GUIDELINES

ISCCM Guidelines for Hemodynamic Monitoring in the Critically Ill

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Abstract

Hemodynamic assessment along with continuous monitoring and appropriate therapy forms an integral part of management of critically ill patients with acute circulatory failure. In India, the infrastructure in ICUs varies from very basic facilities in smaller towns and semi-urban areas, to world-class, cutting-edge technology in corporate hospitals, in metropolitan cities. Surveys and studies from India suggest a wide variation in clinical practices due to possible lack of awareness, expertise, high costs, and lack of availability of advanced hemodynamic monitoring devices. We, therefore, on behalf of the Indian Society of Critical Care Medicine (ISCCM), formulated these evidence-based guidelines for optimal use of various hemodynamic monitoring modalities keeping in mind the resource-limited settings and the specific needs of our patients. When enough evidence was not forthcoming, we have made recommendations after achieving consensus amongst members. Careful integration of clinical assessment and critical information obtained from laboratory data and monitoring devices should help in improving outcomes of our patients.

Keywords: Arterial lactate, Cardiac output measurement, Central venous oxygen saturation, Critically ill adults, Echocardiography, Hemodynamic monitoring, Static parameters, Thermodilution cardiac output, Transpulmonary thermodilution.

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Introduction

Hemodynamic monitoring is an integral part of the management of critically ill patients, especially those with acute circulatory failure. The history of hemodynamic monitoring dates back to ancient times when Galen of Pergamon (130–210 AD) described 27 characteristics from a single beat of pulse based on the speed, frequency, and size that were associated with different causes and outcomes.[1] Scientific and technological advances over the years have led to a sea change in our understanding and ability to monitor the hemodynamic status in real time, with continuous or intermittent noninvasive and invasive techniques and devices.

In patients with acute circulatory failure, the hemodynamic condition often waxes and wanes until overt decompensation, rather than in a linear progression to organ dysfunction. The dynamic variability represents the compensatory mechanisms that occur within the physiological reservoir before overt tissue injury occurs. These can to some extent be indirectly quantified from clinical assessment, absolute physiological values from the monitor, or other clinical and laboratory variables.[2,3] However, in actual practice, these hemodynamic thresholds may not often account for individual variations and dynamic changes, which can potentially lead to misinterpretation or sometimes even underestimation of the instability. Therefore, understanding the limitations of various hemodynamic monitoring techniques and the actual physiological values they reflect is essential to justify the cost, especially in resource-limited settings.

In India, the infrastructure in ICUs varies from very basic facilities in smaller towns and semi-urban areas to world-class, cutting-edge technology in corporate hospitals, in metropolitan cities.[4] The first INDICAPS study, a 4-day point-prevalence study conducted in 2011, which included data from 124 Indian ICUs (4209 patients), found that arterial cannulation was performed in only 19.5%

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patients, while a central venous catheter (CVC) was present in 34.6% patients.[5] In barely 3% of patients, CO and stroke-volume variation (SVV) monitoring was being performed. The second INDICAPS study (5019 patients, 141 ICUs), which surveyed the ICUs between 2018 and 2019, also showed a similar infrequent use of invasive arterial (24.5%) and central venous (34.3%) pressure monitoring. CO and SVV monitoring remained low even in this second survey which happened after a gap of ~8 years.[6]

The wide variation in clinical practices observed in these surveys may be due to lack of awareness, expertise, availability of advanced hemodynamic monitoring devices and high costs. These surveys are suggestive of a need to increase awareness about the utility and limitations of various techniques of hemodynamic monitoring. We, therefore, on behalf of the ISCCM, formulated evidence-based guidelines to guide clinicians for optimal use of various modalities of hemodynamic monitoring in patients with acute circulatory failure, keeping in mind the resource-limited settings and the specific needs of Indian patients.

Scope of the Guidelines

These guidelines have been developed to help clinicians perform hemodynamic monitoring in adult critically ill patients using evidence-based recommendations in variable resource settings. These guidelines are aimed to give clinicians a broad framework for hemodynamic monitoring, however, the details of individual monitoring devices and techniques have not been included. Consensus opinion from the committee experts and other experts who are members of the ISCCM has been taken, wherever robust evidence is lacking or to suit the requirements in the region. These guidelines do not represent the minimum standard of practice, nor are they a substitution for good clinical judgment.

Methods

Committee Composition

The ISCCM executive committee appointed two chairs to constitute a national committee to formulate guidelines for hemodynamic monitoring in the critically ill patients. The committee chairs formed a panel of critical care specialists with clinical experience and expertise in the field of hemodynamic monitoring. Corresponding with individual expertise, the panel was divided into subgroups addressing the following six domains: (i) Definition of shock or acute circulatory failure, (ii) Clinical and point-of-care investigations to determine the presence of acute circulatory failure, (iii) Volume responsiveness, (iv) Role of transthoracic and transesophageal echocardiography (TEE), (v) Fine-tuning of fluid therapy, and (vi) When to use advanced hemodynamic monitoring. Each subgroup was led by a team member and was given the task of summarizing evidence and drafting recommendations in the respective area.

Conflict of Interest

Each panel member declared any conflict of interest based on procedures outlined by the ISCCM, which has been reviewed by the guideline chairs. The views and interests of any commercial entity that provided funding to ISCCM had no influence on the topics discussed and recommendations made.

Meetings

In view of the travel restriction due to the pandemic, all committee meetings were held on an online platform. Conference calls and e-mail correspondence were used to discuss specific issues requiring input from other panel members, including updated literature searches, evidence synthesis, finalizing the recommendations, and responding to peer review.

Formulating Clinical Questions

The panel agreed on eight specific questions pertinent to hemodynamic monitoring of critically ill adults and outlined outcomes of interest for each question a priori:

- How do we assess tissue perfusion clinically?
- Which laboratory parameters do we use to diagnose tissue hypoperfusion and as targets for resuscitation?
- How should the blood pressure be monitored in patients with acute circulatory failure? What should be the blood pressure target for resuscitation of patients with acute circulatory failure?
- What is the role of echocardiography in assessing patients with acute circulatory failure?
- How do we assess fluid responsiveness?
- When do we stop giving fluid to a patient with acute circulatory failure?
- Which patients need advanced hemodynamic monitoring?
- Should changes in microcirculatory perfusion be used to guide the therapy of a patient with acute circulatory failure?

Literature Review

A medical librarian helped to develop a search strategy for each of the guideline questions, using specific vocabulary terms for an updated search of articles from January 2016 to December 2021 in MEDLINE, EMBASE, Cochrane Registry of Controlled Trials, Ovid, Google Scholar, and PubMed. In addition, the panel members were also asked to highlight any additional studies not identified by the search.

Evidence Review and Development of Clinical Recommendations

Two independent reviewers in each group screened titles and abstracts to identify articles related to their subgroup, they also evaluated the full text of articles deemed potentially relevant by any reviewer. Any disagreement was resolved by consensus among the members. We used Grading Recommendations, Assessment, Development, and Evaluation (GRADE) principles to prioritize outcomes, assess the quality of evidence, and determine the strength of outcomes, rather than the formal GRADE process. Thereafter, we used the Evidence-to-Decision framework to facilitate transition from evidence to final recommendations.[7] We classified each recommendation as strong or conditional as per GRADE methodology. A recommendation was accepted if 80% consensus was achieved. We developed best-practice statements based on these recommendations. The committee assessed whether the intervention would provide substantially more benefit than harm. If the benefit was felt to be substantial in our consensus opinion, the recommendation was worded as "we recommend". If we were not confident of substantial benefit as against harm, then we worded it as "We suggest". Where the evidence was not strong but the committee felt that the interventions were beneficial, the statements for the particular intervention have been labeled as Best Practice Statements or BPS.

Recommendations with Evidence Summary

How do We Assess Tissue Perfusion Clinically?

Shock is defined as a life-threatening acute circulatory failure, which leads to either failure of oxygen delivery or utilization by the tissues. Shock may be caused by a single pathology or a combination of different disease processes. Shock, unless identified and corrected promptly, may lead to multiorgan failure and death. It is important to remember that the patient can have shock without being hypotensive, but have hyperlactatemia. Tissue hypoperfusion can be diagnosed using clinical signs and laboratory parameters.

