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Review

Septic cardiomyopathy: Diagnosis and management☆

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ABSTRACT

There is an extensive body of literature focused on sepsis-induced myocardial dysfunction, but results are conflicting and no objective definition of septic cardiomyopathy (SCM) has been established. SCM may be defined as a sepsis-associated acute syndrome of non-ischemic cardiac dysfunction with systolic and/or diastolic left ventricular (LV) dysfunction and/or right ventricular dysfunction. Physicians should consider this diagnosis in patients with sepsis-associated organ dysfunction, and particularly in cases of septic shock that require vasopressors. Echocardiography is currently the gold standard for diagnosis of SCM. Left ventricular ejection fraction is the most common parameter used to describe LV function in the literature, but its dependence on loading conditions, particularly afterload, limits its use as a measure of intrinsic myocardial contractility. Therefore, repeated echocardiography evaluation is mandatory. Evaluation of global longitudinal strain (GLS) may be more sensitive and specific for SCM than LV ejection fraction (LVEF). Standard management includes etiological treatment, adapted fluid resuscitation, use of vasopressors, and monitoring. Use of inotropes remains uncertain, and heart rate control could be an option in some patients.

Introduction

Sepsis is a significant cause of mortality,[1] but sepsis-induced cardiomyopathy, or septic cardiomyopathy (SCM), is not well-characterized with regard to prognosis or treatment. SCM may be defined as depressed intrinsic contractility induced by sepsis. The reported prevalence of SCM varies widely from 10% to 70%.[2] Myocardial dysfunction in sepsis is a poorly understood phenomenon. Although there is an extensive body of literature on this subject, the results are conflicting and no objective definition of SCM has been established.[2–4] In the present study, we will review the recent literature with a focus on the pathophysiology, definition, diagnosis, prognosis, and treatments of SCM.

Pathophysiology

A major impediment to understanding SCM is the variety of definitions by which it is described. Primary myocardial cellular dysfunction in sepsis can manifest in multiple ways, including left and/or right ventricular impairment during systole or diastole, and with or without inadequate cardiac output (CO) and oxygen delivery. Several pathways secondary to pathogens and a dysregulated host immune response have been proposed to explain sepsis-associated changes in myocardial contractility.[3,4] Pathogen-associated molecular patterns (PAMPs), such as lipopolysaccharide, are recognized by toll-like receptors. Endogenous damage-associated molecular patterns (DAMPs) such as heparan sulfate fragments, histones, and high-mobility group protein B1 also trigger multiple intracellular pathways that induce secretion of innate pro-inflammatory cytokines, such as tumor necrosis factor (TNF)-α and interleukin (IL)−1.[5–7] These cytokines were associated with myocardial dysfunction and organ failure in patients with septic shock.[8] In contrast, mediators involving adaptive immunity and repair (the IL17/interferon pathway and vascular endothelial growth factor [VEGF]) were associated with faster resolution of sepsis

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and a higher survival rate.[8] An imbalance between these two types of cytokines may promote myocardial dysfunction in some patients. However, these associations were not observed in another clinical study.[9]

Endothelial and inducible nitric oxide (NO)- synthase plays important roles in myocardial dysfunction. NO can alter preload and afterload, promote down-regulation of beta-adrenergic receptors, reduce response of myofilaments to calcium (Ca^{2+}), and increase mitochondrial permeability.[4]

Mitochondrial dysfunction is multifactorial in sepsis,[10] and can manifest with ultrastructural abnormalities, oxidative phosphorylation disorders, signaling alterations, and impaired biogenesis and mitophagy, resulting in insufficient renewal of mitochondria.[11] Secondary to impairment of the antioxidant capacity of mitochondria, oxidative stress interferes with signaling pathways, and also increases mitochondrial calcium and free fatty acid levels. Calcium dysregulation can also contribute to myocardial dysfunction.[12]

Sympathetic hyperactivation in sepsis can lead to myocardial dysfunction through tachycardia, shortened diastole, and left ventricle (LV) filling, and through conversion of adrenergic G protein coupling from a stimulatory to an inhibitory response.[4] Furthermore, β-adrenergic receptor down-regulation could explain refractory response to catecholamines. The hypothesis that coronary ischemia occurs secondary to microcirculation hypoperfusion has not been seen in some studies,[13,14] but coronary microvascular dysfunction has been observed.[4] Endogenous and/or exogenous adrenergic stimulation may also contribute to SCM, as seen in Takotsubo syndrome. In an autopsy study, myocytolysis, interstitial fibrosis, contraction band necrosis, mononuclear infiltrates, and interstitial edema were observed in >90% of patients, and these findings may be explanatory of stress-induced cardiac lesions.[15]

