This is your toolkit in hemodynamic monitoring

Kaufmann, Thomas; van der Horst, Iwan C C; Scheeren, Thomas W L

Published in:
Current opinion in critical care

DOI:
10.1097/MCC.0000000000000727

This is your toolkit in hemodynamic monitoring

Thomas Kaufmann[a], Iwan C.C. van der Horst[b,c], and Thomas W.L. Scheeren[a]

Purpose of review
To appraise the basic and more advanced methods available for hemodynamic monitoring, and describe the definitions and criteria for the use of hemodynamic variables.

Recent findings
The hemodynamic assessment in critically ill patients suspected of circulatory shock follows a step-by-step algorithm to help determine diagnosis and prognosis. Determination of accurate diagnosis and prognosis in turn is crucial for clinical decision-making. Basic monitoring involving clinical examination in combination with hemodynamic variables obtained with an arterial catheter and a central venous catheter may be sufficient for the majority of patients with circulatory shock. In case of uncertainty of the underlying cause or to guide treatment in severe shock may require additional advanced hemodynamic technologies, and each is utilized for different indications and has specific limitations. Future developments include refining the clinical examination and performing studies that demonstrate better patient outcomes by targeting hemodynamic variables using advanced hemodynamic monitoring.

Summary
Determination of accurate diagnosis and prognosis for patients suspected of circulatory shock is essential for optimal decision-making. Numerous techniques are available, and each has its specific indications and value.

Keywords
cardiac output, circulatory shock, clinical examination, decision-making, hemodynamic monitoring

INTRODUCTION

Hemodynamic monitoring plays a fundamental part in the initial assessment and the subsequent guidance of the treatment of critically ill patients suspected of or suffering from circulatory shock [1,2]. Different methods of monitoring to obtain hemodynamic variables exist, and for the care of critically ill patients, there are recommendations for their use in an escalating or step-by-step manner [3■■].

Every step of the assessment of a patient provides the physician with information regarding diagnosis and a patient's prognosis. Diagnosis is the process of determining the disease or condition that explains a patient's symptoms. Multiple signs and symptoms can be present simultaneously, and each has a specific value (i.e. diagnostic accuracy) in the diagnostic process. Prognosis is the process of predicting the development and outcome of the disease. With prognosis, an educated guess on the improvement or deterioration of the disease can be made, which can then be applied in decision-making. For the processes of diagnosis and prognosis, hemodynamic variables have different values, for example, some might be useful to establish a diagnosis but are not an independent factor in the prognosis and vice versa. Therefore, the process of understanding the obtained results and putting them into clinical context depends on education and the available evidence. The latter can be hampered by the variability in the methodology of current studies [4].

Scenario: a 74-year-old female with a medical history of hypertension, type 2 diabetes, and a previous stroke was admitted to the ICU after she had undergone a laparotomy for bowel perforation. Her

[a]Department of Anesthesiology, University Medical Center Groningen, University of Groningen, Groningen, [b]Department of Intensive Care, Maastricht University Medical Center and [c]Cardiovascular Research Institute Maastricht (CARIM), Maastricht University, Maastricht, The Netherlands

Correspondence to Thomas W.L. Scheeren, Department of Anesthesiology, University Medical Center Groningen, Hanzeplein 1, P.O. Box 30.001, 9700 RB, Groningen, The Netherlands. Tel: +31 503616161; e-mail: t.w.l.scheeren@umcg.nl

Curr Opin Crit Care 2020, 26:303–312
DOI:10.1097/MCC.0000000000000727

KEY POINTS

- The definition and criterion of each hemodynamic variable of the clinical examination in circulatory shock need to be applied uniformly for optimal diagnostic and prognostic value.
- Simple measures of clinical examination, such as CRT, might guide optimal treatment in circulatory shock.
- Basic hemodynamic monitoring of patients with circulatory shock involves the placement of an arterial and central venous catheter, and more advanced monitors may be indicated in more complex shock states.
- Advanced hemodynamic monitors should be selected based on their ability to correctly measure CO and measure other clinically applicable hemodynamic variables.
- The application of advanced hemodynamic monitors in patients with circulatory shock does not automatically imply that patients will have improved outcomes.

current blood pressure is 94/54 mmHg (mean arterial pressure, MAP 67 mmHg), and her heart rate is 78 bpm. She looks pale and clammy on clinical examination, and her extremities are subjectively cold. Capillary refill time (CRT) on the right distal index finger is 4 s, and she has a mottling score of 2 on both knees. You decide to give half a liter of intravenous fluids, and the nurse asks you:

(1) What is the underlying cause of these symptoms? (i.e. diagnosis)
(2) How will she develop in the next hours or days? (i.e. prognosis)

To answer these daily questions, we critically appraise the different methods, your tools, and describe the exact definitions and values of the hemodynamic variables that can be obtained using these methods. We apply these tools in a clinical scenario to guide clinical decision-making in a realistic context.

THE GENERAL IDEA OF HEMODYNAMIC MONITORING

About one-third of patients in the ICU eventually experience circulatory shock, and patients with circulatory shock have increased risks of multiorgan failure, long-term morbidity, and mortality [5]. The underlying pathophysiology of circulatory shock can be complex and depends on the type of shock. For instance, patients can present with hypovolemia, myocardial dysfunction, and alteration of vascular tone. The hemodynamic assessment is considered to be even more difficult if patients are also burdened with comorbidities [6]. Each of the components of circulatory shock needs to be measured correctly as a prerequisite for proper decision-making.

CLINICAL EXAMINATION

Clinical examination of the cardiovascular system can be used to assess perfusion or to estimate cardiac output (CO), and its daily application in critically ill patients makes it the first step of hemodynamic monitoring in suspected circulatory shock. However, much remains unknown about the value of clinical examination in the diagnosis and prognosis of circulatory shock [7]. The issue with the clinical examination is that its extensive use in critically ill patients is contrasted with a limited number of studies assessing its value, which leads to the level of evidence being considered as best practice [1]. One of the reasons is that the introduction of the pulmonary artery catheter (PAC) in the 1970s markedly changed clinical practice and led to a decline in a physician's reliance on clinical examination [8,9]. The introduction of this and other new monitoring techniques has also changed the definition and the significance of the clinical examination, and the integration of bedside diagnostic tools is now an inherent part of the intensivists' curriculum [10].