Recommendations

- We recommend that the clinician looks for clinical signs of peripheral hypoperfusion in all critically ill patients.
- We recommend that all patients be assessed for the presence of altered mentation, tachycardia, hypotension, decreased urine output, and tachypnea.
- If the peripheries are cold on touch, formal measurement of the difference between peripheral and core temperature should be carried out at admission and at frequent intervals during resuscitation.
- We recommend that capillary refill time (CRT) be measured at admission, if it is found to be >4 seconds, frequent measurements should be carried out during resuscitation to check for a change.
- We recommend that patients be assessed for the presence of mottling around the knees, and if present, it should be graded from 0 to 5, and repeated assessment carried out at frequent intervals.
- We recommend that hourly urine output should be measured in all critically ill patients.
- We recommend that a single clinical sign be not relied upon, and overall clinical assessment should be taken into account while assessing the progress of the patient.

Evidence Summary

In the presence of an insult leading to the development of shock, the human body progresses through compensating physiological needs, to decreasing organ perfusion, to overt shock. The signs that are seen are dependent on the importance of the organs to the body based on "inverse priority pattern", i.e., the perfusion reduces first in the organs of least importance (skin and muscles) through to the last but the most important organs, i.e., heart and brain.[8] In the initial interval, neurohumoral response takes over causing vasoconstriction, which then leads to decreased peripheral perfusion with preservation of vital organ perfusion.[9] Therefore, decreased peripheral temperature, i.e., cold extremities, appears first, followed by tachycardia [to increase cardiac output (CO)], then decreasing blood pressure, tachypnea, oliguria, and last changes in mentation occur.

A reduced peripheral perfusion leads to a drop in temperature of the extremities. This decrease in peripheral perfusion also leads to a temperature gradient between central and peripheral areas of the body and can be confirmed by measuring the difference between core temperature/room temperature and great toe.[10,11] Another sign of decreased peripheral perfusion is delayed CRT. This is easily measured at either the fingertips or knees of the patient. Multiple studies have shown an association between delayed CRT and metabolic parameters (lactate) of perfusion, and their impact during resuscitation, particularly in septic shock.[11–15] A trial targeting CRT vs lactate normalization in patients with septic shock found that though CRT-targeted resuscitation did not reduce mortality, it did lead to reduced organ dysfunction at 72 hours.[15] Recently, a point-of-care device for CRT measurement was shown to improve the accuracy of assessment of peripheral perfusion.[16]

Reduced perfusion can lead to changes in consciousness and cognition, leading to obtunded mental status. In critically ill patients, reduced perfusion can present as altered mental status that may range from confusion to delirium and coma. Gofton and Young found that 70% of septic shock patients had neurological symptoms.[17] Kataja found that 68% patients with cardiogenic shock had altered mental status at presentation and this was an independent predictor of mortality.[18]

Normally, the kidneys receive one-fifth of total CO, but of this, 90% goes to the cortex and the rest to the medulla. In patients with adequate renal blood flow, the cortex and medulla respond differently to a decrease in renal perfusion pressure. The medullary microcirculation is pressure-dependent, i.e., it has poor autoregulation. Therefore, it responds poorly to decrease in circulating intravascular volume.[19] Any drop in blood pressure, therefore, leads to a decrease in urine output. In the ICON study, persistent oliguria in the critically ill was found to be associated with increased ICU stay and hospital mortality.[20]

A Mottling score with 6 grades (0–5) has been described, which was shown to correlate with survival in patients with septic shock, this, however, can be used only in patients with fair skin.[21]

Which Laboratory Parameters do We Use to Diagnose Tissue Hypoperfusion and as Targets for Resuscitation?

Recommendations

- We recommend measuring lactate during the initial phase of resuscitation.
- We suggest serial lactate measurement be performed for prognostic purposes.
- We *do not recommend* tailoring resuscitation strategies solely on the basis of elevated lactate.
- We *do not recommend* using nonclearance of lactate as a trigger for fluid therapy.
- We suggest using standard bases excess (SBE) as a tool for triaging patients in shock, especially in the setting of trauma.
- We *do not recommend* using SBE as an alternative to lactate measurement or as a single parameter to guide resuscitation in nontrauma patients.
- We recommend measurement of oxygen saturation (SvO_2)/ $ScvO_2$ in patients having shock.
- A low $ScvO_2$ suggests poor tissue hypoperfusion and patients should be re-evaluated to ascertain the cause of shock and guide further therapy (BPS).
- A high $ScvO_2$ on the other hand may indicate impaired oxygen utilization by the tissues (BPS).

Evidence Summary

Lactate is recommended as a marker of resuscitation and peripheral perfusion. The Surviving Sepsis Campaign integrated lactate measurement into the 1-hour bundle.[22] During critical illness, multiple factors cause elevation in lactate in addition to hypoxia and hypotension.[23] A threshold of 2 mmol/L has now been projected as a marker of organ dysfunction, especially in sepsis.[24] However, hyperlactatemia may be seen without evidence of hemodynamic instability. In addition, not all patients with a diagnosis of shock

manifest lactic acidosis. The original recommendation to measure lactate arose from the concept of "oxygen debt" in 1969.[25] While this was a very simplistic explanation, hyperlactatemia and lactic acidosis are fairly consistent manifestations of cellular hypoxia and represent the severity of shock. Serial lactate measurements then became the standard of care.[26] It was recognized and accepted for long that the responders of fluid resuscitation could be identified by a 10% decrease in blood lactate concentration over 1 hour. Further evidence seemed to suggest that faster clearance of lactate identifies patients with a better prognosis.[27] The ANDROMEDA-SHOCK trial, however, countered the concept of lactate-directed resuscitation.[15] The authors found that lactate-guided therapy resulted in more fluid therapy, more vasopressor usage, and more adrenaline usage, while not resulting in better outcomes. The finding of great concern was that mortality was higher in the lactate-guided therapy group. It has to be remembered that hyperlactatemia in the early hours of resuscitation, especially in sepsis, may not always be due to end-organ hypoperfusion.

Standard Base Excess

Early recognition of shock (especially hypovolemic shock) is a challenge in the acute care setting. The SBE is often used as a marker of systemic metabolic acidosis in the context of shock. Most blood gas analyzers provide both the values. The role of SBE in managing trauma patients is well-documented.[28] Standard base excess might be able to predict mortality better than vital signs or shock index. But this body of evidence comes predominantly from observational studies. Moreover, SBE values are significantly influenced by hyperchloremia in the acute setting. Kidney injury and failure, diabetic ketoacidosis, and chronic CO_2 retention also influence the SBE.[29] Therefore, its application across the spectrum of patients needing hemodynamic optimization is not validated.

Monitoring SvO_2/$ScvO_2$

The ultimate endpoint of resuscitation is to reverse the imbalance between oxygen supply and demand. It was proposed that both mixed venous SvO_2 and $ScvO_2$ can be used to measure the efficacy of resuscitation. A true SvO_2 measure needs a pulmonary artery catheter, while $ScvO_2$ measurement needs an appropriately positioned CVC. The importance of $ScvO_2$ was highlighted in the first early goal directed therapy (EGDT) trial.[30] Since then, several studies have attempted to replicate the results of "normalizing" $ScvO_2$ with no success.[24] The incidence of low $ScvO_2$ in patients needing resuscitation also appears to be low.[31]

How should the Blood Pressure be Monitored in Patients with Acute Circulatory Failure? What should be the Target for Resuscitation of Patients with Acute Circulatory Failure?

Recommendations

- We recommend that in all patients in shock, arterial blood pressure should be monitored invasively.
- We recommend a target MAP of 65–70 mm Hg.

