CHAPTER 4

Hemodynamic Support in the Critically Ill Patient

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OBJECTIVES

This chapter will:

1. Illustrate the general principles of pharmacologic and mechanical hemodynamic support.
2. Review the recent literature dealing with hemodynamic monitoring.
3. Provide some practical suggestions on bedside management of circulatory support.

Circulatory shock is a leading cause of tissue hypoperfusion and multiple organ dysfunction in critically ill patients admitted in intensive care units (ICUs)[1] with an associated mortality rate up to 40%.[2–6] Although circulatory shock commonly is classified into four main categories (i.e., hypovolemic, cardiogenic, obstructive, and distributive), their combination usually is observed in many clinical conditions (e.g., sepsis, right and left ventricular failure, hemorrhage).[7] Because early intervention is crucial for successful treatment of shocked patients, early diagnosis and reliable utilization of available resources are paramount to prevent the worsening of organ function and to improve outcome.[8,9] Essentially, appropriate cardiovascular support is required when circulatory shock occurs to limit cellular hypoxia by increasing the oxygen delivery (DO_2) (e.g., with volume resuscitation, transfusion, vasoconstriction, or oxygenation). From a pathophysiologic point of view, the amount of oxygen actually available depends on "central" and "peripheral" factors. Cardiorespiratory function and hemoglobin concentration are central factors for the DO_2 determinants, whereas the microcirculation regulation and redistribution of cardiac output (CO) to tissues (depending on autonomic control of vascular tone and local microvascular responses) constitute the peripheral side.[10] The optimization of the different components involved in cellular oxygenation (blood flow, perfusion pressure, and arterial oxygen content) requires accurate monitoring and represents the target for pharmacologic and mechanical hemodynamic support therapies in critically ill patients with shock.[8,9]

HEMODYNAMIC MONITORING

Hemodynamic monitoring is a cornerstone in the care of critically ill patients with shock. It allows physicians to identify the pathophysiologic mechanisms sustaining shock, to target therapy delivery on the pathogenesis of the disease, and to evaluate the effects of treatments over time.[11] Coupled with clinical evaluation, hemodynamic monitoring is helpful

to guide the administration of fluids, to titrate the dose of vasoactive drugs, and to potentially indicate, in a timely fashion, when to start a mechanical support.[12] Preload, afterload, and contractility can be evaluated with a number of hemodynamic monitoring tools that differ in invasiveness, technology, advantages, and limitations.[13]

Preload is the major determinant of CO, and fluid loading is usually the first-line intervention in shocked patients. Nonetheless, only half of critically ill patients respond to fluids with an increase in CO (fluid responders; increase in CO by 15%), whereas in the other half, fluid administration is likely to be harmful.[14] To avoid the negative effects of fluid administration in non–fluid responders, fluid responsiveness should be assessed before volume load.[15–17] A consistent degree of uncertainty is related with use of clinical signs, such as tachycardia and hypotension, and static variables, such as central venous pressure and echocardiographic volumes and areas,[13] which have been demonstrated to be reliable predictors of fluid responsiveness only in specific circumstances.[18] On the other hand, ventilator-induced dynamic variables, such as stroke volume variation (SVV), pulse pressure variation (PPV), and plethysmography, have been demonstrated as much more accurate predictors of fluid responsiveness in routine clinical practice.[14] Finally, although highly questioned in the last decade because of its invasiveness, the pulmonary artery catheter (PAC) may provide crucial information, such as pulmonary artery pressures, left-sided filling pressures, and mixed venous oxygen saturation in some specific clinical conditions.[13] Moreover, the PAC still represents the clinical gold standard for CO estimation.[13]

Evolution in technology has introduced into the clinical practice easier, less invasive, and more rapid systems for CO estimation.[19] Among them, pulse contour methods are minimally invasive systems that analyze the arterial pressure waveform from an indwelling arterial catheter and allow the estimation of the patient's stroke volume (SV) and CO.[13] In addition, these devices also may deliver parameters of cardiac function, such as compliance, resistance, or impedance of the cardiovascular tree.[13] Controversy exists regarding the clinical reliability and accuracy of these systems.[19] Echocardiography currently is performed reliably at the bedside and may provide morphologic information and Doppler-based estimations of SV and CO, although not continuously.[9] In combination with the available hemodynamic monitoring tools (invasive, minimally invasive, and noninvasive), the echocardiographic assessment of cardiac function currently is considered central for the correct diagnosis of hemodynamic instability and management of these patients.[9,13]