The diagnostic accuracy of using clinical examination to estimate CO is only similar to that of the flip of a coin [7]. Single variables, such as the mottling score or CRT, should not be used for that purpose as univariable analyses show poor correlations between them and CO, while several variables combined into a structured clinical examination showed good accuracy [7]. No standardized definition exists of how to obtain some of these clinical examination findings, so different methods of measurement were used [7]. The goal of clinical examination of the cardiovascular system is not only to estimate a CO value but also to assess sufficiency of perfusion. The same CO value may be sufficient for perfusion in one patient but insufficient in another.

Recently, a study determined the value of a structured clinical examination in critically ill patients as part of an observational study [11■■]. The authors showed that several clinical examination findings [i.e. blood pressure, central-to-peripheral temperature difference (ΔTc−p), and CRT] were independently associated with cardiac index [11■■]. However, these variables were found to be of insufficient value to estimate cardiac index in multivariable analyses and diagnostic accuracy tests [11■■]. Clinical examination remains the first step to estimate CO in critically ill patients, but additional measurements are necessary to estimate CO accurately and fully evaluate circulatory shock [12]. Clinical examination can also be used to estimate a patient's prognosis. The prognostic value of a model including systolic blood pressure, respiratory rate, central temperature, altered consciousness, and decreased urinary output obtained during the first 24 h of admission was equal to that of contemporary models, such as the Simplified Acute Physiology Score II (SAPS-II) or the Acute Physiology and Chronic Health Evaluation IV (APACHE-IV) [13]. For patients with sepsis and septic shock, the mottling score had a high prognostic value for 14-day mortality, irrespective of the infusion of vasopressors or other perfusion-related variables [14■].

In the ANDROMEDA-SHOCK trial, a resuscitation strategy targeting CRT or lactate for the reduction of mortality was employed in patients with septic shock [15■■]. Although the primary endpoint, a 15% absolute reduction in 28-day mortality between the two groups, was not achieved, trials such as this one show that targeting perfusion variables to reduce mortality and morbidity in septic shock is feasible [15■■]. Secondary analysis of the ANDROMEDA-SHOCK trial using Bayesian methods showed that the CRT-guided resuscitation may result in lower mortality and morbidity when compared with the lactate-targeted strategy based on prior probability distribution [16].

It is necessary to improve the hemodynamic assessment made with clinical examination. Although advanced hemodynamic tools are becoming more widely available, further research into the value of clinical examination may potentially limit inappropriate overuse of advanced monitoring techniques [4]. On the other hand, new tools can also help improve the clinical examination. For example, a device has been developed to objectively measure CRT in an attempt to help standardize this clinical measurement [17,18]. Before these novel devices can be implemented, the obtained values need to be compared with the contemporary method of CRT measurement as used in the ANDROMEDA-SHOCK trial [15■■]

BASIC HEMODYNAMIC MONITORING USING AN ARTERIAL CATHETER AND A CENTRAL VENOUS CATHETER

An initial mean arterial pressure (MAP) of 65 mmHg is the lower limit to target perfusion pressure in all shock states except for hypovolemic shock [1], and this value has been chosen as research has shown that a MAP below this value is associated with complications and increased mortality [19,20]. Placement of an arterial catheter is the clinical standard for blood pressure measurements as it allows reliable and continuous measurements. Accurate measurements are not self-evident, as care has to be taken with the position of the pressure transducer and correct zero adjustment [21]. Artifacts of the signal may be present because of occlusion or compression of the lining, which causes underdamping or overdamping [21]. Blood pressure measurements can also be performed using noninvasive alternatives, such as oscillometry, the volume-clamp method, or applanation tonometry [21]. Although noninvasive alternatives are sometimes used as the standard of care, including in patients with circulatory shock [22], uncertainty exists regarding the interchangeability of the obtained results with these methods compared with those obtained by the arterial catheter [23]. At the moment, the placement of an arterial catheter is recommended as soon as possible to obtain reliable blood pressure measurements [1].

An arterial catheter also facilitates the use of point-of-care blood gas analysis. Several variables can be assessed using blood gas analysis in suspected circulatory shock, and in determining the prognosis of established shock. Lactate is one of the best-known biomarkers for estimating the severity and prognosis of circulatory shock, and is used in the definition of its diagnosis [2]. The difference of partial pressures of CO_2 in venous and arterial blood gas ($P_{v\text{-}a}CO_2$ or CO_2 gap) is a surrogate marker for the adequacy of CO and can be used in algorithms for diagnosis and treatment of circulatory failure [24]. The presence of an elevated $P_{v\text{-}a}CO_2$ (i.e. >6 mmHg) is associated with a reduced lactate clearance in patients with septic shock [25]. Also, normalization of $P_{v\text{-}a}CO_2$ during the treatment of circulatory shock was associated with a decrease in blood lactate levels [26].

A central venous catheter is placed in critically ill patients suspected of circulatory shock to facilitate administration of vasoactive medication and offers continuous monitoring of central venous pressure (CVP), and if placed in the superior caval vein (either via the jugular or subclavian vein), it facilitates the measurements of central venous oxygen saturation ($S_{cv}O_2$). CVP is still the most frequently used variable to guide fluid resuscitation in critically ill patients [27], while it has been demonstrated that CVP, as a single variable, is unreliable for this purpose [28]. Many factors influence the CVP, such as thoracic and abdominal pressures, which make interpretation of this static variable difficult [29]. In general, a low value between 0 and 5 mmHg is considered normal but there are many exceptions to this rule [30]. Furthermore, a significant increase in CVP (i.e. above 12 mmHg) is suggestive for an increase in right atrial pressure.

Utilizing central venous oxygen saturation ($S_{cv}O_2$) in patients with circulatory shock has gained attention since the original early goal-directed therapy trial [31]. A $S_{cv}O_2$ greater than 70% is considered adequate and was used as a target for hemodynamic intervention [31]. $S_{cv}O_2$ is a surrogate measurement for mixed venous oxygen saturation (S_vO_2). The measurement of S_vO_2 requires a PAC, whereas $S_{cv}O_2$ does not. Both measurements give similar information on the balance between oxygen delivery and consumption [32]. Although the absolute values of S_vO_2 and $S_{cv}O_2$ are not interchangeable, the trend of both values can be used similarly for the hemodynamic management of critically ill patients [33]. The $S_{cv}O_2$ measurement is done in the superior vena cava territory, and thus it may be affected by maneuvers, such as deeper levels of sedation and emergency intubation, without necessarily implying a correction in global perfusion [34]. In patients with septic shock, $S_{cv}O_2$ values combined with the $P_{v\text{-}a}CO_2$ predict mortality more reliably than $S_{cv}O_2$ alone [35]. An overview of the abovementioned variables and their definition and value is given in Table 1.

