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Less invasive hemodynamic monitoring in critically ill patients

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Abstract

Over the last decade, the way to monitor hemodynamics at the bedside has evolved considerably in the intensive care unit as well as in the operating room. The most important evolution has been the declining use of the pulmonary artery catheter along with the growing use of echocardiography and of continuous, real-time, minimally or totally non-invasive hemodynamic monitoring techniques. This article, which is the result of an agreement between authors belonging to the Cardiovascular Dynamics Section of the European Society of Intensive Care Medicine, discusses the advantages and limits of using such techniques with an emphasis on their respective place in the hemodynamic management of critically ill patients with hemodynamic instability.

Keywords: Hemodynamic monitoring, Pulse contour analysis, Transpulmonary thermodilution, Pulse pressure variation, Esophageal Doppler, Bioreactance

Introduction

Patients with circulatory shock have a high risk of mortality. Most often, the mechanisms involved in shock are complex and involve more than one of the three major hemodynamic abnormalities, namely hypovolemia, myocardial dysfunction, and alteration in vascular tone. Sometimes, acute respiratory failure is associated with shock, with risks of lung edema with fluid therapy. It is thus fundamental to accurately assess the respective degree of each of these components to select the most appropriate therapeutic options. Clinical examination is essential. Although it is of great value in the initial phase of shock, it suffers from some limitations in reliably identifying the main hemodynamic problem in the complex situations that are frequently encountered in the intensive care unit (ICU) [1–3]. Bedside monitoring methods have been developed to help clinicians to better assess the hemodynamic situation and to evaluate the response to therapy.

Over the last decade, hemodynamic monitoring has evolved considerably in the ICU as well as in the operating room. The most striking evolution has been the declining use of the pulmonary artery catheter (PAC) along with the growing use of either minimally or totally non-invasive hemodynamic monitoring techniques. The reasons for the declining use of the PAC are multiple. They include not only invasiveness (maintenance of a catheter in a pulmonary artery passing through the right ventricle) but also difficulties in appropriately measuring and interpreting the data [4] and findings from randomized clinical trials showing no outcome benefit of using PAC in ICU patients [5]. Some less invasive techniques such as the transpulmonary thermodilution systems still need the placement of a central venous catheter and a femoral artery catheter, which carry risks of bloodstream infections [6], although their use by intensivists that have experience with these systems was shown to be

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associated with a low rate of complications [7]. One of the main particularities of minimally and non-invasive techniques is their ability to provide continuous cardiac output (CO) and fluid responsiveness variables in real time. The importance of the concept of fluid responsiveness, extensively developed during recent years, is emphasized by the two following facts. First, half of ICU patients are fluid non-responders as their CO does not increase with fluid administration [8]. Second, fluid overload in ICU patients was shown to be associated with increased mortality [9]. Bedside techniques that provide indices of fluid responsiveness are helpful to better assess the benefit/risk ratio of fluid therapy because outcome studies using these techniques in ICU patients are still lacking.

In this article, we review the main minimally or non-invasive hemodynamic monitoring techniques. We also define their place in the management of ICU patients, because no strong evidence has emerged in spite of the high number of articles published over the last decade. Most of them included a single-center evaluation and/or a limited number of patients with heterogeneous cardiovascular derangements.

A common characteristic of the minimally and non-invasive techniques is to measure and monitor CO, a macrocirculatory variable which is well known by ICU physicians. However, monitoring CO is far from being enough to manage patients with complex hemodynamic disorders, since this variable is only one piece of the puzzle. Most of the monitoring techniques described in this article provide other relevant hemodynamic variables, which help to better define the macrocirculatory disorders, to select the best therapy, and to monitor its effects.

Minimally (or less invasive) hemodynamic technologies

In this section, we first consider the methods that use the arterial pulse contour analysis and then the esophageal Doppler that uses ultrasound.