Finally, septic endothelial dysfunction, through glycocalyx degradation,[16] can lead to microcirculatory hypoperfusion and capillary leaks, resulting in myocardial edema.[17]

Definitions

Although there is no consensus clear definition of SCM, most review articles and expert opinions agree on a few fundamental features of this unique form of cardiac dysfunction. These features include acute uni- or bi-ventricular systolic or diastolic dysfunction with reduced contractility not due to coronary disease. Whether isolated diastolic LV dysfunction and isolated right ventricle (RV) dysfunction should be part of the definition of SCM is a topic of debate.[4] Septic myocardiopathy is usually described as reversible. Notably, some patients died from fulminant septic shock with associated SCM, and studies till date have not considered the competing risk of death.

A description of five hemodynamics profiles in septic shock has been proposed by Geri et al.[18] using a clustering approach. These profiles are as follows: (1) LV systolic dysfunction, (2) LV hyperkinesia, (3) still hypovolemia, (4) RV failure, and (5) well-resuscitated. This clustering approach failed to identify an LV diastolic dysfunction cluster. However, this dysfunction was uniformly distributed among all clusters except in well-resuscitated patients.

Incidence

The incidence of LV and/or RV dysfunction varies depending on evaluation methods and diagnostic criteria.[2] This heterogeneity of incidence depends also on the timing of echocardiographic evaluation, and timing factors include evaluation before or after resuscitation, correction for preload and afterload, within the first 24 h, or within 72 h. In a study by Boissier et al.,[19] LV dysfunction was diagnosed in 22% of patients assessed using echocardiography within 24 h, but also in an additional 9.8% of patients assessed between 25 h and 72 h. Vieillard-Baron et al.[20] showed an incidence of LV dysfunction in 18% of patients assessed within 6 h, and 60% within 72 h. Therefore, as most echo parameters are dependent on loading conditions, the echo assessment should be repeated at multiple time points.

Study population may influence the incidence of SCM defined by echo criteria. Some studies included both severe sepsis and patients with septic shock, while others included only patients with septic shock. Furthermore, patients with and without mechanical ventilation, and differences in preload and afterload conditions, may influence SCM as defined by echo criteria.

Clinical Presentation

As summarized by L'Heureux et al.[21] clinical features suggesting the diagnosis of SCM can include a "septic, cool extremities phenotype" on clinical exam, failure to respond to a preload challenge, cardiac arrhythmias, and hemodynamic instability despite vasopressor therapy.

Diagnosis

Clinicians should consider a diagnosis of SCM in all septic patients with sepsis-associated organ dysfunction, and particularly in cases of septic shock requiring vasopressor therapy.[2–4] Some commonly reported risk factors for SCM are male sex, younger age, higher lactate levels at admission, and a history of heart failure, although the latter likely reflects preexisting disease.[21]

Given the absence of a consensus regarding definition or criteria, diagnosing SCM can be challenging. Several tools can be used to evaluate LV ejection fraction (LVEF). Echocardiography is the most useful technique for bedside evaluation, but magnetic resonance imaging (MRI)[22] or ventriculography can also be used.

Intrinsic myocardial contractility can be accurately measured by pressure-volume loop analysis using multicrystal sonomicrometry,[23] a conductance catheter,[24] MRI,[25] or radionuclide techniques,[26] but these techniques cannot be used during routine bedside care, particularly in critically ill patients.

Echocardiography

Echocardiography is the gold standard for the diagnosis of SCM. Every hemodynamically unstable patient should be assessed using critical care echocardiography.[27,28] These findings are summarized in Figure 1 and described in more detail below.