In our 74-year-old female example patient, using the clinical examination, we can establish the diagnosis shock with sepsis as an underlying cause, and the diagnosis of septic shock seems very likely. We can consider the prognostic value of the clinical examination findings to get a basic idea for clinical decision-making. Of course, in a real-life scenario, the process of clinical decision-making is much more extensive, with a modifiable conclusion using the clinical course of the disease. In this case, whether a cardiac or pulmonary component is present as well has to be established by more advanced measures aside from clinical examination and laboratory tests. If the hemodynamic instability is progressive, or unresponsive to initial resuscitation, advanced hemodynamic monitoring is indicated or at least an evaluation of CO can be performed as further diagnostic testing is required [1,3■■].

ADVANCED HEMODYNAMIC MONITORING

To determine the optimal applicable method of advanced hemodynamic monitoring in a certain clinical scenario, one must take the measurement performance, the ability to provide continuous CO measurements, the ability to calibrate according to a reference technique, and the ability to measure other hemodynamic variables into account [3■■,53]. Noninvasive hemodynamic monitors are not clinically indicated in the ICU yet, and will therefore, not be discussed here [3■■]. An overview of the advanced hemodynamic monitors is presented in Table 2.

Critical care echocardiography (CCE) is a branch of critical care ultrasonography, which is the umbrella term for the point-of-care application of ultrasonography in the ICU [71]. Over the last decade, CCE has gained general acceptance as a diagnostic tool [54]. The CO measurement performance of CCE compared with the clinical reference PAC has been debated as there is a wide variety in the quality of research. A systematic review with meta-analysis demonstrated that the currently available evidence does not support the interchangeability of CCE and PAC derived CO [55]. However, another systematic review with meta-analysis showed no significant differences and suggested that both techniques may be used interchangeably [57]. Recently, a study showed that CCE derived CO measurements in critically ill patients with sinus rhythm have high precision and can be used to guide interventions such as a fluid challenge [72]. The images required to measure CO may be unobtainable in up to 30% of critically ill patients because of suboptimal positioning and complicating factors, such as a patients' postsurgical state (e.g. after sternotomy), presence of emphysema, or the presence of chest tubes [56,73]. Regardless of these limitations, the use of CCE to measure CO in critically ill patients suspected of circulatory shock is now advocated in the guidelines [1]. CCE has excellent diagnostic value in critically ill patients because of the ability to measure various heart structures and perform different measurements of fluid responsiveness, and therefore, every new ICU physician should at least be able to perform basic CCE [54]. Clustering septic shock patients to increase individual hemodynamic management is possible using clinical examination combined with hemodynamic variables measured by CCE [74]. A more advanced measurement, the global longitudinal strain is a prognostic marker of left ventricular function, and worse values are associated with higher mortality in patients with septic shock [75]. More extensive skills in CCE are required to perform the advanced measurements, and therefore, these values may be even more difficult to obtain in critically ill patients.

Pulse contour analysis allows estimation of CO based on the principle that aortic pulse pressure is proportional to stroke volume (SV) and inversely proportional to aortic compliance [76]. Uncalibrated pulse contour analysis monitors estimate the CO from arterial pressure waveform characteristics and

Table 1. Basic hemodynamic assessment definition and value

Method	Diagnostic variables	Definition	Criterion	Diagnostic value	Prognostic value
Clinical examination	ΔT_{c-p}	The difference between central temperature measured by a bladder thermistor catheter and peripheral temperature measured by a skin probe on the big toe of the foot	Pathological if more than 7 °C [36]	Patients with a higher ΔT_{c-p} have a lower cardiac index [11■■]	Mean 24-h ΔT_{c-p} is correlated to mortality [37]
	Subjective temperature	Subjective temperature measured as 'cool' or 'warm' on the extremities	Cool extremities if all examined extremities were cool, or only the lower extremities were cool despite warm upper extremities [38]	Patients with cool extremities have a lower cardiac index than patients with warm extremities [11■■,38,39]	ICU nonsurvivors more often had cold extremities [13,40]
	Capillary refill time	Measured by applying pressure to the ventral surface of the right index finger distal phalanx with a glass microscope slide. Increased pressure until the skin is blank and then maintained for 10 s [15■■]	Refill time greater than 3 s is defined as abnormal [15■■]	Low correlation with CO [11■■,39] Not different between patients with and without shock [42]	Strong predictive factor of mortality [41], and in-hospital mortality [43]
	Skin mottling	Patchy skin discoloration that usually starts around the knees because of heterogenic small vessel vasoconstriction [44]	Score 0 indicates no mottling Score 1, a small mottling area (coin size) localized to the center of the knee Score 2, a mottling area that does not exceed the superior edge of the kneecap Score 3, a mottling area that does not exceed the middle thigh Score 4, a mottling area that does not go beyond the fold of the groin Score 5, an extremely severe mottling area that goes beyond the fold of the groin [44]	Incidence of 49% in patients with septic shock [45] Low diagnostic accuracy for CO [11■■]	A predictive factor of mortality in critically ill patients [13] and patients with shock [14■,44]
Arterial catheter	Blood pressure monitoring	Continuous monitoring of the pressure of the blood in the circulatory system while maintaining a reliable arterial blood pressure waveform	Guidelines recommend an initial MAP above 65 mmHg in all shock states except for hemorrhagic shock, to be individualized based on clinical evaluation [1]	Circulatory shock does not require the presence of hypotension [1]	MAP is independently associated with mortality in shock [19,20,37,46■]
Blood gas analysis	Lactate	Product of glucose and pyruvate metabolism. In shock states, blood lactate levels increase because of many potential causes [47]. Measured in a reliable way	Increased if > 1.5 mmol/l [2]	The definition of shock is insufficient oxygen delivery to the cells, which leads to hyperlactatemia Cannot be used to differentiate between patients with and without shock [42]	Higher lactate levels were associated with increased mortality [48,49] Better patient outcome is observed with decreasing lactate levels [50]
	$P_{v-a}CO_2$ or CO_2 gap	Marker of the adequacy of blood flow to remove CO_2 from the tissues [24]	Normal if < 6 mmHg and increased if > 6 mmHg [24]	Patients with septic shock with increased $P_{v-a}CO_2$ (>6 mmHg) had a lower CO than those with normal $P_{v-a}CO_2$ [51]	Normalization of $P_{v-a}CO_2$ is associated with a decrease in blood lactate [26]
Central venous catheter	CVP	Pressure measured in the superior vena cava, used as a surrogate for right atrial pressure	Normal between 0 and 5 mmHg [30]	CVP is useful in diagnosing the type of shock. However, unless in the extreme ranges of the variables (such as a CVP of 0 mmHg with bleeding), CVP should always be interpreted together with other variables [1]	Nonsurvivors of shock have a higher CVP at ICU admission and after 24–48 h [19,20]
	$S_{CV}O_2$	Oxygen saturation measured in the superior vena cava used as a surrogate for mixed venous oxygen saturation	Low if < 70%, high if > 80% [31]	Low $S_{CV}O_2$ indicates an inadequacy of oxygen transport or high oxygen consumption [32], especially in the context of hyperlactatemia Normal or high $ScvO_2$ cannot discriminate if oxygen transport is adequate [1]	Persistence of low $S_{CV}O_2$ is associated with higher mortality [52]

