. Uniform definitions for 'clinically acceptable agreement' between innovative noninvasive cardiac output monitoring systems and criterion standard methods are currently missing. Further research must aim to further develop the different technologies for noninvasive continuous cardiac output determination with regard to signal recording, signal processing, and clinical applicability.

Keywords: cardiac output; intensive care unit; monitoring, intraoperative

Determination of blood flow, i.e. cardiac output, is an integral part of advanced haemodynamic monitoring in perioperative and intensive care medicine. Besides the pulmonary artery thermodilution technique using the pulmonary artery catheter (PAC) and transpulmonary thermodilution, less invasive technologies for both intermittent and continuous cardiac output determination have been developed including calibrated and un-calibrated (i.e. calibrated according to algorithms based on biometric data) pulse contour analysis and oesophageal doppler.

In addition, completely noninvasive technologies such as thoracic electrical bioimpedance, thoracic bioreactance, vascular unloading technique, pulse wave transit time, and radial artery applanation tonometry are now available for cardiac output monitoring.

In this review, we focus on noninvasive continuous cardiac output monitoring in perioperative and intensive care medicine. We discuss how novel technologies should be appropriately evaluated with special regard to the statistical methods applied in comparison studies. Finally, we present the underlying principles and validation data of currently available technologies for noninvasive continuous cardiac output determination.

Clinical relevance of cardiac output determination and optimization

The importance of cardiac output – pathophysiologic basics

The outstanding importance of cardiac output becomes clear when considering that the total amount of oxygen delivered by the cardiovascular system can be quantified by calculating oxygen delivery (DO_2):

$$DO_2[\text{ml min}^{-1}] = \text{cardiac output [litre min}^{-1}] \times \text{arterial oxygen content [ml dl}^{-1}] \times 10$$

(with cardiac output [litre min^{-1}] = stroke volume [litre] × heart rate [1 min^{-1}])

† B.S. and M.C. contributed equally to the work.

Knowing a patient's DO_2 and global oxygen consumption (VO_2) the oxygen extraction ratio can be assessed. Critical illness or major surgery induces a systemic inflammatory response syndrome resulting in a marked increase in oxygen demand. To meet this increased oxygen demand in these clinical conditions, compensation mechanisms resulting in an increase in DO_2 are needed. These mechanisms include an increase in cardiac output and oxygen extraction ratio. The inability to increase cardiac output can result in tissue hypoxia and ultimately organ dysfunction. Therefore, to avoid inadequate DO_2 in these patients, therapeutic interventions such as administration of fluids and inotropic agents aim at optimization of cardiac output.

Perioperative medicine

In surgical patients, protocol-based optimization of haemodynamic variables reduces postoperative mortality and morbidity in high-risk surgical patients according to large meta-analyses.[1–3] A recent Cochrane Systematic Review including more than 5000 patients from 31 studies provides evidence that goal-directed therapy aiming to increase global blood flow reduces postoperative complications and hospital length of stay.[4] In addition, improved patient outcome in terms of a reduction in postoperative complications and hospital length of stay by goal-directed haemodynamic therapy was revealed in a recent meta-analysis, also in cardiac surgery patients.[5]

Although this approach is still not widely adopted in routine clinical care, there is considerable evidence to show that goal-directed haemodynamic strategies aiming at an optimization of cardiac output/cardiac index and DO_2 in selected high-risk surgical patients can contribute to a reduction of postoperative morbidity and mortality.[6]

Critical illness

In critically ill patients treated in the intensive care unit (ICU), monitoring of blood flow and tissue oxygenation is an integral part of the management of these patients. The assessment of cardiac output plays a pivotal role in the differential diagnosis of shock states.[7 8]

In addition, cardiac output monitoring is crucial in the identification of patients who are fluid responsive, i.e. patients who are able to increase their stroke volume and cardiac output after a fluid challenge test or a passive leg raising test.[9 10]

Especially in patients with severe sepsis, relative intravascular hypovolemia due to a mediator-induced increased capillary permeability and septic myocardial dysfunction make close monitoring of cardiac preload and cardiac output inevitable.[11]

How should we adequately evaluate innovative noninvasive cardiac output monitoring technologies?

Criterion standard methods

One key problem related to validation studies for novel cardiac output monitoring technologies is that there is no generally accepted consensus on which established monitoring technique should be used as the criterion standard. While pulmonary artery thermodilution measurements using a PAC are generally accepted as the clinical criterion standard method,[12] among other techniques, transpulmonary thermodilution, pulse contour analysis, and echocardiography have also been used in previous validation studies. The question still remains unanswered whether invasive criterion standard technologies such as thermodilution using a PAC or transpulmonary thermodilution are the appropriate comparators when testing innovative noninvasive devices.[13]

Statistical analyses in method comparison studies evaluating innovative cardiac output monitoring technologies

Appropriate statistical analyses are the prerequisite for a sound interpretation of method comparison studies describing the measurement performance of novel cardiac output monitoring technologies.[13] Different statistical methods for the assessment of a system's accuracy, precision, and trending ability in comparison with a criterion standard technology have been described.

First, it should be noted that correlation analysis, although frequently used in method comparison studies evaluating agreement, does not measure *agreement* between two methods, but rather their *relationship*.[14] Therefore, correlation analysis should not be used as the single statistical method in clinical studies comparing new technologies for cardiac output measurement with an established reference technique.

To illustrate the statistical tests discussed in the following, we present two worked examples describing cardiac output measurements obtained with a reference technology in comparison with a studied technology in 20 individual patients at three different time points (Table 1). The two studied methods were chosen to represent good (example 1) and poorer (example 2) measurement performance with regard to absolute accuracy and precision as well as trending of cardiac output values compared with the reference technology.

Bland-Altman analysis including computation of a Bland-Altman plot has become the accepted standard statistical approach for the evaluation of the agreement, i.e. accuracy and precision, of a new cardiac output monitoring system in comparison with criterion standard cardiac output measurements.[14 15] Further development of the initially presented Bland-Altman analysis allows taking multiple and unequal numbers of measurements per individual into account.[14] When applying Bland-Altman analysis to evaluate the agreement of an innovative cardiac output measurement technology in comparison with a criterion standard method for cardiac output assessment, the mean difference (i.e. bias) and the limits of agreement (i.e. 1.96 × standard deviation of the mean difference) reflect the new technology's accuracy and precision, respectively (Fig. 1A and B).

In addition, the percentage error as proposed by Critchley and Critchley can be calculated as 2 times the standard deviation of the mean difference divided by the mean of measurements (Fig. 1A and B).[16]

Besides high accuracy and precision, the ability to accurately follow changes in cardiac output is of crucial importance for