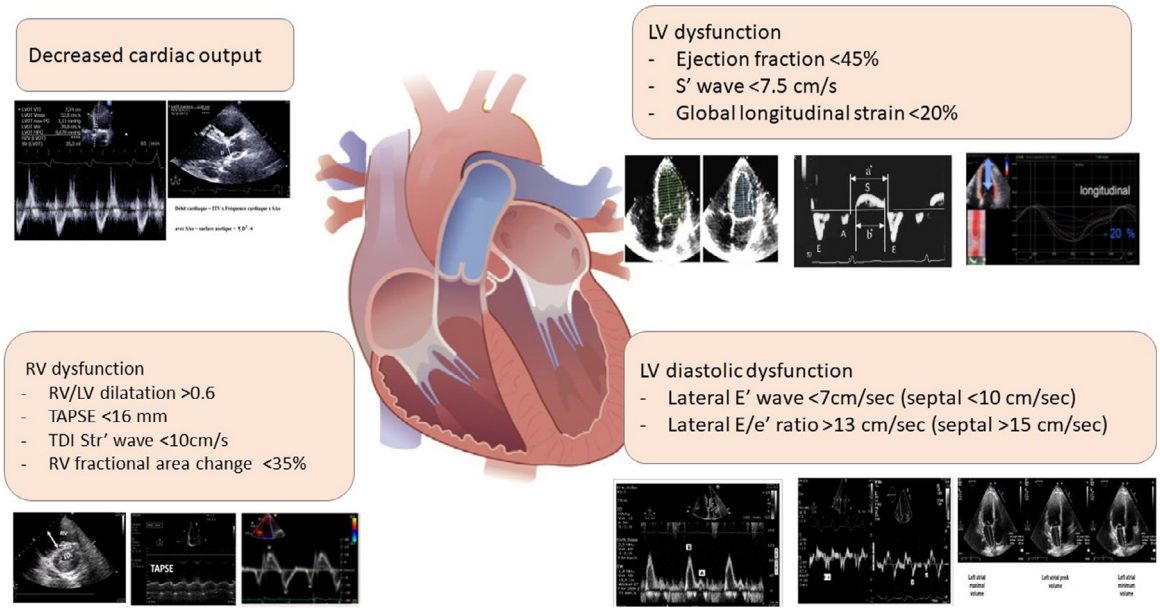

Figure 1. Echo parameters used to diagnose SCM. LV: Left ventricular; RV: Right ventricle; SCM: Septic cardiomyopathy; TDI: Tissue Doppler imaging; TAPSE: Tricuspid annular plane systolic excursion.

LV systolic dysfunction

LVEF systolic dysfunction was observed in the first studies of SCM, and was associated with LV dilation.[29] Systolic function can be assessed using LVEF measured with Simpson's rule or LV fractional area contraction at the midpoint of the LV.[30,31] The initial assumption was that diagnosis of SCM could be made based solely on observation of depressed LVEF (LVEF <45%).

LVEF is simple to evaluate at bed side, but is highly dependent on loading conditions, and is particularly dependent on afterload.[19] Therefore, LVEF is not a sensitive indicator of intrinsic myocardial contractility, but reflects the interaction between LV myocardial contractility and LV afterload.[32] Evaluation of septic myocardial function must account for ventriculo-arterial coupling, with decreased afterload at the early phase of sepsis. This coupling necessitates reevaluation following initial resuscitation with fluid expansion and vasopressors.

Tissue Doppler imaging (TDI)

The peak systolic velocity, as determined by the S' wave measured at the mitral annulus using TDI, may be less dependent on loading conditions than LVEF.[33,34] However, a meta-analysis of 13 studies assessing patients with sepsis found no differences in S' values between survivors and non-survivors.[35] Measurement of S' is limited by angle-dependency, and measurements are unidirectional (longitudinal) and unidimensional (one segment) evaluations. Notably, the feasibility is limited in critically ill patients, about 62%.[19]

Speckle tracking echography (STE)

STE is a recent echocardiographic modality used to evaluate LV deformation over time by following ultrasound echoes called speckles.[36,37] Global longitudinal strain (GLS), which represents the change in length during systole compared to that in diastole, is a good surrogate measure of LV contractility. In addition, GLS may be angle-independent and less dependent on loading conditions.[38,39] Typical GLS values are approximately 20%.[40]

Use of GLS to assess LV systolic function in patients with septic shock resulted in detection of changes in myocardial contractility in 70% of patients (*vs.* 32% of patients evaluated using LVEF), which indicates that GLS may be a more sensitive indicator of systolic dysfunction.[19] In this study, GLS measurement on day 1 predicted secondary LV dysfunction as determined by LVEF on day 2 or 3.[19] Notably, GLS impairment has been shown to be more prevalent in intensive care unit (ICU) patients with septic shock than in those without septic shock.[41]