ΔT_{c-p}, central-to-peripheral temperature difference; CO, cardiac output; CVP, central venous pressure; MAP, mean arterial pressure; $P_{v-a}CO_2$, difference of partial pressures of CO_2 in venous and arterial blood gas; $S_{CV}O_2$, central venous oxygen saturation.

Table 2. Advanced hemodynamic monitoring methods and devices used clinically in the ICU

Method	Indication	Diagnostic variables	Variable to guide treatment	Caution	CO validation
Critical care echocardiography	Indicated as the first measurement of CO in patients suspected of circulatory shock [1]	Left and right heart function Tamponade Cardiac contusion Hemothorax Outflow obstruction Pulmonary edema [54]	CO Fluid responsiveness variables Titration of vasoactive medication by measuring ventricular function [55]	Not considered a monitoring device as continuous measurements are not possible Acoustic windows may not be obtainable in up to 30% of patients [56]	Not interchangeable compared with thermodilution, using data from 799 patients in 24 studies [55] Interchangeable compared with thermodilution, using data from 1996 patients in 68 studies [57]
Pulse contour analysis	Indicated in patients, which require continuous CO measurements to assess fluid responsiveness [3■■]	dP/dt_{max} was proposed as an estimator of left ventricular function [58]; however, recent evidence suggests dP/dt_{max} may be unreliable for this purpose [59]	CO Fluid responsiveness variables [60] Ea_{dyn} may potentially be used to reduce vasopressor doses in patients with sepsis [62,63]	Interpret CO values with caution in patients with arrhythmias or hyperdynamic conditions, such as liver failure or circulatory shock [3■■]	Adequate measurement performance in normal and hypodynamic conditions, but not during hyperdynamic conditions, using data from 2234 patients in 65 studies [61]
Esophageal Doppler	Indicated in patients who require continuous cardiac output measurements [3■■]	None	CO FTc	Limited to patients under sedation or general anesthesia because of the requirement to insert an esophageal probe [3■■]	Accurate measurement performance compared with PAC, using data from 314 patients in 11 studies [79]
Transpulmonary thermodilution	Indicated in patients who have circulatory shock associated with ARDS [3■■]	PVPI and EVLW differentiate pulmonary edema from ARDS [64] CFI is a reliable estimator of left ventricular systolic function [65]	CO Elevated PVPI and EVLW are associated with increased mortality in patients with ARDS [82]	Requires cannulation of the femoral artery and central venous access, which can be associated with complications [66] Obtaining CO values can be limited by factors related to the indicator (e.g. loss of indicator, temperature differences), patient-specific factors (e.g. intracardiac shunts, tricuspid regurgitation, low-flow states) [67]	Accurate measurement performance compared with PAC, using data from 239 patients in 10 studies [67]
Pulmonary artery catheter	Indicated in patients who have circulatory shock associated with right ventricular dysfunction or pulmonary arterial hypertension [3■■]	Used to diagnose right ventricular dysfunction and pulmonary arterial hypertension PCWP can be used for the diagnosis of cardiogenic shock [68]	CO PAP PCWP RAP	Considered as invasive procedure associated with rare but severe complications [69] Obtaining CO values can be limited by factors related to the indicator (e.g. loss of indicator, temperature differences), or patient-specific factors (e.g. intracardiac shunts, tricuspid regurgitation, low-flow states) [52]	The clinical gold standard method for CO measurement [69] Relatively accurate compared with experimental reference standards (e.g. flow probe) [70]

ARDS, acute respiratory distress syndrome; CFI, cardiac function index; CO, cardiac output; dP/dt_{max}, maximum rate of the arterial pressure increase during systole; Ea_{dyn}, dynamic arterial elastance; EVLW, extravascular lung water; FTc, corrected flow time; PAC, pulmonary artery catheter; PAP, pulmonary arterial pressure; PCWP, pulmonary capillary wedge pressure; PVPI, pulmonary vascular permeability index; SV, stroke volume; SVR, systemic vascular resistance; RAP, right atrial pressure.

biometric data. Different derivations of hemodynamic variables obtained using arterial pressure and arterial compliance are used, and CO is determined based on sex, age, weight, and height [77]. Some pulse contour analysis monitors can be calibrated with an independent measurement of CO done by transpulmonary thermodilution. Calibration is done with the injection of a fluid bolus, and placement of a central venous catheter and a femoral arterial catheter are required to do so [78]. A systematic review with meta-analysis has shown that the CO measurement performance of uncalibrated pulse contour analysis monitors was adequate compared with PAC under normal and hypodynamic conditions, but not in hyperdynamic conditions (e.g. septic shock) [61]. Therefore, uncalibrated pulse contour analysis monitors are not suitable for continuous CO measurements in patients suspected of circulatory shock, but can be used in other clinical scenarios in the ICU where assessing trends in CO and fluid responsiveness is indicated.