The hemodynamic monitoring systems have their own advantages and limitations,[13] and selection of the most appropriate system depends on the individual patient, on the device, and on the local expertise available at each institution.[19]

PHARMACOLOGIC CARDIOVASCULAR SUPPORT

A personalized pharmacologic treatment with fluids and vasoactive/inotropic drugs, guided by appropriate monitoring, is crucial in the management of hemodynamic instability. Many drugs administered to critically ill patients have cardiac and vascular effects depending on the dose and on density and distribution of their target receptors.[20] Among them, catecholamines are the most used and recommended in patients with shock.[20] Table 4.1 summarizes the relative potency of the cardiac and peripheral vascular effects of several agents. This distinction is useful to define targets and end points of the treatment, although norepinephrine, well balanced in inotropic and vasoconstrictor effects, represents the most commonly administered drug in hypotensive critically ill patients.[20]

Avoiding and treating arterial hypotension are major targets in patients with hemodynamic instability.[20] Vasopressors usually are recommended even before the diagnostic process is concluded,[20–22] because arterial pressure usually is considered the main end point for vasopressor therapy. As a matter of fact, the achievement of the most effective tissue perfusion does not necessarily equal the restoration of "normal" arterial pressure,[20] and it may be recommended to also titrate vasopressor administration according to different clinical variables, including, among the others, CO, urine output, lactate concentrations, and mixed venous blood saturation.

Adrenergic and nonadrenergic molecules modulate vascular tone.[7] Catecholamines with predominant vasopressor effects mainly activate α-adrenergic receptors, whose expression differs within the cardiovascular system (e.g., minimal in capillaries and progressively increased toward arterioles and venules) and across regional vascular beds (e.g., between mesenteric and skeletal muscle bed).[23] Norepinephrine is the most used catecholamine during shock, followed by dopamine and epinephrine given alone

TABLE 4.1

Vasoactive and/or Inotropic/Chronotropic Effects of the Most Used Drugs

			HEART RATE	CONTRACTILITY	VASOCONSTRICTION
Ca^{2+} sens.		Levosimendan	+	+++	0
PDEI		Enoximone	+	+++	0
		Amrinone	+	+++	0
		Milrinone	+	+++	0
Catecholamine	β	Dobutamine	++	++++++	0
		Dopamine	+/++	+/+++++	+++++
		Epinephrine	+++	++++	++++
	α	Norepinephrine	+	++	+++
		Phenylephrine	0	0	+++
		Vasopressin	0	0	+++++
		Terlipressin	0	0	+++++

The chronotropic, inotropic and vasoactive effects are proportionally expressed for the different agents in terms of no effect (0), weak (+) or strong effect (++/+++).
Ca^{2+} sens, calcium sensitizer; *PDEI,* inhibitors of phosphodiesterase type III.

or in combination.[3] Although several studies failed to demonstrate differences in mortality rate of patients treated with different vasopressors,[7] the most recent guidelines on distributive (septic) and cardiogenic shock suggest using norepinephrine as first choice to reestablish an adequate perfusion pressure.[21,22] Beyond catecholamines, other endogenous noncatecholaminergic hormones have been used largely in clinical practice. In particular, vasopressin (physiologically released in response to osmotic, chemoreceptor, and baroreceptor stimuli) acts on vascular smooth muscle V1 and oxytocin receptors, causing vasoconstriction.[23,24] Terlipressin is a prodrug slowly degraded by liver and kidney peptidases to lysine vasopressin, conferring a significantly longer duration of action after intravenous (IV) bolus than vasopressin. Terlipressin has a greater selectivity for vascular V1 receptors. In septic shock, the administration of exogenous vasopressin (0.01–0.04 $U \cdot min^{-1}$) results in the reversal of vasodilatory shock, mainly because of reversal of a relative deficiency of the hormone seen in established sepsis.[23] Furthermore, V1 and α1-adrenoceptor crosstalk, the amelioration of autonomic dysfunction, the increase of other endogenous vasoconstrictors, and a potential effect on nitric oxide and glucocorticoid production also may contribute to the improvement of catecholamines' effects and the reversal of vasodilatation.[23]