Methods that use arterial pulse contour analysis

General principles

All less invasive and non-invasive devices that estimate stroke volume from the arterial pressure pulse waveform are based on the principle of ventriculo-arterial coupling, in that the arterial pulse pressure and its contour are primarily determined by left ventricular stroke volume and arterial impedance. Each device uses different proprietary algorithms based on slightly different assumptions that make their interoperability questionable [10]. In general, devices that are externally calibrated using an independent estimate of CO tend to be more accurate but do require frequent recalibration [11] if vasomotor tone changes, either spontaneously (e.g., as a result of sepsis) or because of modification of therapy. A major interest of the pulse contour analysis systems is the real-time, short-term tracking of CO changes induced by therapeutic tests such as external (fluid administration) or internal (e.g., passive leg raising) volume challenges. The pulse contour analysis systems also provide automatic calculation of dynamic indices of fluid responsiveness such as pulse pressure variation (PPV) and/or stroke volume variation (SVV). Using PPV and SVV to predict fluid responsiveness is based upon the concept of heart–lung interactions during mechanical ventilation revealing cardiac preload dependence [12]. In situations where PPV and SVV are not valid (e.g., spontaneous breathing activity, arrhythmias, low tidal volume, low lung compliance), monitoring pulse contour CO during internal volume challenges such as passive leg raising or end-expiratory occlusion can reliably predict fluid responsiveness [13, 14].

In clinical practice, the reliability of pulse contour CO and derived variables is decisively dependent on the quality of the arterial pressure signal, i.e., over- and under-damping of the signal, for example induced by bubbles of air within the liquid-filled or unnecessary prolonged arterial lines.

Calibrated arterial pulse analysis systems

Transpulmonary thermodilution and lithium dilution can serve to externally calibrate the pulse contour analysis.

Transpulmonary thermodilution The transpulmonary thermodilution method provides intermittent measurements of CO and other variables by applying the indicator dilution principle based on temperature changes over time (Fig. 1). The transpulmonary thermodilution devices [PiCCO (Pulsion Medical systems, Germany) and VolumeView (Edwards Lifesciences, USA)] are less invasive than the PAC (no catheter traversing the heart) but still require insertion of a central venous catheter (for cold bolus injection) and a thermistor-tipped (femoral) artery catheter. This technique is being used in devices that combine transpulmonary thermodilution and pulse contour analysis. The mathematical analysis of the thermodilution curve (blood temperature vs. time) allows calculation of the following variables: (1) CO; (2) global end-diastolic volume, a volumetric estimate of global preload; (3) cardiac function index and global ejection fraction, indicators of cardiac systolic function; (4) extravascular lung water (EVLW), a quantitative measure of lung edema; and (5) pulmonary vascular permeability index, a marker of lung capillary leak. There is acceptable agreement between transpulmonary thermodilution and intermittent pulmonary artery thermodilution measures of CO in ICU patients [15]. The measurement of CO is reliable provided that three cold boluses are injected [16]. Moreo-