The Esophageal Doppler Monitor (EDM) probe can only be used in sedated patients or patients under general anesthesia as it is placed in the patient's esophagus. EDM uses Doppler ultrasound to measure the velocity of blood flow in the descending aorta. The blood flow in the descending aorta is correlated to CO, under the assumption that the proportion of blood flow to the upper and lower part of the body remains equal. A systematic review with meta-analysis has shown that the CO measurement performance of EDM compared with PAC was adequate [79]. Yet, the probe can be displaced easily, which may limit proper CO measurements and makes the technique more suitable for patients in the operating room [53].

Transpulmonary thermodilution consists of the injection of a cold fluid bolus into the superior vena cava and measuring the subsequent temperature difference in the femoral artery [80]. The method allows measurement and calculation of additional hemodynamic variables, such as extravascular lung water (EVLW), pulmonary vascular permeability index (PVPI), and global end-diastolic volume (GEDV) [78]. A review with meta-analysis has shown good measurement performance for transpulmonary thermodilution compared with the PAC [67]. Continuous, reliable CO measurements, in combination with the additional hemodynamic variables, make the method suitable for monitoring in critically ill patients with a specific indication in acute respiratory distress syndrome (ARDS) [81]. EVLW and the PVPI are independent prognostic factors of mortality in patients with ARDS, which makes monitoring of these variables particularly valuable [82].

The PAC is able to measure additional hemodynamic variables in addition to CO, such as right atrial pressure (RAP) and pulmonary artery pressure (PAP), which make it a valuable tool in the hemodynamic assessment of critically ill patients suspected of circulatory shock with additional right ventricular dysfunction or pulmonary hypertension. The intermittent thermodilution with the PAC is considered the gold standard for clinical CO measurements in critically ill patients. CO measurements are provided using the Stewart–Hamilton equation after injection of a cold bolus of fluid (i.e. the indicator) [67]. Obtaining CO measurements can be limited by factors related to the injection of the indicator (e.g. loss of indicator, temperature differences) or patient-specific factors (e.g. intracardiac shunts, tricuspid regurgitation, low-flow states) [67]. A systematic review with meta-analysis found an adequate CO measurement performance of the PAC compared with experimental reference measurements (i.e. flow probes) [70]. Furthermore, the PAC is the only hemodynamic monitor capable of continuously monitoring the right ventricle, which makes it the monitor of choice in patients with right heart failure, and which allows assessment of the ventilator settings' impact on right ventricular function [83]. Patients with cardiogenic shock can be managed with a PAC, but the use of the PAC was not associated with improved outcome [84].

HOW TO COMBINE THESE TOOLS?

Now that we have the evidence for all individual monitoring tools, let us consider how to combine the measurements in such a manner that we get informed on the underlying cause, the right trigger for intervention, the appropriate hemodynamic target, and the patient's prognosis.

Our example patient deteriorated and had to be mechanically ventilated as a consequence of exhaustion. Mottling on the knees increased after initial resuscitation, higher ventilation pressures were needed over time, and lactate levels remained elevated. An increasing dose of vasopressors had to be administered. CCE was performed and showed no significant cardiac comorbidities except minor tricuspid regurgitation. Additionally, a low CO was recognized combined with signs of fluid responsiveness. An arterial thermistor catheter was placed in the femoral artery, which allowed continuous CO measurements using the transpulmonary thermodilution technique. The decision for this monitoring technique was made because of the potential for the occurrence of ARDS [81].

FUTURE DEVELOPMENTS

Improvements need to be made on all aspects of hemodynamic monitoring to provide the best care for critically ill patients suspected of circulatory shock. Future developments in this field include improving the clinical examination and demonstrating improved patient outcomes by targeting hemodynamic variables using advanced hemodynamic monitoring.

Education to improve the clinical examination by physicians should identify some of the cognitive biases physicians may be subjected to, and teach physicians to negate them [85]. Physicians may be prone to confirmation bias in which they refrain from considering diverging information not supporting their decision. For example, a physician may examine a critically ill patient who is receiving a high dose of norepinephrine infusion, and may believe that the presence of this drug must imply that CO is low. An observational study demonstrated that a crude insight into the thought process behind the estimation of cardiac function by physicians using clinical examination is possible using Bayesian networks [86▪]. The physician can be made aware of their thinking process and can be trained to use or leave out specific values obtained with the clinical examination, or the physician can be trained to reconsider their conclusion when new information is presented. Additionally, machine learning algorithms are increasingly applied in studies to diagnose and predict outcomes of circulatory shock [87]. These types of techniques may be applied to improve the clinical examination as a first step for the evaluation of circulatory shock.

The application of hemodynamic monitors in patients with circulatory shock does not automatically imply that patients will have improved outcomes. For instance, the extensive use of the PAC in the past did not show a benefit on outcomes in critically ill patients [69]. Although CCE is considered to be one of the first additional steps after clinical examination and its diagnostic capabilities are well demonstrated, there is no evidence of a beneficial effect of CCE on patient outcomes as of yet [88]. Patient outcomes can only be improved if monitoring and diagnosis are coupled with successful therapeutic interventions. Recently, a randomized trial was published, which assessed the effect of continuous hemodynamic monitoring of patients with shock using transesophageal echocardiography [89▪▪]. Although hemodynamic instability resolved sooner within the first 72 h of resuscitation using continuous monitoring, no beneficial effect was found on mortality or the overall resolution of hemodynamic instability [89▪▪].

In the near future, the hemodynamic variables obtained with the clinical examination and with more advanced measurements to guide decision-making in circulatory shock can be optimally selected and combined using machine learning and logistic regression models [90].

CONCLUSION

Decision-making in patients suspected of circulatory shock is intricate, and numerous tools are available to guide this process. The clinical examination combined with basic hemodynamic monitoring tools is the first step, but more advanced monitoring tools are often necessary to provide the best care. Future developments are focused on improving the clinical examination and demonstrating improved patient outcomes using targeted variables by advanced hemodynamic monitoring.

Acknowledgements

None.

Financial support and sponsorship

None.