Evaluation of GLS requires good image resolution and endocardium visualization, and a high frame rate, which limits the ability to measure GLS in critically ill patients at bedside (42% *vs.* 97% for LVEF estimated with Simpson or visual evaluation).[19]

Other echocardiographic tools have been used to describe septic LV dysfunction, including the myocardial performance index (also called Tei index), which reflects the time spent in isovolumetric contraction, with lower values reflecting better function.[42,43] Mitral annular plane systolic excursion (MAPSE) may also be a promising tool for evaluation of SCM.[44–46]

LV diastolic dysfunction

Diastolic dysfunction is important to evaluate in the ICU, as it can contribute to acute respiratory distress in some patients and to failure to successfully discontinue mechanical ventilation.[47] In patients with septic shock, diastolic function can be impaired.[48] Similar to LV systolic function, differences in definitions and lack of consensus regarding diagnostic techniques complicate diagnosis of diastolic dysfunction.[49] Lanspa et al.[50] proposed a simplified definition using TDI-derived septal e' wave (<8 cm/s) and E/e' ratio (≤8, between 8 and 13,

and ≥13). This method identified diastolic dysfunction in 87% of patients with severe sepsis or septic shock. In this study, septal e' wave was used because it was easier to record than lateral e' wave (lateral annulus). However, e' wave may overestimate the severity of diastolic dysfunction. Interestingly, lateral e' wave was less sensitive to preload variations.[51] In a meta-analysis conducted by Sanfilippo et al.[52] that assessed seven studies with 636 patients with severe sepsis or septic shock, 48% of patients had diastolic dysfunction. Diastolic dysfunction was diagnosed using TDI septal e' wave, but the included studies did not have consistent cut-off values. Another meta-analysis by Sanfilippo et al.[48] in 2017 that included 17 studies using lateral and/or septal e' and E/e' showed that lateral measurements were more strongly associated with prognosis than septal values.

The most recent recommendations of ASE and European Association of Cardiovascular Imaging, published in 2016, define diastolic dysfunction in patients with normal LVEF as meeting more than two of the following criteria: tricuspid jet velocity >2.8 m/s, left atrial volume >34 mL/m^2, TDI e' wave <7 cm/s in lateral annulus and <10 cm/s in the septal annulus, and E/e' ratio >13 in the lateral and >15 in the septal annulus.[53] However, these parameters are not fully applicable in the ICU setting, and use of TDI e' wave and E/e' ratio remains the most reliable approach because these measures are relatively independent of loading state.[54] The 2016 recommendations allowed for identification of 60% patients with diastolic dysfunction at day 1, among 62 patients with severe sepsis or septic shock.[55] Diastolic function varies with loading conditions, and evaluation of this parameter should be coupled with evaluation of LV filling pressure. In addition, tachycardia related to sepsis and atrial fibrillation (prevalence up to 42% in septic shock cases[56]) can worsen diastolic dysfunction, and may preclude use of diastolic function as a diagnostic measure. A limitation of assessment of systolic functions is that unknown preexisting diastolic dysfunction can affect this measure.

RV dysfunction

The pathogenesis of RV dysfunction is likely multifactorial in sepsis. Hypoxemia, hypercapnia, and mechanical invasive ventilation (particularly in the case of associated acute respiratory distress syndrome) may exacerbate RV dysfunction in sepsis and lead to acute cor pulmonale,[57] even during protective mechanical ventilation.[58]

Right ventricular dysfunction was reported in 50% of patients with severe sepsis and septic shock in two retrospective studies.[59,60] In one study in which 55% of patients were ventilated, RV dysfunction occurred in the absence of LV dysfunction in 47% of cases.[60] Right ventricular dysfunction was defined according to the following ASE criteria: tricuspid annular plane systolic excursion (TAPSE) <16 mm, tricuspid systolic lateral annular velocity (TDI Str' wave) <15 cm/s, and RV fractional area change (FAC) <35%.[61]

However, as with LV systolic and diastolic dysfunction, diagnosis is difficult and diagnostic-technique–dependent. The shape of the RV makes geometrical evaluation difficult, and assessment of RV using TAPSE or S wave is limited to longitudinal evaluation. A previous study defined RV failure as a combination of RV dilatation (RV/LV end-diastolic area >0.6) and systemic congestion (central venous pressure ≥8 mmHg).[57] This study reported RV dysfunction in 42% of 282 ventilated patients in septic shock. Interestingly, 63.5% of these patients with RV failure according to this definition had a normal TAPSE.[57]