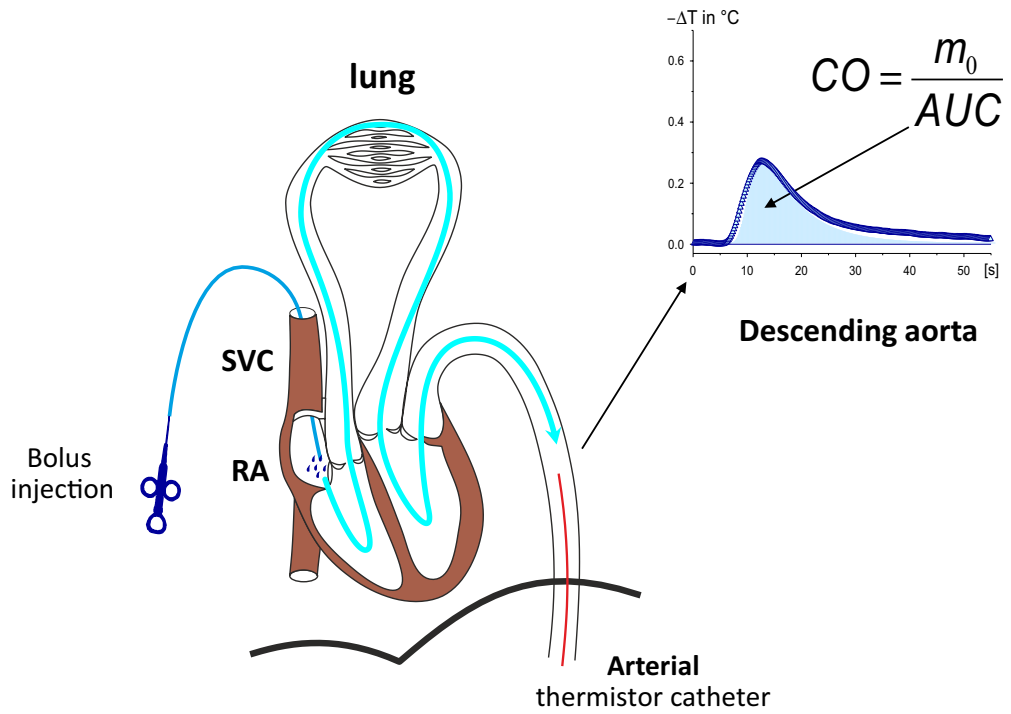

Fig. 1 Thermodilution method for intermittent cardiac output (CO) measurements. After injecting a cold indicator (usually saline) into the right atrium (RA) via a central venous catheter, the resultant thermodilution curve can be derived in the descending aorta (transpulmonary thermodilution). *AUC* area under thermodilution curve, m_0 = amount (or mass) of injected cold at the time of injection (t_0) = (blood temperature minus injectate temperature) × (injectate volume minus dead space volume of catheter), $-\Delta T$ = decrease in blood temperature, °C = degree Celsius, *SVC* superior vena cava, *RA* right atrium

ver, the transpulmonary thermodilution bolus injection is being used to calibrate the artery pressure waveform analysis that provides continuous, real-time calculation of CO by using proprietary algorithms based on the relationship between stroke volume and arterial pressure waveform. An acceptable agreement between arterial pressure-derived and thermodilution CO was reported in hemodynamically unstable patients [17]. However, frequent recalibration is required [11].

One major advantage of the transpulmonary thermodilution devices is that they provide EVLW, which can be used as a safety parameter during fluid therapy, especially in capillary leak states [18], where it was shown to have a prognostic value [19, 20].

Lithium dilution The lithium dilution method (LiDCOplus, LiDCO, UK) is an indicator dilution technique, which provides intermittent CO measurements. A small amount of lithium chloride is injected through a central venous catheter, and changes in lithium levels are detected in the blood drawn from a radial artery catheter over a lithium-selective sensor. The CO is then measured from analysis of the lithium dilution curve (lithium concentration vs. time). This technique has been validated against pulmonary artery thermodilution in humans [21]. As for transpulmonary thermodilution, three measurements should be averaged to achieve a good precision [22]. The major inconvenience of this system is the need for lithium injection, which is less safe than saline injection and cannot be repeated infinitely because of lithium accumulation, and moreover it is costly. The monitor also contains a proprietary algorithm that converts an arterial blood pressure waveform-based signal into an arterial blood flow measurement using a pulse power analysis. In addition the lithium bolus injection serves to calibrate the system, which then provides a beat-to-beat measurement of CO, PPV, and SVV. The lithium dilution system can be used with a radial artery catheter but it does not provide advanced hemodynamic and volumetric variables such as EVLW.

Uncalibrated arterial pressure waveform analysis CO monitors

Some monitors provide real-time CO measurements by deriving the stroke volume from the arterial pressure waveform recorded from an arterial catheter, but they do so without external calibration. Several devices are

commercialized [FloTrac (Edwards Lifesciences, USA), LiDCOrapid (LiDCO UK), ProAQT (Pulsion Medical Systems, Germany)] and use different proprietary algorithms that analyze the characteristics of the arterial pressure waveform along with patient-specific anthropometric and demographic data. By nature, these systems necessarily use a statistical correction that mandates a bias when a specific patient is out of standard range. These devices can be used with any arterial catheter. Knowing that frequent recalibration of pulse contour analysis is actually required in hemodynamically unstable patients to provide reliable data [11], it is clear that the uncalibrated systems must become unreliable when major hemodynamic changes are occurring. Hence, these systems should be restricted to hemodynamically stable patients or when CO monitoring is required for short periods of time, e.g., during surgery. In such situations and provided that CO is normal or low, the most recent versions of uncalibrated CO monitoring devices provide reliable CO measurements [23], as suggested by percentage errors of less than 30 % [24] found in validation studies [23]. However, the upper limit of acceptability of the percentage error also depends on the reproducibility of the compared methods [25], which was not always provided in the studies that reported percentage error values. The derived PPV and/or SVV is very suitable for predicting fluid responsiveness in the operating room setting, where these indices are generally reliable [26] and, as such, used in many goal-directed algorithms for guiding intraoperative fluid management. Finally, the ability of uncalibrated CO monitors to track short-term changes in CO following fluid infusion could be acceptable [27], although divergent results were reported [23].