Conflicts of interest

T.W.L.S. received research grants and honoraria from Edwards Lifesciences and Masimo Inc. (Irvine, California, USA) for consulting and lecturing, and from Pulsion Medical Systems S.E. (Feldkirchen, Germany) for lecturing. T.K. and I.vd.H. have no conflicts of interest.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

▪ of special interest
▪▪ of outstanding interest

1. Cecconi M, De Backer D, Antonelli M, *et al.* Consensus on circulatory shock ▪▪ and hemodynamic monitoring. Task force of the European Society of Intensive Care Medicine. Intensive Care Med 2014; 40:1795–1815.
2. Vincent J-L, De Backer D. Circulatory shock. N Engl J Med 2013; 369: ▪▪ 1726–1734.
3. Saugel B, Vincent J-L. Cardiac output monitoring: how to choose the optimal ▪▪ method for the individual patient. Curr Opin Crit Care 2018; 24:165–172.

This review provided a comprehensive overview of the application of cardiac output monitors in critically ill patients or patients undergoing surgery.

4. Elder A, Japp A, Verghese A. How valuable is physical examination of the cardiovascular system? BMJ 2016; 354:i3309.
5. Sakr Y, Reinhart K, Vincent J-L, *et al.* Does dopamine administration in shock influence outcome? Results of the Sepsis Occurrence in Acutely Ill Patients (SOAP) Study. Crit Care Med 2006; 34:589–597.
6. Saugel B, Malbrain MLNG, Perel A. Hemodynamic monitoring in the era of evidence-based medicine. Crit Care 2016; 20:401.
7. Hiemstra B, Eck RJ, Keus F, van der Horst ICC. Clinical examination for diagnosing circulatory shock. Curr Opin Crit Care 2017; 23:293–301.
8. Swan HJ, Ganz W, Forrester J, *et al.* Catheterization of the heart in man with use of a flow-directed balloon-tipped catheter. N Engl J Med 1970; 283: 447–451.
9. Eisenberg PR, Jaffe AS, Schuster DP. Clinical evaluation compared to pulmonary artery catheterization in the hemodynamic assessment of critically ill patients. Crit Care Med 1984; 12:549–553.

10. Domain 2: diagnosis: assessment, investigation, monitoring and data interpretation [cited 2019 Dec 22]. Available at: http://www.cobatrice.org/Data/ModuleGestionDeContenu/PagesGenerees/en/02-competencies/0B-diagnosis/8.asp. Accessed April 11th, 2020.

11. Hiemstra B, Koster G, Wiersema R, *et al.,* SICS Study Group. The diagnostic ■■ accuracy of clinical examination for estimating cardiac index in critically ill patients: the Simple Intensive Care Studies-I. Intensive Care Med 2019; 45:190–200.

This observational study applied a standardized clinical examination to estimate cardiac index in acutely admitted critically ill patients.

12. De Backer D, Vieillard-Baron A. Clinical examination: a trigger but not a substitute for hemodynamic evaluation. Intensive Care Med 2019; 45:269–271.

13. Hiemstra B, Eck RJ, Wiersema R, *et al.,* SICS Study Group. Clinical examination for the prediction of mortality in the critically ill. Crit Care Med 2019; 47:1301–1309.

14. Dumas G, Lavillegrand JR, Joffre J, *et al.* Mottling score is a strong predictor of ■ 14-day mortality in septic patients whatever vasopressor doses and other tissue perfusion parameters. Crit Care 2019; 23:211.

This observational study demonstrated the strong prognostic value of the mottling score in patients with septic shock.

15. Hernández G, Ospina-Tascón GA, Damiani LP, *et al.* Effect of a resuscitation ■■ strategy targeting peripheral perfusion status vs serum lactate levels on 28-day mortality among patients with septic shock. JAMA 2019; 321:654.

This randomized controlled trial demonstrated the feasibility and potential positive effect of targeting peripheral perfusion (capillary refill time) as a goal for resuscitation in septic shock

16. Zampieri FG, Damiani LP, Bakker J, *et al.* Effects of a resuscitation strategy targeting peripheral perfusion status versus serum lactate levels among patients with septic shock. A Bayesian reanalysis of the ANDROMEDA-SHOCK Trial. Am J Respir Crit Care Med 2020; 201:423–429.

17. Kawaguchi R, Nakada TA, Oshima T, *et al.* Optimal pressing strength and time for capillary refilling time. Crit Care 2019; 23:4.

18. Shinozaki M, Nakada TA, Kawaguchi R, *et al.* Feedback function for capillary refilling time measurement device. Crit Care 2019; 23:295.

19. Varpula M, Tallgren M, Saukkonen K, *et al.* Hemodynamic variables related to outcome in septic shock. Intensive Care Med 2005; 31:1066–1071.

20. Dünser MW, Takala J, Ulmer H, *et al.* Arterial blood pressure during early sepsis and outcome. Intensive Care Med 2009; 35:1225–1233.

21. Saugel B, Dueck R, Wagner JY. Measurement of blood pressure. Best Pract Res Clin Anaesthesiol 2014; 28:309–322.

22. Chatterjee A, Depriest K, Blair R, *et al.* Results of a survey of blood pressure monitoring by intensivists in critically ill patients: a preliminary study. Crit Care Med 2010; 38:2335–2338.

23. Lakhal K, Ehrmann S, Boulain T. Noninvasive BP monitoring in the critically ill: time to abandon the arterial catheter? Chest 2018; 153:1023–1039.

24. Scheeren TWL, Wicke JN, Teboul JL. Understanding the carbon dioxide gaps. Curr Opin Crit Care 2018; 24:181–189.

25. Mesquida J, Saludes P, Gruartmoner G, *et al.* Central venous-to-arterial carbon dioxide difference combined with arterial-to-venous oxygen content difference is associated with lactate evolution in the hemodynamic resuscitation process in early septic shock. Crit Care 2015; 19:1–7.

26. Mallat J, Pepy F, Lemyze M, *et al.* Central venous-to-arterial carbon dioxide partial pressure difference in early resuscitation from septic shock: a prospective observational study. Eur J Anaesthesiol 2014; 31:371–380.

27. Cecconi M, Hofer C, Teboul JL, *et al.* Fluid challenges in intensive care: the FENICE study: a global inception cohort study. Intensive Care Med 2015; 41:1529–1537.

28. Marik PE, Cavallazzi R. Does the central venous pressure predict fluid responsiveness? An updated meta-analysis and a plea for some common sense. Crit Care Med 2013; 41:1774–1781.

29. De Backer D, Vincent JL. Should we measure the central venous pressure to guide fluid management? Ten answers to 10 questions. Crit Care 2018; 22:1–6.