Evidence Summary

Cohn, in 1967, described how inaccurate the palpatory and auscultatory methods of noninvasive blood-pressure measurements were as compared with invasive blood-pressure measurement.[32] Meidert et al. recently reported that in ED patients, oscillometric method was unable to detect hypotension in patients with shock, since the MAP measured by this method was erroneous, nearly 15% higher compared with invasive blood-pressure measurement.[33]

The aim of resuscitation in shock states is to restore adequate tissue perfusion. Varpula et al. chose different mean arterial pressure (MAP) thresholds, 60, 65, 70, and 75 mm Hg, and looked at the effect of maintaining these target pressures on patient outcomes. They found that MAP of 65 mm Hg and $ScvO_2$ >70% were independent predictors of mortality.[34] Dünser et al. calculated the time integral of drop in arterial blood pressure for systolic pressure, mean perfusion pressure [MPP = MAP–central venous pressure (CVP)] for the first 24-hour stay in the ICU, and correlated it with ICU outcomes.[35] They found that MAP threshold of ≥60 mm Hg was as good as higher MAP levels. However, acute renal failure was likely to occur if the MAP was <75 mm Hg. A *post hoc* analysis of different quartiles of MAP values and vasopressor load found that increasing MAP to values higher than 70 mm Hg does not offer any advantage, contrarily, use of higher doses of vasopressor may cause an increased mortality.[36] Asfar et al. found no difference in outcomes when targeting low (65–70 mm Hg) or high (80–85 mm Hg) MAP thresholds, in patients with septic shock, however, there was an increased incidence of atrial fibrillation in the high-target group.[37] Another trial comparing normal vs higher blood-pressure targets did not find any improvement in outcomes of patients with shock.[38] Prolonged high dose of vasopressor therapy may be associated with adverse cardiac events and worse outcomes, due to certain adverse effects of exogenous vasopressor load.[35,38,39] A systematic review of trials comparing high vs lower blood pressure did not find any patient-related adverse events in the lower target group, but suggested that higher blood-pressure targets may increase mortality, for patients who are on high doses of vasopressors.[40]

What is the Role of Echocardiography in Assessing Patients with Acute Circulatory Failure?

Recommendations

- We recommend use of transthoracic echocardiography (TTE) for initial evaluation of type of shock.
- We recommend that a stepwise, protocolized, echocardiographic approach be used.
- Echocardiography can be used to determine the type of shock, if the reason is not clinically obvious (BPS). Subsequently, it should be used for sequential evaluation (BPS).
- We recommend a detailed echocardiographic evaluation, after initial rapid evaluation to confirm the findings.
- We suggest the use of TEE for hemodynamic monitoring only if an operator skilled in its use is available.
- We recommend using TEE over TTE for hemodynamic monitoring in the following situations:
  - Poor thoracic echo window that precludes TTE.
  - Patients in prone position.
  - During cardiac arrest, to diagnose the cause of the arrest and to assess the adequacy of compressions.
  - Pulmonary embolism due to a proximal pulmonary artery thrombus.
  - Thoracic aortic dissection.
  - Post-cardiac surgery hypotension.
- We suggest obtaining the following views at a minimum with TEE done for assessing a hemodynamically unstable patient:
  - Transgastric short-axis view.
  - Mid-esophageal 4-chamber (ME4C) view.

  - Mid-esophageal bicaval view.
  - Mid-esophageal descending aorta view.
- We recommend using a two-point compression technique (femoral and popliteal) for rapid screening for DVT.

Evidence Summary

Echocardiography is the perfect hemodynamic tool for the initial evaluation of the patient in shock due to reasons such as immediate availability of results to detect the mechanism of shock, guidance for hemodynamic management (fluid responsiveness/impairment of left or right ventricular (RV) function/increased RV afterload), and rapid evaluation of response therapy.[41,42]

A clinician should be trained in rapid cardiac assessment by echo (RACE), to assess a deteriorating patient using 2D and M-mode echocardiography, to detect major abnormalities with initiation of treatment. This can be followed by a more detailed assessment at a later stage. RACE involves assessment of left ventricular function, including ejection fraction, regional wall-motion abnormalities; signs of right heart failure; inferior vena cava assessment, and pericardial pathologies. RACE should be also accompanied by other scans [lung ultrasound (LUS), DVT scan, etc.] to confirm diagnosis and guide therapy. For this reason, several integrated protocols for shock assessment have been devised, which allow stepwise protocolized approach. One such protocol is the Rapid Ultrasound in Shock (RUSH) protocol.[43] The RUSH protocol consists of three components: "the pump", "the tank", and "the pipes", allowing an experienced ultrasound operator to easily complete the entire protocol in 5–10 minutes. Several studies of RUSH protocol have shown excellent accuracy for all types of shock.[44,45]

Transthoracic echocardiography is noninvasive, quicker, and cheaper than TEE. In addition, availability of transesophageal probe and the training required to use it may be a barrier to using TEE. If available, TEE has a distinct advantage over TTE for hemodynamic monitoring in patients with a poor transthoracic echo window. Transthoracic echocardiography cannot be performed when patients are in prone position, while TEE can.[46] In cardiac arrest, TEE is useful to determine the cause of the arrest and allows for continuous monitoring of the adequacy of resuscitation, which is not possible with TTE.[47] In aortic dissection, TEE offers much superior visualization of the thoracic aorta than TTE.[48] Postoperative bleeding with localized tamponade in the post-cardiac surgery patient requires TEE as it is difficult to rule it out using TTE. Transesophageal echocardiography is also superior to TTE for the visualization of a central pulmonary embolus.[49]

Transesophageal echocardiography has been shown to have a greater diagnostic accuracy and therapeutic impact compared with TTE in hemodynamically unstable patients.[50] It is also less operator-dependent and needs a shorter training time to achieve competency.[51] Although more invasive than TTE, it has a low risk of complications—that are mostly very minor.[52]

How do We Assess Fluid Responsiveness?

Fluid responsiveness is a state when the left ventricle is able to increase its stroke volume (SV) or CO in response to fluid administration.[53–56]Administering a fluid challenge will help determine fluid responsiveness, however, this may be harmful in nonresponders. Repeated fluid boluses increase the risk of fluid overload and may worsen outcomes, especially in patients with septic shock and acute respiratory distress syndrome.[57] Thus, administering fluid to a "fluid non-responder" is not only ineffective, but may be harmful. Therefore, after initial resuscitation, predicting whether a fluid bolus will increase CO or not before administering fluid, is essential to avoid harm. Dynamic parameters are more reliable than static parameters like CVP and pulmonary artery occlusion pressure (PAOP) to assess fluid responsiveness. The dynamic parameters in current clinical use are pulse-pressure variation (PPV), SVV, using tidal volume challenge (TVC) and lung recruitment to improve the reliability of PPV, respiratory variation of vena cava diameters (rvIVC), and end-expiratory occlusion test (EEOT), and noninvasive tests such as plethysmographic-variability index (PVI).[58,59] Central venous catheter is placed in critically ill patients both for CVP monitoring and safe venous access for administration of vasopressors and other irritant medications. Central venous pressure is considered a surrogate of right ventricular end-diastolic pressure (RVEDP), which in turn is considered to be a reflection of RV preload and is the commonest. However, CVP interpretation and extrapolation to clinical practice has several limitations.[54]

Recommendations

- We *recommend against* the use of CVP to predict fluid responsiveness.
- In spontaneously breathing patients in shock, we suggest using focused cardiac ultrasound to accurately identify patients with low CVP, provided the patient is not gasping for breath and has smooth breathing pattern.
- A very low CVP may indicate low preload, on the other hand, a very high CVP may indicate an adequately filled vasculature. If the patient is still in shock, we feel other approaches need to be adopted for further evaluation and therapy (BPS).
- We suggest that a fluid challenge be used to identify patients who will benefit from fluid therapy, provided there is no contraindication to fluid administration.
- We recommend that at least 4 mL/kg crystalloid be given over 5–10 minutes for performing fluid-challenge test.
- If advanced devices for monitoring are not available, we suggest using the CVP and MAP to observe a response to fluid-challenge test.
- We feel that a mini fluid challenge should be used only if advanced echocardiographic expertise interpretation is available (BPS).
- We recommend using dynamic parameters such as PPV, SVV, Δ-IVC, EEOT, and TVC over static parameters for hemodynamic monitoring, when available, in mechanically ventilated patients.
- We recommend using pulse-pressure variation, which is available with most modern monitors used for invasive arterial pressure, as the preferred dynamic measure, since it is likely to be available in all settings, even in areas with limited resources.
- We recommend using TVC with PPV and SVV to predict fluid responsiveness in patients ventilated using low tidal volume.
- When TVC is used with PPV, direct CO measurements are not required (BPS).
- Among dynamic parameters, we recommend using the EEOT, TVC, and PLR, as these tests are the most reliable in predicting fluid responsiveness in patients ventilated using low tidal volume.
- We recommend that EEOT be assessed by direct measurement of CO, as it is less reliable when its effects are measured using arterial pressure.
- We recommend using ΔVmaxAo and ΔSVC over ΔIVC, as they have greater diagnostic accuracy, provided required expertise for TEE is available.

- We recommend using passive leg-raising test (PLR) to predict fluid responsiveness in both nonventilated and ventilated patients.
- We recommend performing PLR using a direct measurement of CO or stroke volume, since it is less reliable when performed using invasive arterial pressure waveform.
- Since PLR may not be useful in patients with intra-abdominal hypertension, we suggest using some other measure for fluid responsiveness in its place.
- We recommend against using PLR in patients with intracranial hypertension, or other conditions where head-low position may adversely affect the patients.