The pressure-recording analytical method monitors CO in real time using a proprietary algorithm that takes into account the area under the systolic part of the arterial pressure curve and the mean arterial pressure [28]. This technology, implemented in the MostCare device (Vytech, Italy), does not require any calibration or adjustments based on user-entered data. When compared to thermodilution, divergent results were reported [29, 30].

Uncalibrated CO systems do not provide other hemodynamic variables than CO, PPV, or SVV. This represents an important disadvantage for the complex hemodynamic situations compared to the advanced monitoring methods such as the PAC or the transpulmonary thermodilution systems.

Esophageal Doppler

Esophageal Doppler (CardioQ, Deltex Medical, UK) provides real-time estimation of blood flow in the descending thoracic aorta from the aortic blood velocity and the aortic diameter. On the basis of the hypothesis of a constant distribution of CO between the upper territories and the descending aorta, the CO value is inferred from the descending aorta blood flow value. The validity of CO estimation by esophageal Doppler was confirmed in both critically ill and patients undergoing surgery [31]. However, some limitations must be known. First, the distribution of CO between the upper and the lower parts of the arterial system can be affected by changes in the sympathetic tone, which occur frequently in patients with shock and/or receiving vasoactive drugs. Second, the diameter of the descending aorta is not measured but estimated from the patient's characteristics. However, the aorta at this level is compliant enough to change its diameter in response to changes in mean arterial pressure [32]. Thus, currently available esophageal Doppler systems that only estimate the aortic diameter bear a risk of poorly tracking the real changes in CO during shock resuscitation [32]. On the other hand, old models of esophageal Doppler probes that measure the aortic diameter carry some risk of error of measurement of stroke volume, as even a limited error in the diameter can have a significant impact as the radius is dependent on the square of that value. Finally, movements of the Doppler probe often occur in less-sedated patients, resulting in loss of the signal with the necessity of repositioning the probe. For these reasons, the use of esophageal Doppler is more questionable in the ICU than in the operating room setting, where its use for goal-directed hemodynamic management was shown to decrease postsurgical morbidity [33]. Nevertheless, esophageal Doppler can be helpful in sedated ICU patients for assessing short-term changes in CO such as those induced by fluid loading or passive leg raising, especially when no other hemodynamic monitoring systems are available.

Non-invasive techniques

Fully non-invasive techniques providing CO estimation have been introduced recently [34–36].

Continuous analysis of the arterial pressure waveform is possible by using either the volume clamp method [Clearsight (Edwards Lifesciences, USA), ex Nexfin (BMYE, NL), CNAP (CNSystems, Austria)] or the radial artery applanation tonometry (T-Line, Tensys, USA) [35–37]. As delineated in Fig. 2, the volume clamp method derives the finger arterial pressure waveform from the cuff pressure that is needed to keep the blood volume (assessed by photoplethysmography) in the finger arteries constant throughout the cardiac cycle [37]. The continuous radial artery applanation tonometry technique records the arterial pressure waveform using a sensor that is electromechanically driven over the radial artery [37] (Fig. 2). By applying proprietary algorithms for pulse contour analysis to the non-invasively obtained arterial pressure