Right ventricular strain using STE may be a promising tool to detect RV dysfunction, but the associations between RV strain and TAPSE or other parameters used to assess RV function are moderate. Further studies are needed to determine whether RV dysfunction is a consequence of abnormal loading conditions or intrinsic to myocardial dysfunction.[59]

Invasive monitoring

Afterload-related cardiac performance (ACP) can be a useful indicator of SCM. Normal CO does not rule out SCM because decreased systemic vascular resistance (SVR-afterload) may falsely elevate the measured CO. Furthermore, CO does not necessarily reflect intrinsic cardiomyocyte contractility. The derived calculation for ACP is as follows: ACP (%) = CO measured/CO predicted × 100%, with >80% considered normal. Predicted CO is calculated as a function of SVR as follows: CO predicted = $\beta 0 * \mathrm{SVR}^{\beta 1}$ ($\beta 0 = 394.07$, $\beta 1 = -0.64$), which includes a mathematical coupling of measurement errors as a limit. A few studies have found an association between low ACP and mortality in patients with severe sepsis or septic shock.[62–64]

Ventriculoarterial coupling represents the interaction between myocardial contractile function and the arterial system as two interconnected systems. This can be assessed by determining the ratio of LV end-systolic maximal elastance ($LVend - systolicmaximal\ elastance = \frac{systolic\ arterial\ pressure\ [mmHg]}{LVend-systolic\ volume\ [mL]}$) and LV end-systolic arterial elastance($LVend - systolicarterial\ elastance = \frac{systolic\ arterial\ pressure\ [mmHg]}{stroke\ volume\ [mL]}$), results in $\frac{stroke\ volume(mL)}{LVend-systolic\ volume\ (mL)}$ using echocardiography; even the reference method is an invasive measure with pressure-volume loops.[65] Ventriculoarterial decoupling (reflecting by a decreased ratio) is associated with impaired LV performance, but studies have failed to show a correlation with LVEF in patients with sepsis.[66] Assessment of ventriculoarterial coupling may be useful for understanding the interaction between contractility and the vascular system and to guide therapies, but further studies are needed.

Biomarkers

Measurement of serum cardiac biomarkers may be complementary to echocardiographic assessment.[67–69] Troponin elevation is frequently observed in sepsis and septic shock, even in the absence of myocardial dysfunction. A meta-analysis showed that increased troponin was associated with increased mortality.[68] However, troponin elevation is frequently observed in critically ill patients regardless of reasons for admission. Furthermore, assays for troponin have become increasingly sensitive,[70] and the association between troponin and hospital mortality is substantially attenuated after controlling for confounding factors.[71] The causes of troponin elevation are likely multifactorial, and increases are associated with myocardial membrane leakage and/or cytokine apoptosis, but not macrothrombi.[67]

Troponin elevation was also associated with severity of RV dilatation. This association has also been observed with acute pulmonary embolism and LV diastolic dysfunction.[69] It is unclear whether troponin elevation or peak troponin correlates with SCM diagnosis.[72–74] Notably, acute kidney injury and