Inotropic therapy is administered when myocardial contractility is impaired[20] in condition of cardiogenic shock (e.g., myocardial infarction) or combined forms of distributive-cardiogenic shock (e.g., sepsis).[25] Inotropes can be divided into catecholaminergic and noncatecholaminergic agents. Norepinephrine, showing a well-balanced α1-β1 effect, and epinephrine, predominant inotropic β1 affinity, belong to the first category (catecholamines): β-receptors stimulation results in significant chronotropic and inotropic activity eventually causing CO, heart rate (HR), mean arterial pressure, and coronary blood flow to increase.[23] Although less pronounced than β-adrenoceptor, cardiac dopaminergic receptors mostly show inotropic effects; accordingly, dopamine is considered a predominant inotropic agent. Furthermore, beyond this effect, medium doses of dopamine (5–15 $mcg \cdot kg \cdot min^{-1}$) are associated with β-adrenoceptor stimulation, leading to a further increase in CO and HR.[23] Finally, dobutamine is a synthetic catecholamine with β-adrenoceptor effects (with a 3:1 ratio to β1 and β2 adrenoceptors) and a mild α1-adrenoceptor affinity at higher doses.[23] According to its pharmacologic characteristics, dobutamine is used widely in the short-term treatment of severe heart failure and cardiogenic shock.[22,23] Principal side effects of catecholamines include increase of myocardial oxygen consumption and arrhythmias. Inotropic noncatecholaminergic drugs include the inhibitors of phosphodiesterase type 3 (PDEI) and the calcium sensitizer levosimendan. Amrinone, milrinone, and enoximone are PDEI, which enhance cyclic adenosine monophosphate (cAMP) and protein kinase A (PKA) levels through non–receptor-dependent mechanisms and increase inotropy, chronotropy, and lusitropy while decreasing preload and afterload.[23] These agents are potent pulmonary vasodilators and are considered particularly useful in the treatment of acute severe right heart failure and pulmonary hypertension.[23] Finally, levosimendan is a calcium sensitizer, and it is the only inotrope that does not increase the intracellular myocardial cAMP levels at clinically recommended doses.[23] In particular, unlike other inotropes, levosimendan does not exert its action through potentially harmful increases in intracellular Ca^{2+}. This may explain why this agent does not impair diastolic relaxation and cardiac rhythm and it is considered to optimize myocardial energetics.[23] Levosimendan binds to the N-terminal of troponin C with high affinity and prolongs the interaction of myosin and actin filaments through inhibition of troponin I.[23] Importantly, the levosimendan metabolite OR-1896 has similar calcium-sensitizing actions to the parent molecule, maintaining the inotropic effect of levosimendan for several days once the infusion is stopped.[23] The cardiovascular effects of levosimendan include increase in HR when high doses of loading and infusion are used, possibly via baroreceptor-mediated pathways. In vascular tissue, levosimendan acts as a vasodilator by decreasing the sensitivity of myofilaments to Ca^{2+} and activating K^+ channels. This results in hyperpolarization, decreased Ca^{2+} entry, and vasodilatation.[23]

NONPHARMACOLOGIC CARDIOVASCULAR SUPPORT

When pharmacologic vasoactive and inotropic therapy, even at maximal doses, is insufficient to prevent tissue hypoxia and organ damage, or patients are becoming refractory to ongoing drug administration because of prolonged illness, mechanical circulatory support (MCS) can be considered. Different tools are now available, and the selection of the most appropriate device depends on the supposed duration of the support, the nature of cardiocirculatory dysfunction, and the acuity of presentation. MCS encompasses a spectrum of devices aimed to partially or completely replace cardiac function temporarily or for long-term application. Temporary MCS refers to devices generally used for less than 30 days and includes the intraaortic balloon pump (IABP), the venous-arterial extracorporeal oxygenation (VA-ECMO), the Impella (Abiomed Inc., Danvers, MA) the TandemHeart, the CentriMag (CardiacAssist, Pittsburg, PA), the Thoratec (pVAD) (Thoratec Corporation, Pleasanton, CA), and the Abiomed BVS 5000 (Abiomed Inc., Danvers, MA). The long-term MCS, also known as a ventricular-assist device (VAD), is a system dedicated to patients with end-stage heart failure as a bridge to transplantation or as a destination therapy.