30. Magder S. Understanding central venous pressure: Not a preload index? Curr Opin Crit Care 2015; 21:369–375.

31. Rivers E, Nguyen B, Havstad S, *et al.* Early goal-directed therapy in the treatment of severe sepsis and septic shock. N Engl J Med 2001; 345: 1368–1377.

32. van Beest P, Wietasch G, Scheeren T, *et al.* Clinical review: use of venous oxygen saturations as a goal - a yet unfinished puzzle. Crit Care 2011; 15:232.

33. Dueck MH, Klimek M, Appenrodt S, *et al.* Trends but not individual values of central venous oxygen saturation agree with mixed venous oxygen saturation during varying hemodynamic conditions. Anesthesiology 2005; 103: 249–257.

34. Hernandez G, Peña H, Cornejo R, *et al.* Impact of emergency intubation on central venous oxygen saturation in critically ill patients: a multicenter observational study. Crit Care 2009; 13:R63.

35. Du W, Liu DW, Wang XT, *et al.* Combining central venous-to-arterial partial pressure of carbon dioxide difference and central venous oxygen saturation to guide resuscitation in septic shock. J Crit Care 2013; 28:1110.e1–1110.e5.

36. Curley FJ, Smyrnios NA. Routine monitoring of critically ill patients. J Intensive Care Med 1990; 5:153–174.

37. Houwink API, Rijkenberg S, Bosman RJ, van der Voort PHJ. The association between lactate, mean arterial pressure, central venous oxygen saturation and peripheral temperature and mortality in severe sepsis: A retrospective cohort analysis. Crit Care 2016; 20:56.

38. Kaplan LJ, McPartland K, Santora TA, Trooskin SZ. Start with a subjective assessment of skin temperature to identify hypoperfusion in intensive care unit patients. J Trauma 2001; 50:620–627.

39. Schey BM, Williams DY, Bucknall T. Skin temperature as a noninvasive marker of haemodynamic and perfusion status in adult cardiac surgical patients: An observational study. Intensive Crit Care Nurs 2009; 25:31–37.

40. Hasdai D, Holmes DR, Califf RM, *et al.* Cardiogenic shock complicating acute myocardial infarction: predictors of death. GUSTO Investigators. Global Utilization of Streptokinase and Tissue-Plasminogen Activator for Occluded Coronary Arteries. Am Heart J 1999; 138(1 Pt 1):21–31.

41. Ait-Oufella H, Bige N, Boelle PY, *et al.* Capillary refill time exploration during septic shock. Intensive Care Med 2014; 40:958–964.

42. Filho RR, de Freitas Chaves RC, Assunção MSC, *et al.* Assessment of the peripheral microcirculation in patients with and without shock: a pilot study on different methods. J Clin Monit Comput 2019. [Epub ahead of print]. doi: 10.1007/s10877-019-00423-8.

43. Champion HR, Sacco WJ, Hannan DS, *et al.* Assessment of injury severity: the triage index. Crit Care Med 1980; 8:201–208.

44. Ait-Oufella H, Lemoinne S, Boelle PY, *et al.* Mottling score predicts survival in septic shock. Intensive Care Med 2011; 37:801–807.

45. Coudroy R, Jamet A, Frat JP, *et al.* Incidence and impact of skin mottling over the knee and its duration on outcome in critically ill patients. Intensive Care Med 2015; 41:452–459.

46. Maheshwari K, Nathanson BH, Munson SH, *et al.* The relationship between ■ ICU hypotension and in-hospital mortality and morbidity in septic patients. Intensive Care Med 2018; 44:857–867.

This study demonstrated that critically ill patients already have an increased risk of acute kidney injury, myocardial injury, and mortality if mean arterial pressure drops below 85 mmHg.

47. Hernandez G, Bellomo R, Bakker J. The ten pitfalls of lactate clearance in sepsis. Intensive Care Med 2019; 45:82–85.

48. Wacharasint P, Nakada TA, Boyd JH, *et al.* Normal-range blood lactate concentration in septic shock is prognostic and predictive. Shock 2012; 38:4–10.

49. Das BP, Sharma M, Bansal S, *et al.* Prognostic value of tissue oxygen monitoring and regional cerebral oxygen saturation monitoring and their correlation in neurological patients with sepsis: a preliminary, prospective, observational study. J Neurosurg Anesthesiol 2018; 32:77–81.

50. Vincent J-L, Quintairos e Silva A, Couto L, Taccone FS. The value of blood lactate kinetics in critically ill patients: a systematic review. Crit Care 2016; 20:257.

51. Bakker J, Vincent JL, Gris P, *et al.* Veno-arterial carbon dioxide gradient in human septic shock. Chest 1992; 101:509–515.

52. Protti A, Masson S, Latini R, *et al.* Persistence of central venous oxygen desaturation during early sepsis is associated with higher mortality: a retrospective analysis of the ALBIOS Trial. Chest 2018; 154:1291–1300.

53. Jozwiak M, Monnet X, Teboul JL. Monitoring: from cardiac output monitoring to echocardiography. Curr Opin Crit Care 2015; 21:395–401.

54. Vieillard-Baron A, Millington SJ, Sanfillipo F, *et al.* A decade of progress in critical care echocardiography: a narrative review. Intensive Care Med 2019; 45:770–788.

55. Wetterslev M, Møller-Sørensen H, Johansen RR, Perner A. Systematic review of cardiac output measurements by echocardiography vs. thermodilution: the techniques are not interchangeable. Intensive Care Med 2016; 42: 1223–1233.

56. Koster G, Van Der Horst ICC. Critical care ultrasonography in circulatory shock. Curr Opin Crit Care 2017; 23:326–333.

57. Zhang Y, Wang Y, Shi J, *et al.* Cardiac output measurements via echocardiography versus thermodilution: a systematic review and meta-analysis. PLoS One 2019; 14:1–17.

58. Scolletta S, Bodson L, Donadello K, *et al.* Assessment of left ventricular function by pulse wave analysis in critically ill patients. Intensive Care Med 2013; 39:1025–1033.

59. Vaquer S, Chemla D, Teboul JL, *et al.* Influence of changes in ventricular systolic function and loading conditions on pulse contour analysis-derived femoral dP/dt max. Ann Intensive Care 2019; 9:1–10.

