EDITORIAL

Sepsis and the Heart: More to Learn

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Sepsis is a major contributor to the case mix of an intensive care unit. The evolving definitions of sepsis have included organ dysfunction at the core of diagnosing the syndrome.[1] Several organ dysfunctions have been defined and the severity of such dysfunction can also be quantified.[2] One of the organ dysfunctions that are less clearly defined relates to the impact of sepsis on the heart. No objective definition for sepsis-induced cardiomyopathy (SICM) has been established despite the fact that the reported prevalence of this condition varies between 10 and 70%. Part of the variation is due to the influence of various aspects of sepsis like source, severity, adequacy of resuscitation, antimicrobials used, and hemodynamic consequences. The most widely agreed criteria to define SICM[3] include the following:

- Acute and reversible dysfunction within 7–10 days
- Global, biventricular dysfunction (either systolic, diastolic, or both)
- Dilatation of the left ventricle
- Reduced fluid and catecholamine response
- Exclusion of acute coronary syndrome.

In this issue of the journal, Bansal et al.[4] reported the results of their prospective observational study evaluating the incidence and outcome of the condition. Traditionally, a patient with sepsis with cool extremities unresponsive to fluids and vasopressors is considered as a prototype of SICM.[5]

Several risk factors have been known to be associated with SCM. Advanced age, higher disease severity, diabetes mellitus, and preexisting heart failure are considered to be determinants of the genesis of SCM.[5] In the current study, the authors documented diabetes and pneumonia as predictors of SCM. Both the SOFA and the APACHE scores were higher among patients with SCM and left ventricular (LV) dysfunction.

The exact pathophysiology of SCM is unclear. Initially, it was considered to be similar to coronary artery disease, but that viewpoint is no longer accepted. Chemical mediators such as endotoxins, cytokines, and nitric oxide are now considered to be central to the pathogenesis of SCM.[6] The imbalance between the pro- and the anti-inflammatory cytokines, which determines the progress of sepsis, seems to be the key to the genesis of SCM as well. The current focus during resuscitation is on maintaining the integrity of the glycocalyx.[7] Disruption to the glycocalyx can cause alterations to the microvascular flow and generate myocardial edema, which could explain the mechanism underlying SCM. This could be aggravated by the mitochondrial dysfunction[8] and calcium dysregulation[9] associated with sepsis.

No specific diagnostic test is exclusive to the diagnosis of SCM. New-onset atrial fibrillation is a common occurrence among septic patients and could possibly reflect the myocardial changes associated with sepsis.[10] A type I Brugada pattern mimicking ST elevation occurs fairly frequently among febrile patients.[11] Bansal et al., in the current study, have not reported any specific ECG pattern among patients with SCM.

Echocardiography is by far the most widely available tool for assessing patients suspected to have SCM. The left ventricular ejection fraction (LVEF) is quite often considered as a benchmark to identify depressed LV function. However, in the context of sepsis, the reduced afterload that exists as part of the distributive shock tends to "pseudo-normalize" the ejection fraction (EF).[12] The impact of vasopressors and inotropes on the EF also needs to be reported while describing the LVEF among septic patients. The current study reports an LVEF of 35% among patients with SCM and LV dysfunction.

Assessment of stroke volume (SV) and cardiac index (CI) using the left ventricular outflow tract diameter and velocity-time integral is a standard component of hemodynamic assessment of unstable patients. These measurements are relatively easy to obtain and have prognostic significance. However, the tachycardia and altered afterload that accompany sepsis confound the interpretation of these parameters and reduce their applicability in diagnosing SCM.

The right ventricle (RV) is an integral part of the hemodynamic homeostasis and is frequently affected by the fluid and vasopressor therapy used in managing septic shock. It is reported that RV dysfunction is seen in nearly 60% of patients with sepsis and could be a determinant of mortality.[13] The parameters which guide the assessment of the RV include a comparison of the end-diastolic areas of both ventricles, the fractional area change of the RV along with the tricuspid annular plane systolic excursion, and tissue Doppler imaging (TDI) of the tricuspid annulus as well as the RV free wall. Getting a proper window of the RV to assess these parameters among septic patients, who are quite often ventilated mechanically, remains a challenge, and the skill acquisition has a steep learning curve.

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While assessment of systolic function of both the ventricles is essential to identify cardiac dysfunction, assessment of diastolic function cannot be overlooked. Diastolic dysfunction is quite common among patients with septic shock. An abnormal septal relaxation assessed by TDI (e' wave <8 cm/second) has been identified as an important echocardiographic marker of adverse outcomes among patients with septic shock.[14] Similarly, measurement of peak early diastolic transmitral velocity during the passive filling phase (E) and comparing it with the peak early mitral diastolic annular TDI velocity (e')—E/e'—tends to predict mortality among septic patients. Lower e' and higher E/e' ratios have been confirmed as predictors of mortality among septic patients in a recent meta-analysis.

A more recently accepted parameter to identify cardiac dysfunction in sepsis is global longitudinal strain (GLS) assessed by a technique called speckle tracking. Normal values of GLS are reported to be –17% to –23%, with the more negative value denoting better cardiac function. A small pilot study reported a GLS of –14% among patients with septic shock, even among those who were labeled as having a "normal" LVEF.[15] Speckle tracking is considered to be immune to the effect of afterload reduction associated with sepsis. But this technique needs special software and high imaging quality.

The role of biomarkers—troponin I and brain natriuretic peptide (BNP)—appears to be limited in diagnosing SCM. The biomarkers seem to reflect the myocardial injury and the ventricular strain, irrespective of the etiology. They do not seem to discriminate SCM from other forms of heart failure associated with sepsis. They may have a larger role in prognosis rather than diagnosis.[16]

The management of SCM hinges on the management of the underlying sepsis. The use of dobutamine to improve LV systolic function among septic patients is not strongly recommended.[17] Levosimendan also did not show major benefit in large studies.[18] Attempts to manage the diastolic dysfunction with beta-blockers have also not yielded consistent positive results.[19]

Conclusion

The following points are concluded:

- SCM is a distinct, probably under diagnosed condition.
- Excluding a diagnosis of SCM based solely on EF might be an erroneous approach.
- Severity of the sepsis and extent of hemodynamic instability determine the severity of SCM.
- Newer echocardiographic techniques like speckle tracking offer a more specific diagnostic option.
- Therapy is guided by treatment of underlying sepsis.

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