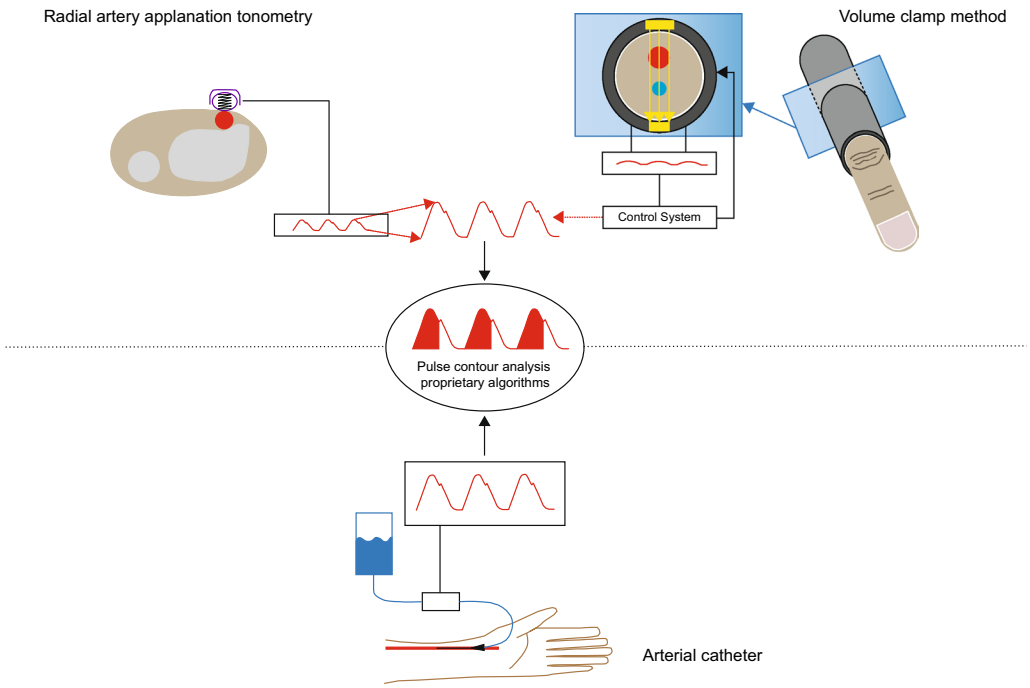

Fig. 2 Pulse contour analysis-derived cardiac output. Different techniques either non-invasive (radial artery applanation tonometry, volume clamp method) or invasive (using an arterial catheter) can provide continuous and real-time CO from the pulse contour analysis

waveforms, these uncalibrated techniques provide CO estimations in a continuous manner. For the volume clamp method, validation studies showed good agreement and trending ability compared with reference techniques in the perioperative context [38, 39]. However, poorer results were reported after cardiac surgery and in ICU patients [40–43], maybe as a result of alterations in vasomotor tone [35, 36]. The radial applanation tonometry method is novel and the first clinical data are promising [44, 45], but further confirmatory studies are required. Though easy to apply, each of the available systems still has specific limitations in its clinical applicability [35, 46]. The main limitations of the volume clamp method are peripheral edema and severe vasoconstriction [35]. The quality of the radial artery applanation tonometry signal can also be impaired by movement of the extremity where the sensor is placed [35].

Other techniques that non-invasively estimate CO in real time are electrical bioimpedance and bioreactance as well as the pulse wave transit time method [34–36].

Bioimpedance [BioZ (Cardiodynamics, USA), Aesculon (Osypka Medical, Germany)] and bioreactance (NICOM, Cheetah Medical, Israel) systems derive CO from changes in thoracic impedance or phase shift in voltage over the cardiac cycle because pulsatile changes in intrathoracic blood volume induce changes in the electrical conductivity of the thorax [34, 35, 47]. These systems use skin surface electrodes that apply a low-amplitude and high-frequency electrical current, which traverses the thorax. Clinical validation studies showed contradicting results [48–50]. Bioreactance systems afforded acceptable results in cardiac surgery patients [48] but not in non-cardiac surgical ICU patients [49, 50]. CO measurements can be disturbed by a variety of factors, such as pleural effusions, pulmonary edema, arrhythmias, electrical interference, internal or external pacemakers, or movement.

The continuous and real-time estimation of CO based on the pulse wave transit time method (esCCO, Nihon Kohden, Japan) requires an electrocardiogram and a pulse oximetry plethysmographical waveform [34, 35]. In theory, the pulse wave transit time (i.e., the time between the appearance of the R wave and the arrival of the pulse wave at the finger level) is inversely correlated with the stroke volume [35]. However, most studies comparing the pulse wave transit time-derived CO with reference methods in ICU patients showed clinically unacceptable disagreement [51–54]. This might be explained by the fact that CO estimation from pulse wave transit time can be impeded in patients with vasoconstriction, cold extremities, and arrhythmias. Administration of vasopressors also limits the use of plethysmographic variability indices to assess fluid responsiveness in critically ill patients [55, 56], whereas such indices are of great value in the intraoperative setting [57, 58].