Evidence Summary

Central Venous Pressure Measurement: Studies have shown that CVP is an unreliable marker of fluid responsiveness.[54–56] Dynamic hemodynamic variables consistently perform better than CVP in predicting fluid responsiveness. However, at extremes of values (CVP <6 and >12 mm Hg), CVP seems to perform better to predict fluid responsiveness.[57] A recent analysis of a large database in China, demonstrated that measuring CVP was associated with reduced risk-adjusted 28-day mortality among septic patients, this benefit was proportionally mediated through reduction of serum lactate.[58]

Fluid-challenge Test: One of the most frequent dilemmas while resuscitating sick patients is whether the patient should be given fluids. Fluid-challenge test is a method to identify patients who may benefit from an increase in intravascular volume. It is, in other words, a dynamic test for the circulation. Given the fact that positive fluid balance could be detrimental to patients during the later stages of resuscitation, it is crucial to identify those who will actually benefit from an increase in intravascular volume. The fundamental principle is that, for a fluid bolus to increase the SV and thereby the CO, the administered volume should be able to stretch the right heart (i.e., increase the RV end-diastolic volume).[59] The postulated volume that is expected to achieve this result in physiological state is 3 mL/kg or 200 mL.[59] A dose of 4 mL/kg over 5 minutes was found to be superior to infusion of 1, 2, or 3 mL/kg (body weight) of crystalloid over 5 minutes.[60] It should be remembered that not all patients who are fluid-responsive, need fluids. This decision has to be taken based on the assessment of perfusion. A positive response to FC would imply a 10–15% increase in SV or CO. The parameter, which identifies this increase in SV or CO, is not the same in all-clinical settings. Mean arterial pressure is the most universally applied measure. Urine output, point-of-care ultrasound echocardiography, and CO monitoring have also been used. The choice of fluid used for the FC is quite often a crystalloid. The rate of fluid administration is equally important. A short infusion time of 5–10 minutes is considered optimal. A mini-fluid challenge involving an infusion of 100 mL of colloid over 1 minute targeting VTi has also been proposed but has not been validated.[61]

Dynamic Measures of Fluid Responsiveness: Dynamic parameters are based on heart–lung interactions, and predict fluid responsiveness by measuring the changes in SV or CO due to changes induced in preload, due to pressure changes in the thorax, and due to mechanical ventilation. Several dynamic tests and parameters have been used to predict fluid responsiveness. They involve inducing or observing variations in cardiac preload, and measuring the resultant changes in CO or SV. The magnitude of these changes can help predict how much change will be induced in these parameters by fluid administration. These include tests based on heart–lung interaction and one test that does not: the passive leg-raising test (PLRT). Dynamic parameters and tests based on heart–lung interactions include PPV, SVV, using TVC to improve the reliability of PPV, rvIVC and EEOT, lung recruitment, and noninvasive tests such as PVI.[62,63] The most common limitations of the tests using heart–lung interactions are spontaneous breathing, low lung compliance, ventilation using low tidal volume (Vt), and arrhythmias. The rvIVC however is not affected by the presence of arrhythmias and TVC can be reliably used in patients ventilated using low V_T.[62] Three meta-analyses found that arterial waveform-derived parameters, PPV and SVV, can reliably predict fluid responsiveness in mechanically ventilated patients. The respiratory variations of superior vena cava diameter (rvIVC), however, are not affected by the presence of arrhythmias and both rvIVC along with TVC can be reliably used in patients ventilated using low V_T.[63–65] Si et al. conducted a systematic review and meta-analysis to assess the reliability of EEOT to predict fluid responsiveness in mechanically ventilated patients. The mean threshold was an EEO-induced increase in CI of more than 4.9 ± 1.5%.[66] However, the accuracy of EEOT was shown to be reliable when its hemodynamic effects were assessed by direct measurement of CO than using arterial pressure. Messina et al. conducted a meta-analyses and systematic review to check the reliability of the EEOT and of the mini-fluid challenge for predicting fluid responsiveness.[67] The areas under the curve (AUC) for EEOT was 0.96, with pooled sensitivity and specificity of 0.86 and 0.91, respectively. They concluded that EEOT and the mini-FC reliably predict fluid responsiveness.

The largest prospective multicenter study (540 ventilated adults) compared echocardiographic indices used to predict fluid responsiveness, i.e., rvSVC, rvIVC, and Doppler velocity in the left ventricular outflow tract (ΔVmaxAo).[68] The ΔVmaxAo had the best sensitivity and rvSVC the best specificity in predicting fluid responsiveness. Though rvSVC had a greater diagnostic accuracy than rvIVC (AUC was 0.752 and 0.635, respectively), its measurement requires TEE. The most commonly used echocardiographic variable in clinical practice is rvIVC. Vignon et al. conducted a systematic review and meta-analysis (20 studies and 761 patients) to assess the diagnostic accuracy of rvIVC in detecting fluid responsiveness.[69] Pooled sensitivity and specificity of rvIVC in 330 spontaneously breathing patients were 0.80 [95% confidence interval (CI) 0.68–0.89] and 0.79 (95% CI 0.60–0.90). Pooled sensitivity and specificity of rvIVC in 431 mechanically ventilated patients were 0.79 (95% CI 0.67–0.86) and 0.70 (95% CI 0.63–0.76).[70]

Among the limitation with the use of parameters and tests to predict fluid responsiveness, ventilation using low tidal volume is the most common in clinical practice.[62] Recently, Alvarado Sánchez et al. conducted the first systematic review and meta-analysis on predictors of fluid responsiveness in critically ill patients mechanically ventilated with low tidal volumes (Vt ≤8 mL kg), including 33 studies and 1352 patients.[71] The AUC values for predictors of fluid responsiveness were: for PPV = 0.82, Δ-IVC = 0.86, SVV = 0.90, m-FC = 0.84, PLR = 0.84, EEOT = 0.92, and TVC = 0.92. They concluded that using TVC to improve reliability of PPV, EEOT, and SVV has excellent operative performance, while Δ-IVC, PLR, m-FC, and PPV had good operative performance as predictors of

fluid responsiveness.[72] The lung-recruitment tests and noninvasive tests such as plethysmography-variability index (PVI) have shown promising results is small studies, but warrant further investigations before they can be recommended for routine clinical practice.[62] We can use heart–lung interaction to detect fluid responsiveness only in patients on controlled mechanical ventilation. For those who are breathing spontaneously, one should use PLR that is also known as internal or self-fluid challenge. While using PLR to detect fluid responsiveness, continuous CO monitoring is mandatory, where a 15% increase in stroke volume, following PLR, predicts fluid responsiveness.

When do We Stop Giving Fluid to a Patient with Acute Circulatory Failure?

Recommendations

- If desaturation occurs, or crepitations develop, during fluid infusion, the patient should undergo urgent re-evaluation of ongoing fluid therapy (BPS).
- We recommend that in the absence of frank pulmonary edema and pneumothorax, repeated LUS be performed to assess and monitor the risk of fluid overload to guide fluid therapy.
- We recommend closer clinical and LUS monitoring in patients with elevated LV-filling pressures (E/e′>15) as they may be at a higher risk of increased extravascular lung water (EVLW) with a fluid bolus.
- We recommend that fluid therapy may be continued for patients with cardiovascular instability, provided the GEDVI is less than 800 mL and Extravascular Lung Water Index (EVLWI) does not exceed 10 mL/kg.
- In patients with high EVLWI (>12 mL/kg), fluid infusion should be stopped and other therapies such as vasopressors or inodilators may be instituted as indicated.