Temporary Mechanical Circulatory Support

The IABP is the most widely used and the most inexpensive form of cardiac mechanical support. It consists of an 8- to 9-French (Fr) inflatable balloon catheter, typically placed through the femoral artery, in the descendent thoracic aorta distal to the left subclavian artery. It is connected to a console that delivers helium to inflate the balloon during the diastolic phase of the cardiac cycle (synchronized with the electrocardiogram or the arterial pressure waveform). The balloon inflation increases the diastolic pressure by obstructing the lumen of the descending aorta, with the main target of increasing the coronary blood flow. After the diastolic phase, the presystolic deflation reduces left ventricular afterload by means of a vacuum effect, thus reducing myocardial oxygen consumption. IABP, by increasing mean arterial pressure, may improve global systemic perfusion especially in conditions of cardiogenic shock.[26] IABP is suggested strongly during mechanical complications of acute myocardial infarction as a bridge to definitive surgical management,[27,28] and it has been used in many conditions of hemodynamic instability (e.g., acute severe mitral regurgitation or as prophylactic measure during and after percutaneous coronary intervention and coronary artery

bypass graft surgery[29]). Nevertheless, some concerns over its efficacy have emerged from recent randomized controlled trials and meta-analyses,[30–36] leading to a downgrading of its recommendation in the most recent guidelines on cardiogenic shock.[27,28] General contraindications for IABP use are moderate to severe aortic insufficiency, which may worsen with the increase in diastolic pressure, aortic dissection, and abdominal aortic aneurysm.[37] Interestingly, in a recent meta-analysis including 2539 patients, Wang et al. studied the role of preoperative prophylactic IABP on postoperative AKI, hospital and 30-day mortality. These authors concluded that the beneficial hemodynamic effects of IABP may improve perfusion of vital organs, such as the kidney, the brain, and the lungs, consequently reducing postoperative mortality and AKI incidence.[38]

VA-ECMO is an artificial extracorporeal therapy that consists of a specific heart-lung machine aimed at providing temporary respiratory and/or circulatory support. Its use has increased dramatically over the few last years for the treatment of potentially reversible cardiac or cardiorespiratory failure.[39] Because of its particular field of application, no randomized trials using VA-ECMO currently exist, but a recent meta-analysis including 1866 patients receiving ECMO for treatment of cardiogenic shock and cardiac arrest showed a rate of survival to hospital discharge between 20.8% and 65.4%.[40] VA-ECMO is probably recommended for the treatment for myocarditis, refractory arrhythmias, after heart or lung transplantation, and age less than 63 years.[41]

The Impella is a percutaneously inserted, miniaturized MCS, driving a continuous flow through an axial pump contained in a pigtail catheter, placed via the femoral artery. With the Impella the blood is pumped from the left ventricle into the ascending aorta at a rate of 2.5 to 5.0 L/min. The Impella RP has been manufactured recently for right-sided support by drawing blood from the inferior vena cava and pumping it into the pulmonary artery.[37,42] The TandemHeart system is an extracorporeal, centrifugal, continuous flow pump, which can be used for left, right, and biventricular failure. Blood is drained from the left atrium by a percutaneously inserted catheter, and it is pumped into the femoral artery, bypassing, and therefore unloading, the left ventricle (2.5–5 L/min) that works in parallel with the device. If right ventricular has to be supported, the inflow cannula is placed in the right atrium while the outflow one is placed in the pulmonary artery.[37,43] Other short-term MCS can be placed via a sternotomy instead of from a peripheral percutaneous access. Among them CentriMag (Thoratec Corp, Pleasanton CA, USA), the Thoratec (pVAD) (Thoratec, Pleasanton, CA), and the Abiomed BVS 5000 (ABIOMED Inc, USA) are the most commonly used systems. The CentriMag is a centrifugal, continuous-flow extracorporeal pump and is one of the most commonly implanted devices via sternotomy.[37,44] Depending on the configuration, it can provide left, right, or biventricular support.[37,45] Thoratec pVAD and Abiomed BVS 5000 are external, pulsatile, pneumatically driven pumps that are implanted surgically for left and right or biventricular support that are placed surgically for bridge-to-transplantation or bridge-to-recovery and postcardiotomy recovery.[37,46]