What is the place of less invasive hemodynamic monitoring in the ICU?

There is a wide consensus to recommend insertion of arterial and central venous catheters and early performance of echocardiography in patients with shock [59]. The presence of an arterial catheter allows measurements of systolic arterial pressure (a reflection of the left ventricular afterload), diastolic arterial pressure (an indicator of the arterial tone), mean arterial pressure (a determinant of organ perfusion pressure used as a major target for hemodynamic resuscitation), and pulse pressure, which if low is an indicator of a low stroke volume, especially in patients with stiff arteries. In addition, the arterial catheter provides the value of PPV, which under appropriate conditions of interpretation is a good predictor of fluid responsiveness [15, 21]. In addition, the arterial catheter allows one to easily perform repeated blood sampling for laboratory tests, including arterial blood gas measurements. The presence of a central venous catheter, which is inserted at least when vasoactive drugs are required, allows measurements of central venous pressure (CVP) and central venous oxygen saturation ($ScvO_2$). It must be stressed that the CVP has limited value in predicting fluid responsiveness [60–62], knowing that extreme values, although rarely encountered in ICU patients, still keep some value [62]. Nevertheless, measuring changes in CVP can be helpful to monitor the response to fluid therapy. In this regard, the CVP could be used as a stopping rule (safety end-point) but not as a target for fluid resuscitation [63]. It is also important to know the CVP value for estimating the perfusion pressure of most organs, which is assumed to be reflected better by the difference between mean arterial pressure and CVP rather than by the sole mean arterial pressure [64]. This could be particularly important to take into account in cases of profound hypotension and high CVP. The $ScvO_2$ is used as a surrogate of mixed venous blood oxygen saturation (SvO_2), which reflects in real time the balance between oxygen consumption and oxygen delivery. Hence, a low $ScvO_2$ may indicate insufficient global oxygen delivery in case of shock and incite one to increase it. However, there are situations where absolute values as well as dynamic changes of $ScvO_2$ and SvO_2 differ [65]. Finally, coupling arterial and central venous blood sampling allows calculation of the venous-to-arterial carbon dioxide pressure difference (PCO_2 gap), which could be a good indicator of the adequacy of CO relative to the actual global metabolic conditions and could be helpful in conditions where oxygen extraction is altered while $ScvO_2$ is within the normal range. In this particular case, an abnormally high PCO_2 gap (>6 mmHg) could suggest that CO should be elevated to improve tissue oxygenation. Echocardiography, which is not a hemodynamic monitoring device but rather a diagnostic tool, is recommended to be performed as soon as possible to quickly obtain important information on the systolic and diastolic ventricular functions [55]. It also allows one to evaluate valvular competency and diagnose/exclude obstructive shock (e.g., pericardial tamponade), knowing that CO measurements by echocardiography are not interchangeable with thermodilution CO measurements [66].

Combination of all the pieces of information drawn early from both clinical examination (mottling score, capillary refill time, etc.) and basic hemodynamic exploration (arterial catheter, central venous catheter, and echocardiography) is of importance to understand the underlying mechanisms of the shock state and to select the most logical initial therapy. If the hemodynamic status improves with this therapy, it is reasonable to continue with the same monitoring until complete resolution of the shock state (Fig. 3). If, however, the patient does not respond (or insufficiently responds) to the initial therapy, it is recommended to obtain more information, in particular to measure CO to better evaluate the necessity to apply further fluids or inotropes and track the hemodynamic response to these therapeutic measures [59]. In such complex situations, the use of advanced hemodynamic systems [59, 67] can be considered (Fig. 3). Insertion of a PAC can be indicated in the presence of a severe right ventricular dysfunction [59] diagnosed by echocardiography. This approach bears the advantage of monitoring SvO_2 and of measuring pulmonary artery pressure and pulmonary artery occlusion pressure, knowing that this pressure shares the same limitations as CVP for assessing fluid responsiveness. Transpulmonary thermodilution systems on the other hand can take advantage of measuring EVLW [18], especially in the context of acute respiratory distress syndrome (ARDS) [59]. In case of severe ARDS associated with shock, it has been suggested to consider using advanced monitoring devices at an earlier phase (Fig. 3), when it is anticipated that the basic hemodynamic monitoring will not be sufficient to define a logical therapeutic approach [59, 67]. It must be stressed that a randomized study showed that hemodynamic management guided by transpulmonary thermodilution vs. PAC did not affect outcomes of patients with shock [68], knowing that the use of PAC in ICU patients was never demonstrated to improve outcome [5]. On the other hand, it was also shown in a randomized trial that fluid management guided by EVLW vs. pulmonary artery occlusion pressure resulted in a better maintained fluid balance and a shorter duration of mechanical ventilation and ICU length of stay in critically ill patients [69]. However, results of such randomized studies [68, 69] should be cautiously interpreted since therapeutic algorithms based on measurements with any single device can be criticized [70].