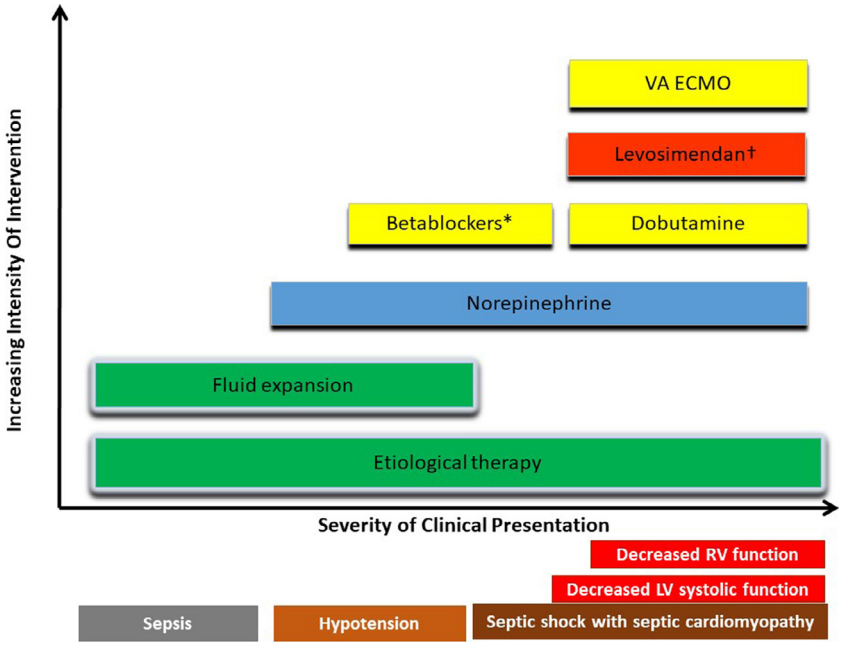

Figure 2. Potential therapeutic options according to the severity of SCM. Green boxes represent therapies with strong recommendations, strong quality of evidence. Blue box represents therapies with strong recommendations, moderate quality of evidence. Yellow Boxes represent therapies with weak recommendations requiring confirmation in prospective clinical trials. Red Boxes represents therapies which should not be used due to weak recommendations, low quality of evidence. *Beta blockers could be discussed in patients with tachycardia with diastolic dysfunction, but are not recommended in cases of systolic dysfunction or cardiogenic shock. †Levosimendan should not be used due to lack of efficacy, poor safety profile, cost, and the limited availability. ECMO: Extracorporeal membrane oxygenation; SCM: Septic cardiomyopathy.

chronic kidney disease can increase the level of troponin independent of myocardial factors.

Troponin assessment, in conjunction with an electrocardiogram, is useful to rule out acute coronary syndrome with ST elevation and myocarditis.

Natriuretic peptides also have prognostic value for patients with sepsis,[3,4] as levels are increased in cases of LV or RV wall stress. However, natriuretic peptide levels are also associated with other conditions.[75] Overall, increased cardiac biomarkers reflect illness severity and prognosis in patients with sepsis, but they are not specific to diagnosis of SCM.

Prognosis of SCM

The first studies assessing SCM reported a lower mortality rate in patients with decreased LVEF and cardiac index.[29,76–80] Increased LVEF and hyperkinesia might be associated with a higher mortality rate because this may reflect persistent profound vasoplegia.[19,78,79] The results regarding the prognostic value of LVEF in patients with severe sepsis and septic shock are conflicting and a recent meta-analysis did not find any association between mortality and LVEF[52,81–85] or TDI S' wave.[35]

According to several studies and a meta-analysis, GLS could be a significant predictor of higher mortality.[86–88] Notably, sepsis may promote cardiovascular disease secondary to persistent systemic inflammation.[89] Abnormal LV strain during sepsis (either too high or too low) was associated with major adverse cardiovascular events in patients with pre-existing cardiac disease.[90]

An association between septic diastolic dysfunction and mortality was also described in several studies, a systematic review, and a meta-analysis.[48,52,91,92] However, this study was limited by small sample size and sample heterogeneity. A prospective observational study is ongoing, aiming to assess the prognostic value of diastolic and systolic left ventricular function in 440 patients with septic shock (Vignon et al.[51] PRODIASYS, NCT02918214).

Some studies have shown that isolated RV dysfunction was associated with worse survival.[59,60,93,94] A recent database study suggested that echocardiographic assessment of myocardial function influenced hemodynamic management of patients with sepsis, which resulted in earlier discontinuation of vasopressor administration, and decreased 28-day mortality.[95]

Management

Although questions remain regarding hemodynamic support for septic shock,[96] initial treatment depends on early recognition and etiological treatment, fluid expansion, and administration of vasopressors Figure 2.

Left ventricular systolic dysfunction

As the prognostic value of septic LV dysfunction is unclear, treatment of this dysfunction is also debated. However, therapies aimed at supporting cardiac function are based on assessment of global parameters such as hypoperfusion signs, and are not solely based on echographic values or images.

The Surviving Sepsis Campaign 2016–2018 strongly recommends norepinephrine as the first line vasopressor for treatment of septic shock, although evidence for this treatment is based on moderate quality evidence. Dobutamine can be added in cases

with persistent hypoperfusion despite adequate fluid loading and administration of vasopressors, although this is not strongly recommended, and is based on low quality evidence.[97]

A randomized controlled study by Hernandez et al.[98] reported no improvement of microcirculation perfusion parameters despite significant increases in heart rate, cardiac index, and LVEF in patients with septic shock receiving dobutamine compared to those who received placebo. However, the dobutamine dose was constant (5 μg • kg^{-1} • min^{-1}) and few patients were on mechanical ventilation. An ongoing RCT is being conducted to evaluate treatment with dobutamine *vs.* placebo in 270 patients with septic LV dysfunction (Vignon et al.,[51] ADAPT study, ClinicalTrials.gov Identifier: NCT04166331).