Evidence Summary

Pulmonary edema, accumulation of excessive fluid in the alveoli, is frequently seen in critically ill patients, due to increased hydrostatic pressure (cardiogenic) or increased efflux of fluid into interstitial spaces as a result of sepsis-induced abnormalities in the vascular permeability.[72,73] This can lead to desaturation, can be assessed clinically on auscultation, on X-ray, and by performing LUS. Using transpulmonary thermodilution or dye-dilution technique, we can measure the preload (Global End-diastolic Volume Index – GEDVI) and quantify the amount of fluid in the pulmonary interstitium (EVLWI).[74,75]

Global End-diastolic Volume Index/Extravascular Lung Water Index/Pulmonary Vascular Permeability Index

Chew et al. demonstrated that EVLW-related parameters improved the diagnosis of sepsis-associated lung injury at all severities.[76] A systematic review of 9 studies, which included 690 patients, found that EVLWI was a good predictor of mortality in critically ill patients.[77] However, EVLWI may also be increased in patients with pneumonia and pleural effusion.[74,78] The presence of pneumonia or pleural effusion is clinically evident. In the absence of these clinical conditions, GEDVI and EVLWI can be used to differentiate between cardiogenic and noncardiogenic pulmonary edema and fluid therapy can be implemented appropriately. Mayr et al. reported that B-line scores derived from LUS (either 4-sector or 28-sector scans) were accurately able to predict the EVLWI in critically ill patients.[79]

The normal values for GEDVI (600–800 mL/m^2), EVLWI (12 mL/kg), and PVPI (extravascular lung water/pulmonary blood volume) ≤2 should be kept in mind for fine-tuning fluid therapy in critically ill patients.[80]

Echocardiography to Assess the Safety of Filling Pressure in Volume-responsive Patients

Excessive fluid administration can lead to deleterious effects in multiple organs, manifesting first in the lungs. Once the patient in shock is found to be preload-responsive, it is important to assess the risk of increasing EVLW. A simple pragmatic way to do this is to be cautious with fluid boluses in all patients with severe hypoxemia and bilateral lung infiltrates. The utility of LUS to assess safety of filling has been already described in another section.

rvIVC has been shown to correlate with EVLW.[81] However, there is no evidence to show that IVC diameters or variation predicts increase in EVLW with fluid loading.

Echocardiographic LV systolic dysfunction has been shown to correlate with EVLW determined ultrasonologically.[82] However, this does not predict an increase in EVLW with fluid administration.[83] These patients are however at higher risk of fluid overload and need closer monitoring during fluid resuscitation. In patients with a grossly dilated RV with RV systolic dysfunction, fluid administration can lead to overdistension of the RV, and precipitate RV ischemia due to the increased wall tension.[84]

Estimation of LV-filling pressures helps to determine if the patient is at risk of lung-fluid intolerance. The ratio of E to e′ correlated well with the LV-filling pressures in most patients in sinus rhythm. An E/e′ ratio of >15 suggests elevated LV-filling pressures. Using the medial mitral annulus has been shown to be better than the lateral mitral annulus for this purpose.[85]

Elevated filling pressures have shown a correlation with EVLW and predict cardiogenic pulmonary edema during weaning failure. However, elevated LV-filling pressures do not unequivocally predict a rise in EVLW with a fluid bolus.[86] This is because an increase in EVLW with fluid administration also depends on pulmonary capillary permeability, serum albumin levels, and the presence of pulmonary vascular remodeling in patients with long-standing elevated filling pressures.[87] The identification of elevated filling pressures on echocardiography only helps to suggest that the patient may be at a higher risk of increased EVLW, needing closer clinical and LUS monitoring during further fluid administration.

Which Patients Need Advanced Hemodynamic Monitoring?

When initial fluid administration and vasopressor therapy fail to resolve shock, a re-evaluation of the patient condition becomes essential. In a patient with complex cardiovascular disorders, basic hemodynamic monitoring consisting of invasive arterial and CVP monitoring may be inadequate to guide therapy and more advanced hemodynamic monitoring may be required.

Recommendations

- We recommend using either pulmonary artery catheterization or transpulmonary thermodilution in patients with shock and complex etiology.
- We recommend using transpulmonary thermodilution technique, if available, to differentiate and manage unstable patients with complex cardiopulmonary pathophysiology.
- We recommend using pulmonary artery catheter in patients with cardiogenic shock on mechanical circulatory-assist devices.

- We suggest use of pulmonary artery catheters (PACs) in patients with RV failure.

Evidence Summary

Recently, Kouz et al. studied the correlation between MAP and CO, in patients undergoing complex abdominal surgeries. They found that there was no meaningful correlation between MAP and CO. They attributed this to variation in the vascular tone and volume status of the patients.[88] Therefore, it is logical to measure CO directly and optimize therapy in patients with complex etiology of shock, large fluid shifts, and those with multiple-organ dysfunction and failure. There is also increased interest in the use of PACs in patients with cardiogenic shock. The data from Cardiogenic Shock Working Group (CSWG) registry from 8 tertiary care centers of patients with cardiogenic shock, who were on mechanical circulatory support, suggested that use of PAC was associated with lower in-hospital mortality.[89] Osman et al. also reported decreased mortality in patients with cardiogenic shock who were on mechanical circulatory support, with the use of PAC, in a propensity-matched cohort of nearly 400,000 patients.[90] Pan et al., in a retrospective analysis of over 500 patients, found that therapy utilizing transpulmonary thermodilution CO monitoring resulted in a moderately low CO and lower EVLWI, without compromising organ function. The patients with cardiogenic shock had lower EVLWI as compared with those with ARDS and mortality was lower in patients with cardiogenic shock.[91]

In the critically ill patients, when the patients' hemodynamic status does not improve after initial resuscitation, or if the patient has shock of mixed or complex etiology, use of advanced hemodynamic monitoring, consisting of devices such as pulmonary artery catheter or transpulmonary thermodilution catheter, can help us to determine the ongoing need for further fluids or resuscitation, vasopressors, or inotropic agents. They can be used not only as diagnostic tools to clarify the patient status in complex scenarios of shock (due to a combination of etiologies) but can also guide further therapy.

Should Changes in Microcirculatory Perfusion be Used to Guide Therapy in a Patient with Acute Circulatory Failure?

Recommendations

- We *do not recommend* monitoring the microcirculation and using microcirculation-targeted therapy in routine patient management.
- We recommend that its use be restricted only to research settings.

Evidence Summary

The principal role of the circulation is to deliver nutrients to the organs and remove waste products. This is mainly accomplished by the delivery of red blood cells (RBC) into the microcirculation and the passive diffusion of oxygen from the RBCs to the tissue cells. When requirements are not met, organ dysfunction occurs before ultimately failing. Therefore, the goal in treating circulatory dysfunction is to restore adequate perfusion of the microcirculation. The oxygen content [hemoglobin (Hb) and Hb saturation] also determines the amount of oxygen delivered to the organs.

Different handheld microscopes are used for direct observation of microcirculation, mostly applied to the sublingual area. The advantage of these devices is that they are noninvasive and easy and quick to use. Exploration of the microcirculation is intermittent but can be frequently repeated without inconvenience to the patient. Importantly, evaluation of the microcirculation requires acquisition of good-quality images and a strict protocol for image analysis.

The ultimate goal of resuscitation is the improvement in microcirculatory perfusion, the question is whether these currently used signs of shock and the improvement in these signs actually correspond to the changes in the microcirculation. Recent studies have shown that during the development of shock, the deterioration in the macrocirculatory parameters is followed by the deterioration of microcirculatory perfusion. However, in many cases, the restoration of adequate macrocirculatory parameters is frequently not associated with improvement in microcirculatory perfusion.[92,93] This is again variable, depending on the etiology and type of shock. This may result in both overresuscitation and underresuscitation, leading to increased morbidity and mortality.

Fluids given in the early stages and dobutamine may somewhat improve the microcirculation, but their effects are quite variable. Vasodilatory agents may improve microvascular perfusion, but they lack selectivity and increase flow in already-perfused areas as well. Modulation of endothelial nitric oxide synthase with various agents (including vitamin C) appears promising. Hence, it is important to understand the microcirculatory changes that occur with various therapies to plan resuscitation targets for the future. At this stage, it seems premature to address this question. While there is no doubt that a better understanding of the pathophysiologic processes is desired, the major limitation is that we lack therapies specifically acting at the microcirculatory level.

Conclusion

A group of nine experts from the ISCCM formulated these pragmatic recommendations for hemodynamic monitoring in Indian ICUs with variable resource settings. Almost all recommendations are based on studies performed in resource-rich environments. These will need to be adapted at individual provider level and ICU level based on available expertise and resources. The CRT was identified as a promising clinical tool for hemodynamic monitoring, whose role is being evaluated in a large randomized controlled trial. Prospective research on the utility and outcomes of hemodynamic monitoring in Indian ICUs is necessary to determine the modalities best suited for our circumstances.