Long-Term Mechanical Circulatory Support

Impressive advances in technology have changed the landscape of how end-stage heart failure is treated. Novel devices can be implanted for long-term ventricular assistance into the thorax, generally powered by a small external battery connected to the device via a tunneled driveline. Different indications for long-term VAD implantation can be considered: (1) bridge-to-transplantation for patients actively listed at the time of VAD implantation because of limited donor availability; (2) bridge to candidacy: VAD implanted to clarify or improve an aspect of patients' candidacy before transplantation (e.g., pulmonary hypertension, weight loss, improvement in organ function); (3) bridge to recovery: it is an uncommon strategy in which short-term (<30 days) MCS usually are implanted; (4) destination therapy for patients not considered candidates for cardiac transplantation.

CONCLUSION

Shock frequently is observed in the ICU and is characterized by a high mortality rate. An appropriate hemodynamic monitoring is quintessential to identify the pathophysiologic mechanisms sustaining shock and to guide treatments. Pharmacologic treatments may be personalized to the specific patient's needs. Nevertheless, norepinephrine represents the most recommended drug for hypotensive patients suggested in recent guidelines.[21,22] When pharmacologic therapy is insufficient to restore a sufficient hemodynamic status that prevents further tissue hypoxia and organ damage, mechanical circulatory support may be considered for shocked patients.

Key Points

1. A timely diagnosis and an appropriate treatment are crucial to prevent the worsening of organ function and improving outcome in patients with shock.
2. Hemodynamic monitoring allows the identification of pathophysiologic mechanisms sustaining shock, the delivery of pathogenesis-targeted therapy, and the evaluation of treatment during time.
3. The optimal monitoring system depends on the individual patient, on device, and on local expertise available at the institution.
4. A personalized pharmacologic treatment with fluids and vasoactive/inotropic drugs, guided by monitoring and pathophysiology, is crucial in the management of hemodynamic instability.
5. Norepinephrine, well balanced in inotropic and vasoconstrictor effects, represents the most recommended drug in hypotensive patients.
6. When the standard drug therapy is insufficient to prevent tissue hypoxia and organ damage, mechanical circulatory support can be considered.

Key References

7. Gamper G, Havel C, Arrich J, et al. Vasopressors for hypotensive shock. *Cochrane Database Syst Rev*. 2016;(2):CD003709.
9. 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.
14. Marik PE, Cavallazzi R, Vasu T, et al. Dynamic changes in arterial waveform derived variables and fluid responsiveness

in mechanically ventilated patients: a systematic review of the literature. *Crit Care Med*. 2009;37:2642.
24. Gordon AC, Mason AJ, Thirunavukkarasu N, et al. Effect of Early Vasopressin vs Norepinephrine on Kidney Failure in Patients With Septic Shock: The VANISH Randomized Clinical Trial. *JAMA*. 2016;316:509.
37. Saffarzadeh A, Bonde P. Options for temporary mechanical circulatory support. *J Thorac Dis*. 2015;7:2102.

A complete reference list can be found online at ExpertConsult.com.