Alterations in myocardial adrenergic responsiveness have been reported in patients with septic shock.[99] However, catecholamines can cause many adverse effects, including cardiotoxicity.[15,100] which has prompted additional scrutiny on whether use of catecholamine administration should be limited. Levosimendan is a calcium sensitizer that acts in a catecholamine-independent manner to minimize effects on oxygen demand, arrhythmias, and catecholamine resistance resulting from sepsis. Preliminary trials of levosimendan reported reduced mortality in patients with septic shock patients, but no benefit was found in a subsequent larger study.[101–103] Therefore, the Surviving Sepsis campaign does not recommend use of levosimendan for treatment of septic shock owing to little evidence for therapeutic value, poor safety profile, cost, and limited availability of the drug.[97]

Early venoarterial extracorporeal membrane oxygenation (ECMO) may be suitable for some patients with refractory sepsis-induced cardiogenic shock following correction of vasoplegia.[104–106]

LV diastolic dysfunction

Tachycardia and tachyarrhythmias in septic shock can worsen LV systolic and diastolic dysfunctions, and some studies have evaluated the use of short-acting beta-blockers, such as esmolol[107,108] or landiolol[109,110] to treat tachyarrhythmias with the goal of improving the prognoses of patients with septic shock.[111,112] However, few of these studies specifically evaluated SCM. In a study by Kakihana et al.,[109] mean LVEF was 55% ± 15%, and cardiogenic shock was an exclusion criterion. Beta-blockers should be used with caution and in very few patients. Systolic dysfunction should be a contraindication for use of beta blockers in such patients.[113] In a small sample size study that assessed nine patients at the early phase of tachycardic and hyperkinetic septic shock, esmolol had exacerbated hypotension and decreased cardiac index.[114] Morelli et al.[115] described the use of the systolic-dicrotic notch pressure difference to identify tachycardic patients at risk of decompensation following heart rate reduction. A smaller difference was associated with compensatory tachycardia from reduced LV contractility, with high risk of decompensation in conjunction with heart rate reduction. This systolic-dicrotic notch pressure difference was measured by the arterial dP/dt max, obtained by analysis of the radial arterial pressure waveform contour, and used as a surrogate for ventriculoarterial coupling.

Ivabradine, a selective inhibitor of If channels in the sinoatrial node, can lower heart rate without inducing negative inotropy, which is associated with beta blockers. An ongoing randomized trial is evaluating the effects of ivabradine against placebo in patients with septic shock (Mekontso-Dessap A, Ivabradine for Heart Rate Control In Septic Shock (IRISS), NCT04031573).

Right ventricular dysfunction

In a study assessing patients with septic shock under mechanical ventilation, patients with congestive RV failure with RV dilation responded to fluid challenge in 30% of cases, despite significant pulse pressure variation.[57] Fluid expansion should be performed with caution and with strict hemodynamic monitoring[57] following the early phase of resuscitation in patients with septic shock with RV dysfunction.

Limitations of the Literature

Most of the studies assessing SCM are small, observational, or retrospective, have heterogeneous samples with regard to severity (sepsis or septic shock, ventilated or not), and differ in timing of evaluation, treatment outcomes, co-morbidities, and pre-existing cardiac function. Longitudinal studies that include pre-admission echocardiography data are lacking, largely because these studies are difficult to perform. These factors have limited development of a consensus regarding definition, incidence, and prognosis of SCM.

Case heterogeneity and suboptimal reporting of a number of items has been emphasized in a review by the PRICES expert panel of European Society of Intensive Care Medicine (ESICM),[116] and some recommendations have been changed to explicitly state which parameters and information should be included in the design of further echocardiography research studies.[117] Moreover, few studies have evaluated the impact of biological sex on SCM,[118] which has been shown to influence pathology and response to treatment in animal studies.[119,120]

Conclusions

Septic myocardial dysfunction is common in septic shock, but definitions vary (LV and/or RV, systolic and/or diastolic dysfunction). Further studies are needed to improve our understanding of the pathophysiology of SCM, to discriminate adaptive mechanisms to intrinsic myocardial decrease leading to hypoperfusion and organ failure, and to evaluate treatments.

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Conflicts of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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