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References

1. Harris CRS. Galen's Pulse-Lore. The Heart and the Vascular System in Ancient Greek Medicine from Alcmaeon to Galen. Oxford, UK: Clarendon Press; 1973.
2. Zimmerman JE, Kramer AA, McNair DS, Malila FM. Acute Physiology and Chronic Health Evaluation (APACHE) IV: Hospital mortality assessment for today's critically ill patients. Crit Care Med 2006; 34(5):1297–1310. DOI: 10.1097/01.CCM.0000215112.84523.F0.
3. Higgins TL, Teres D, Copes WS, Nathanson BH, Stark M, Kramer AA. Assessing contemporary intensive care unit outcome: An updated Mortality Probability Admission Model (MPM0-III). Crit Care Med 2007;35(3):827–835. DOI: 10.1097/01.CCM.0000257337.63529.9F.
4. Kulkarni AP, Zirpe KG, Dixit SB, Chaudhry D, Mehta Y, Mishra RC, et al. Development of critical care medicine in India. J Crit Care 2020;56:188–196. DOI: 10.1016/j.jcrc.2019.11.017.
5. Divatia JV, Amin PR, Ramakrishnan N, Kapadia FN, Todi S, Sahu S, et al. Intensive care in India: The Indian intensive care case mix and practice patterns study. Indian J Crit Care Med 2016;20(4):216–225. DOI: 10.4103/0972-5229.180042.
6. Divatia JV, Mehta Y, Govil D, Zirpe K, Amin PR, Ramakrishnan N, et al. Intensive Care in India in 2018–2019: The second Indian intensive care case mix and practice patterns study. Indian J Crit Care Med 2021;25(10):1093–1107. DOI: 10.5005/jp-journals-10071-23965.
7. Atkins D, Best D, Briss PA, Eccles M, Falck-Ytter Y, Flottorp S, et al. Grading quality of evidence and strength of recommendations. BMJ 2004;328(7454):1490. DOI: 10.1136/bmj.328.7454.1490.
8. Bonanno FG. Clinical pathology of the shock syndromes. J Emerg Trauma Shock 2011;4(2):233–243. DOI:10.4103/0974-2700.82211.
9. Schlichtig R, Kramer DJ, Pinsky MR. Flow redistribution during progressive hemorrhage is a determinant of critical O2 delivery. J Appl Physiol (1985) 1991;70(1):169–178. DOI: 10.1152/jappl.1991.70.1.169.
10. Joly HR, Weil MH. Temperature of the great toe as an indication of the severity of shock. Circulation 1969;39(1):131–138. DOI: 10.1161/01.cir.39.1.131.
11. Hernandez G, Pedreros C, Veas E, Bruhn A, Romero C, Rovegno M, et al. Evolution of peripheral vs metabolic perfusion parameters during septic shock resuscitation. A clinical-physiologic study. J Crit Care 2012;27(3):283–288. DOI: 10.1016/j.jcrc.2011.05.024.
12. Ait-Oufella H, Bige N, Boelle PY, Pichereau C, Alves M, Bertinchamp R. Capillary refill time exploration during septic shock. Intensive Care Med 2014;40(7):958–964. DOI: 10.1007/s00134-014-3326-4.
13. Lara B, Enberg L, Ortega M, Leon P, Kripper C, Aguilera P. Capillary refill time during fluid resuscitation in patients with sepsis-related hyperlactatemia at the emergency department is related to mortality. PLoS One 2017;12(11):e0188548. DOI: 10.1371/journal.pone.0188548.
14. Castro R, Kattan E, Ferri G, Pairumani R, Valenzuela ED, Alegría L, et al. Effects of capillary refill time-vs. lactate-targeted fluid resuscitation on regional, microcirculatory and hypoxia-related perfusion parameters in septic shock: A randomized controlled trial. Ann Intensive Care 2020;10(1):150. DOI: 10.1186/s13613-020-00767-4.
15. Hernández G, Ospina-Tascón GA, Damiani LP, Estenssoro E, Dubin A, Hurtado J, et al. Effect of a resuscitation strategy targeting peripheral perfusion status vs serum lactate levels on 28-day mortality among patients with septic shock: The ANDROMEDA-SHOCK randomized clinical trial. JAMA 2019;321(7):654–664. DOI: 10.1001/jama.2019.0071.
16. Sheridan DC, Cloutier RL, Samatham R, Hansen ML. Point-of-care capillary refill technology improves accuracy of peripheral perfusion assessment. Front Med (Lausanne) 2021;8:694241. DOI:10.3389/fmed.2021.694241.
17. Gofton TE, Young GB. Sepsis-associated encephalopathy. Nat Rev Neurol 2012;8(10):557–566. DOI: 10.1038/nrneurol.2012.183.
18. Kataja A, Tarvasmäki T, Lassus J, Køber L, Sionis A, Spinar A, et al. Altered mental status predicts mortality in cardiogenic shock–Results from the CardShock study. Eur Heart J Acute Cardiovasc Care 2018;7(1):38–44. DOI: 10.1177/2048872617702505.
19. Legrand M, Payen D. Understanding urine output in critically ill patients. Ann Intensive Care 2011;1(1):13. DOI:10.1186/2110-5820-1-13.
20. Vincent JL, Ferguson A, Pickkers P, Jakob SM, Jaschinski U, Almekhlafi GA, et al. The clinical relevance of oliguria in the critically ill patient: analysis of a large observational database. Crit Care 2020;24(1):171. DOI:10.1186/s13054-020-02858-x.
21. Ait-Oufella H, Lemoinne S, Boelle PY, Galbois A, Baudel JL, Lemant J, et al. Mottling score predicts survival in septic shock. Intensive Care Med 2011;37(5):801–807. DOI: 10.1007/s00134-011-2163-y.
22. Levy MM, Evans LE, Rhodes A. The surviving sepsis Campaign Bundle: 2018 update. Intensive Care Med. 2018;44(6):925–928.
23. Allen M. Lactate and acid base as a hemodynamic monitor and markers of cellular perfusion. Pediatr Crit Care Med 2011;12 (4 Suppl):S43–S49. DOI: 10.1097/PCC.0b013e3182211aed.
24. Greenwood JC, Orloski CJ. End points of sepsis resuscitation. Emerg Med Clin North Am 2017;35(1):93–107. DOI: 10.1016/j.emc.2016.09.001.
25. Broder G, Weil MH. Excess lactate: An index of reversibility of shock in human patients. Science 1964;143(3613):1457–1459. DOI: 10.1126/science.143.3613.1457.
26. Vincent JL, Dufaye P, Berré J, Leeman M, Degaute JP, Kahn RJ. Serial lactate determinations during circulatory shock. Crit Care Med 1983;11(6):449–451. DOI: 10.1097/00003246-198306000-00012.
27. Vincent JL, Quintairos E Silva A, Couto Jr L, Taccone FS. The value of blood lactate kinetics in critically ill patients: A systematic review. Crit Care 2016;20(1):257. DOI: 10.1186/s13054-016-1403-5.
28. Berend K. Diagnostic use of base excess in acid-base disorders. N Engl J Med 2018;378(15):1419–1428. DOI: 10.1056/NEJMra1711860.
29. Connelly CR, Schreiber MA. Endpoints in resuscitation. Curr Opin Crit Care 2015;21(6):512–519. DOI: 10.1097/MCC.0000000000000248.
30. Rivers E, Nguyen B, Havstad S, Ressler J, Muzzin A, Knoblich B, et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. N Engl J Med 2001;345(19):1368–1377. DOI: 10.1056/NEJMoa010307.
31. Angus DC, Barnato AE, Bell D, Bellomo R, Chong C-R, Coats TJ, et al. A systematic review and meta-analysis of early goal-directed therapy for septic shock: The ARISE, ProCESS and ProMISe Investigators. Intensive Care Med 2015;41(9):1549–1560. DOI: 10.1007/s00134-015-3822-1.
32. Cohn JN. Blood pressure measurement in shock: Mechanism of inaccuracy in auscultatory and palpatory methods. JAMA 1967;199(13):972–976. DOI:10.1001/jama.1967.03120130058009.
33. Meidert AS, Dolch ME, Mühlbauer K, Zwissler B, Klien M, Briegel J, et al. Oscillometric versus invasive blood pressure measurement in patients with shock: A prospective observational study in the emergency department. J Clin Monit Comput 2021;35(2):387–393. DOI: 10.1007/s10877-020-00482-2.
34. Varpula M, Tallgren M, Saukkonen K, Voipio-Pulkki L-M, Pettilä V. Hemodynamic variables related to outcome in septic shock. Intensive Care Med 2005;31(8):1066–1071. DOI: 10.1007/s00134-005-2688-z.
35. Dünser MW, Takala J, Ulmer H, Mayr VD, Luckner G, Jochberger S, et al. Arterial blood pressure during early sepsis and outcome. Intensive Care Med 2009;35(7):1225–1233. DOI: 10.1007/s00134-009-1427-2.
36. Dünser MW, Ruokonen E, Pettilä V, Ulmer H, Torgersen C, Schmittinger CA, et al. Association of arterial blood pressure and vasopressor load with septic shock mortality: A post hoc analysis of a multicenter trial. Crit Care 2009;13(6):R181. DOI: 10.1186/cc8167.
37. Asfar P, Meziani F, Hamel J-F, Grelon F, Megarbane B, Anguel N, et al. High versus low blood-pressure target in patients with septic shock. N Engl J Med 2014;370(17):1583–1593. DOI: 10.1056/NEJMoa1312173.
38. Lamontagne F, Meade MO, Hébert PC, Asfar P, Lauzier F, Seely AJE, et al. Canadian Critical Care Trials Group. Higher versus lower blood pressure targets for vasopressor therapy in shock: A multicentre pilot randomized controlled trial. Intensive Care Med2016;42(4):542–550. DOI: 10.1007/s00134-016-4237-3.