References

1. Poeze M, Greve JWM, Ramsay G. Meta-analysis of hemodynamic optimization: relationship to methodological quality. *Crit Care*. 2005;9:R771.
2. Esteban A, Frutos-Vivar F, Ferguson ND, et al. Sepsis incidence and outcome: contrasting the intensive care unit with the hospital ward. *Crit Care Med*. 2007;35:1284.
3. 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.
4. Alberti C, Brun-Buisson C, Chevret S, et al. Systemic inflammatory response and progression to severe sepsis in critically ill infected patients. *Am J Respir Crit Care Med*. 2005;171:461.
5. Cannon CM, Braxton CC, Kling-Smith M, et al. Utility of the shock index in predicting mortality in traumatically injured patients. *J Trauma*. 2009;67:1426.
6. Babaev A, Frederick PD, Pasta DJ, et al. Trends in management and outcomes of patients with acute myocardial infarction complicated by cardiogenic shock. *JAMA*. 2005;294:448.
7. Gamper G, Havel C, Arrich J, et al. Vasopressors for hypotensive shock. *Cochrane Database Syst Rev*. 2016;(2):CD003709.
8. Lemson J, Nusmeier A, van der Hoeven JG. Advanced hemodynamic monitoring in critically ill children. *Pediatrics*. 2011; 128:560.
9. 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.
10. Vincent JL, De Backer D. Oxygen transport-the oxygen delivery controversy. *Intensive Care Med*. 2009;409.
11. Pinsky MR. Hemodynamic evaluation and monitoring in the ICU. *Chest*. 2007;132:2020.
12. Hayes MA, Timmins AC, Yau EH, et al. Elevation of systemic oxygen delivery in the treatment of critically ill patients. *N Engl J Med*. 1994;330:1717.
13. Vincent J-L, Pelosi P, Pearse R, et al. Perioperative cardiovascular monitoring of high-risk patients: a consensus of 12. *Crit Care*. 2015;19:224.
14. Marik PE, Cavallazzi R, Vasu T, et al. Dynamic changes in arterial waveform derived variables and fluid responsiveness in mechanically ventilated patients: a systematic review of the literature. *Crit Care Med*. 2009;37:2642.
15. Cecconi M, Parsons AK, Rhodes A. What is a fluid challenge? *Curr Opin Crit Care*. 2011;17:290.
16. Weil MH, Henning RJ. New concepts in the diagnosis and fluid treatment of circulatory shock. Thirteenth annual Becton, Dickinson and Company Oscar Schwidetsky Memorial Lecture. *Anesth Analg*. 1979;58:124.
17. Vincent J-L, Weil MH. Fluid challenge revisited. *Crit Care Med*. 2006;34:1333.
18. Marik PE, Baram M, Vahid B. Does central venous pressure predict fluid responsiveness? A systematic review of the literature and the tale of seven mares. *Chest*. 2008;134:172.
19. Vincent JL, Rhodes A, Perel A, et al. Clinical review: Update on hemodynamic monitoring - a consensus of 16. *Crit Care*. 2011;15:229.
20. Hollenberg SM. Vasoactive drugs in circulatory shock. *Am J Respir Crit Care Med*. 2011;183:847.
21. Dellinger RP, Levy MM, Rhodes A, et al. Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock, 2012. *Intensive Care Med*. 2013;39:165.
22. Ponikowski P, Voors AA, Anker SD, et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). Developed with the special contribution. *Eur J Heart Fail*. 2016;18:891.
23. Bangash MN, Kong ML, Pearse RM. Use of inotropes and vasopressor agents in critically ill patients. *Br J Pharmacol*. 2012;165:2015.
24. Gordon AC, Mason AJ, Thirunavukkarasu N, et al. Effect of Early Vasopressin vs Norepinephrine on Kidney Failure in Patients With Septic Shock: The VANISH Randomized Clinical Trial. *JAMA*. 2016;316:509.
25. Pierrakos C, Velissaris D, Scolletta S, et al. Can changes in arterial pressure be used to detect changes in cardiac index during fluid challenge in patients with septic shock? *Intensive Care Med*. 2012;38:422.
26. Williams DO, Korr KS, Gewirtz H, et al. The effect of intraaortic balloon counterpulsation on regional myocardial blood flow and oxygen consumption in the presence of coronary artery stenosis in patients with unstable angina. *Circulation*. 1982;66:593.
27. O'Gara PT, Kushner FG, Ascheim DD, et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarctiona report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2013;61:e78.