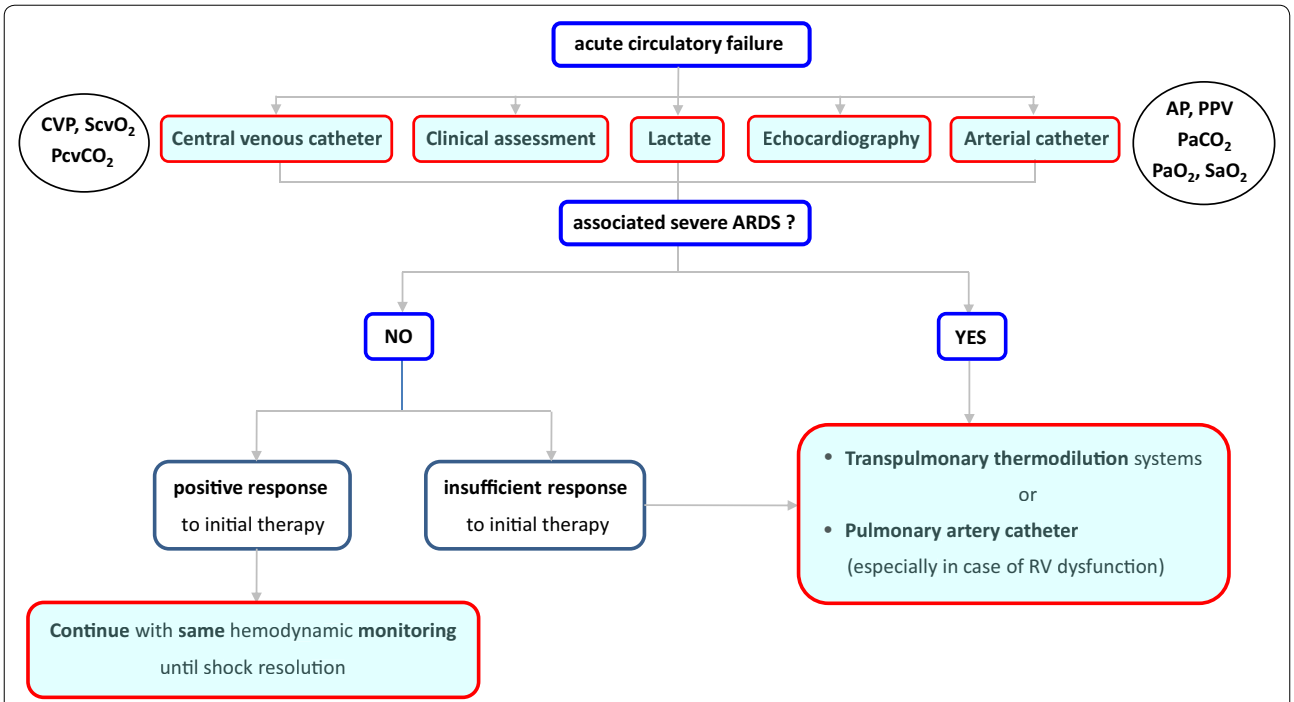

Fig. 3 Simplified algorithm for the choice of hemodynamic monitoring in patients with acute circulatory failure. *AP* arterial pressure, *ARDS* acute respiratory distress syndrome, *CVP* central venous pressure, $PaCO_2$ carbon dioxide pressure in the arterial blood, PaO_2 oxygen pressure in the arterial blood, $PcvCO_2$ carbon dioxide pressure in the central venous blood, *PPV* pulse pressure variation, *RV* right ventricular, SaO_2 arterial blood oxygen saturation, $ScvO_2$ central venous blood oxygen saturation

The place of devices using uncalibrated arterial pressure waveform analysis is more limited in the context of shock, as they rapidly become less reliable and cannot provide other variables than CO, PPV, and/or SVV, which are too limited in the context of complex shock when different mechanisms may coexist and when associated with ARDS.