39. Andreis DT, Singer M. Catecholamines for inflammatory shock: A Jekyll-and-Hyde conundrum. Intensive Care Med 2016;42(9): 1387–1397. DOI: 10.1007/s00134-016-4249-z.
40. Lamontagne F, Day AG, Meade MO, Cook DJ, Guyatt GH, Hylands M, et al. Pooled analysis of higher versus lower blood pressure targets for vasopressor therapy septic and vasodilatory shock. Intensive Care Med 2018;44(1):12–21. DOI: 10.1007/s00134-017-5016-5.
41. De Backer D, Giglioli S. Echocardiographic approach to shock. J Emerg Crit Care Med 2019;3:35. DOI: 10.21037/jeccm.2019.07.06.
42. Cecconi M, De Backer D, Antonelli M, Beale R, Bakker J, Hofer C, et al. Consensus on circulatory shock and hemodynamic monitoring. Task force of the European Society of Intensive Care Medicine. Intensive Care Med 2014;40(12):1795–1815. DOI: 10.1007/s00134-014-3525-z.
43. Perera P, Mailhot T, Riley D, Mandavia D. The RUSH exam: Rapid Ultrasound in SHock in the evaluation of the critically ill. Emerg Med Clin North Am 2010;28(1):29–56, vii. DOI: 10.1016/j.emc.2009.09.010.
44. Rahulkumar HH, Bhavin PR, Shreyas KP, Krunalkumar HP, Atulkumar S, Bansari C. Utility of point-of-care ultrasound in differentiating causes of shock in resource-limited setup. J Emerg Trauma Shock 2019;12(1):10–17. DOI: 10.4103/JETS.JETS_61_18.
45. Keikha M, Salehi-Marzijarani M, Soldoozi Nejat R, Sheikh Motahar Vahedi H, Mirrezaie SM. Diagnostic accuracy of rapid ultrasound in shock (RUSH) exam: A systematic review and meta-analysis. Bull Emerg Trauma 2018;6(4):271–278. DOI: 10.29252/beat-060402.
46. Mekontso Dessap A, Proost O, Boissier F, Louis B, Roche Campo F, Brochard L. Transesophageal echocardiography in prone position during severe acute respiratory distress syndrome. Intensive Care Med 2011;37(3):430–434. DOI: 10.1007/s00134-010-2114-z.
47. Blaivas M. Transesophageal echocardiography during cardio-pulmonary arrest in the emergency department. Resuscitation 2008;78(2):135–140. DOI: 10.1016/j.resuscitation.2008.02.021.
48. Hartnell G, Costello P. The diagnosis of thoracic aortic dissection by noninvasive imaging procedures. N Engl J Med 1993;328(22):1637. DOI: 10.1056/NEJM199306033282213.
49. Vieillard-Baron A, Qanadli SD, Antakly Y, Fourme T, Loubières Y, Jardin F, et al. Transesophageal echocardiography for the diagnosis of pulmonary embolism with acute cor pulmonale: A comparison with radiological procedures. Intensive Care Med 1998;24(5):429–433. DOI: 10.1007/s001340050591.
50. Vignon P, Mentec H, Terré S, Gastinne H, Guéret P, Lemaire F. Diagnostic accuracy and therapeutic impact of transthoracic and transesophageal echocardiography in mechanically ventilated patients in the ICU. Chest 1994; 106(6):1829–1834. DOI: 10.1378/chest.106.6.1829.
51. Charron C, Vignon P, Prat G, Tonnelier A, Aegerter P, Boles J-M, et al. Number of supervised studies required to reach competence in advanced critical care transesophageal echocardiography. Intensive Care Med 2013;39(6):1019–1024. DOI: 10.1007/s00134-013-2838-7.
52. Hüttemann E, Schelenz C, Kara F, Chatzinikolaou K, Reinhart K. The use and safety of transoesophageal echocardiography in the general ICU–A minireview. Acta Anaesthesiol Scand 2004;48(7):827–836. DOI: 10.1111/j.0001-5172.2004.00423.x.
53. Cecconi M, Hofer C, Teboul J-L, Pettila V, Wilkman E, Molnar Z, et al. Fluid challenges in intensive care—the FENICE study: A global inception cohort study. Intensive Care Med 2015;41(9):1529–1537. DOI: 10.1007/s00134-015-3850-x.
54. 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(7):1774–1781. DOI: 10.1097/CCM.0b013e31828a25fd.
55. Osman D, Ridel C, Ray P, Monnet X, Anguel N, Richard C, et al. Cardiac filling pressures are not appropriate to predict hemodynamic response to volume challenge. Crit Care Med 2007;35(1):64–68. DOI: 10.1097/01.CCM.0000249851.94101.4F.
56. Michard F, Teboul JL. Predicting fluid responsiveness in ICU patients: A critical analysis of the evidence. Chest 2002;121(6):2000–2008. DOI: 10.1378/chest.121.6.2000.
57. Eskesen TG, Wetterslev M, Perner A. Systematic review including re-analyses of 1148 individual data sets of central venous pressure as a predictor of fluid responsiveness. Intensive Care Med 2016;42(3): 324–332. DOI: 10.1007/s00134-015-4168-4.
58. Chen H, Zhu Z, Zhao C, Guo H, Chen D, Wei Y, et al. Central venous pressure measurement is associated with improved outcomes in septic patients: an analysis of the MIMIC-III database. Crit Care 2020;24(1):433. DOI: 10.1186/s13054-020-03109-9.
59. Cecconi M, Parsons AK, Rhodes A. What is a fluid challenge? Curr Opin Crit Care 2011;17(3):290–295. DOI: 10.1097/MCC.0b013e32834699cd.
60. Aya HD, Rhodes A, Chis Ster I, Fletcher N, Grounds RM, Cecconi M. Hemodynamic effect of different doses of fluids for a fluid challenge: A quasi-randomized controlled study. Crit Care Med 2017;45(2): e161–e168. DOI: 10.1097/CCM.0000000000002067.
61. Muller L, Toumi M, Bousquet PJ, Riu-Poulenc B, Louart G, Candela D, et al. An increase in aortic blood flow after an infusion of 100 ml colloid over 1 minute can predict fluid responsiveness: The mini-fluid challenge study. Anesthesiology 2011;115(3):541–547. DOI: 10.1097/ALN.0b013e318229a500.
62. Shi R, Monnet X, Teboul J-L. Parameters of fluid responsiveness. Curr Opin Crit Care 2020;26(3):319–326. DOI: 10.1097/MCC.0000000000000723.
63. Myatra SN, Prabu NR, Divatia JV, Monnet X, Kulkarni AP, Teboul JL, et al. The changes in pulse pressure variation or stroke volume variation after a "Tidal Volume Challenge" reliably predict fluid responsiveness during low tidal volume ventilation. Crit Care Med 2017;45(3):415–421. DOI: 10.1097/CCM.0000000000002183.
64. Marik PE, Cavallazzi R, Vasu T, Hirani A. Dynamic changes in arterial waveform derived variables and fluid responsiveness in mechanically ventilated patients: A systematic review of the literature. Crit Care Med 2009;37(9):2642–2647. DOI: 10.1097/CCM.0b013e3181a590da.
65. Hong JQ, He HF, Chen ZY, Du ZS, Liu WF, Weng PQ, et al. Comparison of stroke volume variation with pulse pressure variation as a diagnostic indicator of fluid responsiveness in mechanically ventilated critically ill patients. Saudi Med J 2014;35(3):261–268. PMID: 24623206.
66. Yang X, Du B. Does pulse pressure variation predict fluid responsiveness in critically ill patients? A systematic review and meta-analysis. Crit Care 2014;18(6):650. DOI: 10.1186/s13054-014-0650-6.
67. Si X, Song X, Lin Q, Nie Y, Zhang G, Xu H, et al. Does end expiratory occlusion test predict fluid responsiveness in mechanically ventilated patients? A systematic review and meta-analysis. Shock 2020;54(6):751–760. DOI: 10.1097/SHK.0000000000001545.
68. Messina A, Dell'Anna A, Baggiani M, Torrini F, Maresca GM, Bennett V, et al. Functional hemodynamic tests: A systematic review and a meta-analysis on the reliability of the end-expiratory occlusion test and of the mini-fluid challenge in predicting fluid responsiveness. Crit Care 2019;23(1):264. DOI: 10.1186/s13054-019-2545-z.
69. Vignon P, Repessé X, Bégot E, Léger J, Jacob C, Bouferrache K, et al. Comparison of echocardiographic indices used to predict fluid responsiveness in ventilated patients. Am J Respir Crit Care Med 2017;195(8):1022–1032. DOI: 10.1164/rccm.201604-0844OC.
70. Das SK, Choupoo NS, Pradhan D, Saikia P, Monnet X. Diagnostic accuracy of inferior vena caval respiratory variation in detecting fluid unresponsiveness: A systematic review and meta-analysis. Eur J Anaesthesiol 2018; 35(11):831–839. DOI: 10.1097/EJA.0000000000000841.
71. Alvarado Sánchez JI, Caicedo Ruiz JD, Diaztagle Fernández JJ, Amaya Zuñiga WF, Ospina-Tascón GA, Cruz Martínez LE. Predictors of fluid responsiveness in critically ill patients mechanically ventilated at low tidal volumes: Systematic review and meta-analysis. Ann Intensive Care 2021;11(1):28. DOI: 10.1186/s13613-021-00817-5.
72. Iqbal MA, Gupta M. Cardiogenic pulmonary edema. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2021.
73. Lee WL, Slutsky AS. Sepsis and endothelial permeability. N Engl J Med 2010;363(7):689–691. DOI: 10.1056/NEJMcibr1007320.
74. Michard F, Alaya S, Zarka V, Bahloul M, Richard C, Teboul JL. Global end-diastolic volume as an indicator of cardiac preload in patients