28. Steg PG, James SK, Atar D, et al. ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. *Eur Heart J*. 2012;33:2569.
29. Ihdayhid AR, Chopra S, Rankin J. Intra-aortic balloon pump: indications, efficacy, guidelines and future directions. *Curr Opin Cardiol*. 2014;29:285.
30. Keeley EC, Boura JA, Grines CL. Primary angioplasty versus intravenous thrombolytic therapy for acute myocardial infarction: a quantitative review of 23 randomised trials. *Lancet*. 2003;361:13.
31. Patel MR, Smalling RW, Thiele H, et al. Intra-aortic balloon counterpulsation and infarct size in patients with acute anterior myocardial infarction without shock: the CRISP AMI randomized trial. *JAMA*. 2011;306:1329.
32. Cassese S, de Waha A, Ndrepepa G, et al. Intra-aortic balloon counterpulsation in patients with acute myocardial infarction without cardiogenic shock. A meta-analysis of randomized trials. *Am Heart J*. 2012;164:58.
33. Bahekar A, Singh M, Singh S, et al. Cardiovascular outcomes using intra-aortic balloon pump in high-risk acute myocardial infarction with or without cardiogenic shock: a meta-analysis. *J Cardiovasc Pharmacol Ther*. 2012;17:44.
34. Goldberg RJ, Spencer FA, Gore JM, et al. Thirty-year trends (1975 to 2005) in the magnitude of, management of, and hospital death rates associated with cardiogenic shock in patients with acute myocardial infarction: a population-based perspective. *Circulation*. 2009;119:1211.
35. Zeymer U, Hochadel M, Hauptmann K-E, et al. Intra-aortic balloon pump in patients with acute myocardial infarction complicated by cardiogenic shock: results of the ALKK-PCI registry. *Clin Res Cardiol*. 2013;102:223.
36. Thiele H, Zeymer U, Neumann F-J, et al. Intra-aortic balloon counterpulsation in acute myocardial infarction complicated by cardiogenic shock (IABP-SHOCK II): final 12 month results of a randomised, open-label trial. *Lancet (London, England)*. 2013;382:1638.
37. Saffarzadeh A, Bonde P. Options for temporary mechanical circulatory support. *J Thorac Dis*. 2015;7:2102.
38. Wang J, Yu W, Gao M, et al. Preoperative Prophylactic Intraaortic Balloon Pump Reduces the Incidence of Postoperative Acute Kidney Injury and Short-Term Death of High-Risk Patients Undergoing Coronary Artery Bypass Grafting: A Meta-Analysis of 17 Studies. *Ann Thorac Surg*. 2016;101:2007.
39. Sauer CM, Yuh DD, Bonde P. Extracorporeal membrane oxygenation use has increased by 433% in adults in the United States from 2006 to 2011. *ASAIO J*. 2015;61:31.
40. Cheng R, Hachamovitch R, Kittleson M, et al. Complications of extracorporeal membrane oxygenation for treatment of cardiogenic shock and cardiac arrest: a meta-analysis of 1,866 adult patients. *Ann Thorac Surg*. 2014;97:610.
41. Schmidt M, Burrell A, Roberts L, et al. Predicting survival after ECMO for refractory cardiogenic shock: the survival after veno-arterial-ECMO (SAVE)-score. *Eur Heart J*. 2015;36:2246.
42. O'Neill WW, Kleiman NS, Moses J, et al. A prospective, randomized clinical trial of hemodynamic support with Impella 2.5 versus intra-aortic balloon pump in patients undergoing high-risk percutaneous coronary intervention: the PROTECT II study. *Circulation*. 2012;126:1717.
43. Burkhoff D, Cohen H, Brunckhorst C, et al. A randomized multicenter clinical study to evaluate the safety and efficacy of the TandemHeart percutaneous ventricular assist device versus conventional therapy with intraaortic balloon pumping for treatment of cardiogenic shock. *Am Heart J*. 2006;152:469.

44. Borisenko O, Wylie G, Payne J, et al. Thoratec CentriMag for temporary treatment of refractory cardiogenic shock or severe cardiopulmonary insufficiency: a systematic literature review and meta-analysis of observational studies. *ASAIO J*. 2014;60:487.
45. Mohite PN, Zych B, Popov AF, et al. CentriMag short-term ventricular assist as a bridge to solution in patients with advanced heart failure: use beyond 30 days. *Eur J Cardiothorac Surg*. 2013;44:e310.
46. Hsu P-L, Parker J, Egger C, et al. Mechanical circulatory support for right heart failure: current technology and future outlook. *Artif Organs*. 2012;36:332.