Esophageal Doppler and less invasive uncalibrated devices are predominantly reserved for the perioperative setting [71] where goal-directed hemodynamic optimization based on algorithms using variables included these monitoring devices may result in improved outcomes [33], in particular when these devices allow using goal-directed fluid therapy based on dynamic variables of preload responsiveness [72, 73]. Non-invasive hemodynamic monitors are currently not recommended for use in patients with shock since these patients need arterial catheterization anyway.

What could the future of hemodynamic monitoring be?

It is hard to predict the future, but for hemodynamic monitoring, the future will become more non-invasive for sure. Visualization of complex information, either by creating more detailed real, anatomical images [74], such as by pocket-size 2D and (in the future) 3D ultrasound, or functional images, e.g., by electrical impedance tomography, will also increase the amount of information available at the bedside [75, 76]. Further intelligent visual postprocessing of hemodynamic information in graphical displays will potentially facilitate the understanding of complex pathophysiology [77]. This will be advanced by an increasing connectivity of different monitoring systems, which will maybe further push the development of tools for predictive analytics [78]. For sure, telemetric monitoring will become available for much more complex physiological signals, which will offer the opportunity to expand patient surveillance beyond the doors of the ICU [74]. For more than one decade, clinical research has been performed in the field of the monitoring of microcirculation. In spite of abundant literature on the potential interest of such monitoring to manage patients with shock, in part explained by dissociation between the macrocirculation and the microcirculation [79], no bedside monitors are currently available for clinical practice [59]. It is expected that technological developments in this field will allow one to better select and adjust therapies for treating patients with shock states.

Conclusion

During the few last years, hemodynamic monitoring has evolved considerably from invasiveness to less or no

invasiveness and from intermittent to continuous and real-time measurements of hemodynamic variables. New parameters such as fluid responsiveness indices (PPV, SVV), EVLW, and volumetric measures of preload have also been implemented in less invasive hemodynamic monitors making them particularly attractive to manage patients with complex shock. Non-invasive monitors are increasingly used in high-risk surgical patients. Continual technological refinements will probably make them become the hemodynamic monitoring of the future.

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Compliance with ethical standards

Conflicts of interest
JLT is a member of the medical advisory board of Pulsion Medical Systems and received honoraria from Edwards Lifesciences and Masimo Inc. for consulting. BS is a member of the medical advisory board of Pulsion Medical Systems and a received institutional research grants, unrestricted research grants, and refunds of travel expenses from Tensys Medical Inc. BS received honoraria for giving lectures for CNSystems Medizintechnik AG. MC consulted and lectured for Edwards Lifesciences and LiDCO. He received support from Edwards Lifesciences, LiDCO, Deltex Medical, Applied Physiology, Masimo, Bmeye, Cheetah Medical, Imacor (travel expenses, honoraria, advisory board, unrestricted educational grant, and research material). DDB received honoraria for lectures for Edwards Lifesciences and Nihon Kohden. DDB received grant/material for studies for Edwards Lifesciences, Maquet, Vytech, Cheetah, Imacor, and Nihon Kohden. XM is a member of the medical advisory board of Pulsion Medical systems and received honoraria from Cheetah Medical for consulting. AP is a member of the medical advisory board of Pulsion Medical Systems and is a consultant for Masimo Inc. MRP is a consultant for Edwards Lifesciences, Masimo Inc., and LiDCO and has stock options in LiDCO and Cheetah Medical companies. DAR is a member of the medical advisory board of Pulsion Medical Systems and gave lectures for Edwards Lifesciences. AR has no conflict of interest to declare. PS was a consultant for Cheetah Medical and for Edwards Lifesciences. TS received honoraria from Edwards Lifesciences and Masimo Inc. for consulting. TS received honoraria from Pulsion Medical Systems for lecturing. JLV has no conflict of interest to declare.

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