with septic shock. Chest 2003;124(5):1900–1908. DOI: 10.1378/chest.124.5.1900.
75. Michard F. Bedside assessment of extravascular lung water by dilution methods: Temptations and pitfalls. Crit Care Med 2007;35(4):1186–1192. DOI: 10.1097/01.CCM.0000259539.49339.66.
76. Chew MS, Ihrman L, During J, Bergenzaun L, Ersson A, Undén J, et al. Extravascular lung water index improves the diagnostic accuracy of lung injury in patients with shock. Crit Care 2012;16(1):R1. DOI: 10.1186/cc10599.
77. Zhang Z, Lu B, Ni H. Prognostic value of extravascular lung water index in critically ill patients: A systematic review of the literature. J Crit Care 2012;27(4):420.e1–420.e8. DOI: 10.1016/j.jcrc.2011.09.006.
78. Kushimoto S, Taira Y, Kitazawa Y, Okuchi K, Sakamoto T, Ishikura H, et al. The clinical usefulness of extravascular lung water and pulmonary vascular permeability index to diagnose and characterize pulmonary edema: A prospective multicenter study on the quantitative differential diagnostic definition for acute lung injury/acute respiratory distress syndrome. Crit Care 2012;16(6):R232. DOI: 10.1186/cc11898.
79. Mayr U, Lukas M, Habenicht L, Wiessner J, Heilmaier M, Ulrich J, et al. B-lines scores derived from lung ultrasound provide accurate prediction of extravascular lung water index: An observational study in critically ill patients. J Intensive Care Med 2022;37(1):21–31. DOI:10.1177/0885066620967655.
80. Monnet X, Anguel N, Osman D, Hamzaoui O, Richard C, Teboul JL. Assessing pulmonary permeability by transpulmonary thermodilution allows differentiation of hydrostatic pulmonary edema from ALI/ARDS. Intensive Care Med 2007;33(3):448–453. DOI: 10.1007/s00134-006-0498-6.
81. Schefold JC, Storm C, Bercker S, Pschowski R, Oppert M, Krüger A, et al. Inferior vena cava diameter correlates with invasive hemodynamic measures in mechanically ventilated intensive care unit patients with sepsis. J Emerg Med 2010;38(5):632–637. DOI: 10.1016/j.jemermed.2007.11.027.
82. Frassi F, Gargani L, Gligorova S, Ciampi Q, Mottola G, Picano E. Clinical and echocardiographic determinants of ultrasound lung comets. Eur J Echocardiogr 2007;8(6):474–479. DOI: 10.1016/j.euje.2006.09.004.
83. Updaw R, Passmore L, Mitten-Long D, Pierce C, Ross A, Wells G, et al. Fluid resuscitation volume for septic shock patients was not decreased for echocardiogram-determined left ventricular (LV) systolic dysfunction patients when managed with early goal-directed therapy (EGDT). Chest 2007;132(4). DOI: 10.1378/chest.132.4_meetingabstracts.
84. Mercat A, Diehl JL, Meyer G, Teboul JL, Sors H. Hemodynamic effects of fluid loading in acute massive pulmonary embolism. Crit Care Med 1999;27(3):540–544. DOI: 10.1097/00003246-199903000-00032.
85. Srivastava PM, Burrell LM, Calafiore P. Lateral vs medial mitral annular tissue Doppler in the echocardiographic assessment of diastolic function and filling pressures: which should we use? Eur J Echocardiogr 2005;6(2):97–106. DOI: 10.1016/j.euje.2004.07.005.
86. Takayama Y, Iwasaka T, Sugiura T, Sumimoto T, Takeuchi M, Tsuji H, et al. Increased extravascular lung water in patients with low pulmonary artery occlusion pressure after acute myocardial infarction. Crit Care Med 1991;19(1):21–25. DOI: 10.1097/00003246-199101000-00009.
87. Staub NC. Pulmonary edema: Physiologic approaches to management. Chest 1978;74(5):559–564. DOI: 10.1378/chest.74.5.559.
88. Kouz K, Bergholz A, Timmermann LM, et al. The relation between mean arterial pressure and cardiac index in major abdominal surgery patients: A prospective observational cohort study. Anesth Analg 2022;134(2):322–329. DOI: 10.1213/ANE.0000000000005805.
89. Garan AR, Kanwar M, Thayer KL, Whitehead E, Zweck E, Hernandez-Montfort J, et al. Complete hemodynamic profiling with pulmonary artery catheters in cardiogenic shock is associated with lower in-hospital mortality. JACC Heart Fail 2020;8(11):903–913. DOI: 10.1016/j.jchf.2020.08.012.
90. Osman M, Syed M, Patel B, Munir MB, Kheiri B, Caccamo M, et al. Invasive hemodynamic monitoring in cardiogenic shock is associated with lower in-hospital mortality. J Am Heart Assoc 2021;10(18):e021808. DOI: 10.1161/JAHA.121.021808.
91. Pan P, Su LX, Zhou X, Long Y, Liu DW, Wang XT. Critical hemodynamic therapy oriented resuscitation helping reduce lung water production and improve survival. Chin Med J (Engl) 2019;132(10):1139–1146. DOI:10.1097/CM9.0000000000000205.
92. Ince C, Boerma EC, Cecconi M, Backer DD, Shapiro NI, Duranteau J, et al. Second consensus on the assessment of sublingual microcirculation in critically ill patients: Results from a task force of the European Society of Intensive Care Medicine. Intensive Care Med 2018;44(3):281–299. DOI: 10.1007/s00134-018-5070-7.
93. De Backer D, Bakker J, Cecconi M, Hajjar L, Liu DW, Lobo S, et al. Alternatives to the Swan-Ganz catheter. Intensive Care Med 2018;44(6):730–741. DOI: 10.1007/s00134-018-5187-8.