60. Monnet X, Marik PE, Teboul JL. Prediction of fluid responsiveness: an update. Ann Intensive Care 2016; 6:111.

61. Slagt C, Malagon I, Groeneveld ABJ. Systematic review of uncalibrated arterial pressure waveform analysis to determine cardiac output and stroke volume variation. Br J Anaesth 2014; 112:626–637.

62. Guinot PG, Bernard E, Levrard M, *et al.* Dynamic arterial elastance predicts mean arterial pressure decrease associated with decreasing norepinephrine dosage in septic shock. Crit Care 2015; 19:14.

63. Monge García MI, Pinsky MR, Cecconi M. Predicting vasopressor needs using dynamic parameters. Intensive Care Med 2017; 43:1841–1843.

64. Monnet X, Anguel N, Osman D, *et al.* Assessing pulmonary permeability by transpulmonary thermodilution allows differentiation of hydrostatic pulmonary edema from ALI/ARDS. Intensive Care Med 2007; 33:448–453.

65. Nakwan N, Chichareon P, Khwannimit B. A comparison of ventricular systolic function indices provided by VolumeView/EV1000TM and left ventricular ejection fraction by echocardiography among septic shock patients. J Clin Monit Comput 2019; 33:233–239.
66. Belda FJ, Aguilar G, Teboul JL, *et al.* Complications related to less-invasive haemodynamic monitoring ‡. Br J Anaesth 2011; 106:482–486.
67. Reuter DA, Huang C, Edrich T, *et al.* Cardiac output monitoring using indicator-dilution techniques: basics, limits, and perspectives. Anesth Analg 2010; 110:799–811.
68. Thiele H, Ohman EM, de Waha-Thiele S, *et al.* Management of cardiogenic shock complicating myocardial infarction: an update 2019. Eur Heart J 2019; 40:2671–2683.
69. Rajaram SS, Desai NK, Kalra A, *et al.* Pulmonary artery catheters for adult patients in intensive care. Cochrane database Syst Rev 2013; 373: CD003408.
70. Thiele RH, Bartels K, Gan TJ. Cardiac output monitoring: a contemporary assessment and review. Crit Care Med 2015; 43:177–185.
71. Millington SJ, Goffi A, Arntfield RT. Critical care echocardiography: a certification pathway for advanced users. Can J Anesth 2018; 65:345–349.
72. Jozwiak M, Mercado P, Teboul JL, *et al.* What is the lowest change in cardiac output that transthoracic echocardiography can detect? Crit Care 2019; 23:116.
73. Koster G, Kaufmann T, Hiemstra B, *et al.* Feasibility of cardiac output measurements in critically ill patients by medical students. Ultrasound J 2020; 12:. [Epub ahead of print]. doi: 10.1186/s13089-020-0152-5.
74. Geri G, Vignon P, Aubry A, *et al.* Cardiovascular clusters in septic shock combining clinical and echocardiographic parameters: a post hoc analysis. Intensive Care Med 2019; 45:657–667.
75. Sanfilippo F, Corredor C, Fletcher N, *et al.* Left ventricular systolic function evaluated by strain echocardiography and relationship with mortality in patients with severe sepsis or septic shock: a systematic review and meta-analysis. Crit Care 2018; 22:183.
76. Jozwiak M, Monnet X, Teboul JL. Pressure waveform analysis. Anesth Analg 2018; 126:1930–1933.
77. Langewouters GJ, Wesseling KH, Goedhard WJ. The pressure dependent dynamic elasticity of 35 thoracic and 16 abdominal human aortas in vitro described by a five component model. J Biomech 1985; 18:613–620.
78. Monnet X, Teboul JL. Transpulmonary thermodilution: advantages and limits. Crit Care 2017; 21:1–12.
79. Dark PM, Singer M. The validity of trans-esophageal Doppler ultrasonography as a measure of cardiac output in critically ill adults. Intensive Care Med 2004; 30:2060–2066.
80. Teboul JL, Saugel B, Cecconi M, *et al.* Less invasive hemodynamic monitoring in critically ill patients. Intensive Care Med 2016; 42:1350–1359.
81. Thompson BT, Chambers RC, Liu KD. Acute respiratory distress syndrome. N Engl J Med 2017; 377:562–572.
82. Jozwiak M, Silva S, Persichini R, *et al.* Extravascular lung water is an independent prognostic factor in patients with acute respiratory distress syndrome. Crit Care Med 2013; 41:472–480.
83. Demiselle J, Mercat A, Asfar P. Is there still a place for the Swan-Ganz catheter? Yes. Intensive Care Med 2018; 44:954–956.
84. Sionis A, Rivas-Lasarte M, Mebazaa A, *et al.* Current use and impact on 30-day mortality of pulmonary artery catheter in cardiogenic shock patients: results from the CardShock Study. J Intensive Care Med 2019. [Epub ahead of print]
85. Saposnik G, Redelmeier D, Ruff CC, Tobler PN. Cognitive biases associated with medical decisions: a systematic review. BMC Med Inform Decis Mak 2016; 16:138.
86. ▪ Kaufmann T, Castela Forte J, Hiemstra B, *et al.,* SICS Study Group. A Bayesian Network Analysis of the diagnostic process and its accuracy to determine how clinicians estimate cardiac function in critically ill patients: prospective observational cohort study. JMIR Med Inform 2019; 7:e15358.

This study applied a machine learning algorithm to help determine how clinicians estimate cardiac output using clinical examination in critically ill patients.

87. Medic G, Kosaner Kließ M, Atallah L, *et al.* Evidence-based clinical decision support systems for the prediction and detection of three disease states in critical care: a systematic literature review. F1000Res 2019; 8:1728.
88. Singh K, Mayo P. Critical care echocardiography and outcomes in the critically ill. Curr Opin Crit Care 2018; 24:316–321.
89. ▪▪ Merz TM, Cioccari L, Frey PM, *et al.* Continual hemodynamic monitoring with a single-use transesophageal echocardiography probe in critically ill patients with shock: a randomized controlled clinical trial. Intensive Care Med 2019; 45:1093–1102.

This randomized controlled trial was one of the first to try and provide evidence on the benefit of continuous hemodynamic monitoring in critically ill patients with shock.

90. Lucas A, Williams AT, Cabrales P. Prediction of recovery from severe hemorrhagic shock using logistic regression. IEEE J Transl Eng Heal Med 2019; 7:1900509.