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FINANCIAL/NONFINANCIAL DISCLOSURES: None declared.

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DOI: https://doi.org/10.1016/j.chest.2019.05.006

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The Challenging Diagnosis of Septic Cardiomyopathy

To the Editor:

We read with interest the "septic heart" review in the February issue of *CHEST*.[1] The authors highlight the urgent need for a clear definition of septic cardiomyopathy. The main challenges in this definition are the evaluation of the cardiovascular context (in particular, evaluation of cardiac function in the setting of highly variable preload and afterload conditions), and the lack of longitudinal echocardiography data starting from premorbid heart function with serial echocardiographic evaluations performed during the course of the critical illness and eventually following recovery.

We applaud the authors[1] for their efforts and fully endorse the need for a standardized definition of septic cardiomyopathy; however, at present, there are not enough data to support a precise definition of septic cardiomyopathy. The first characteristic proposed by the authors (Table 1) is a combination of left ventricular (LV) dilatation with normal/low filling pressure (LVFP). A dilated left ventricle has increased end-diastolic volume (and, in most cases, end-diastolic pressure). It seems unlikely that well-resuscitated patients with manifestations of septic cardiomyopathy can exhibit a dilated left ventricle without increased LVFP. Indeed, a meta-analysis reported significantly higher ratio of the E wave to e' wave obtained with tissue doppler imaging (E/e' - surrogate of LVFP) in patients with sepsis who were nonsurvivors. However, in the vast majority of the included studies, survivors also had abnormal E/e′ values, confirming the large prevalence of raised LVFP during sepsis.[2]

The second proposed criteria—"reduced ventricular contractility"—is generic and incorporated into the third proposed characteristic, which includes a wide spectrum of biventricular dysfunction, with systolic or diastolic abnormalities. In the context of sepsis, it is important to clearly differentiate LV diastolic dysfunction (associated with worse outcomes) from LV systolic dysfunction (which has not shown similar associations[3]). Accordingly, patients with LV diastolic dysfunction may warrant a careful approach in terms of fluid resuscitation (which should be based not only on indexes of fluid responsiveness), modulation of afterload, and optimization of heart rate.[4]

Finally, the authors discussed the potential role of a speckle-tracking echocardiography (STE).[1] As the authors suggest, STE is a promising technique in the context of sepsis. We endorse this idea and note that data were recently reported in support of this technique. Indeed, a meta-analysis found an association between worse LV function as assessed according to STE (global longitudinal strain) and higher mortality in patients with sepsis.[5] Of course, prior to firm conclusions being made regarding STE, further research is required with

TABLE 1] Proposed "Main Characteristics" of Septic Cardiomyopathy by Martin et al[1]

Acute cardiac dysfunction unrelated to ischemia with one or more of the following:
• Left ventricular dilatation with normal-filling or low-filling pressure
• Reduced ventricular contractility
• Right ventricular dysfunction or left ventricular (systolic or diastolic) dysfunction with a reduced response to volume infusion

large robust studies, keeping in mind that STE parameters are also affected by preload and afterload conditions.

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DOI: https://doi.org/10.1016/j.chest.2019.04.136

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Response

To the Editor:

We thank Dr Sanfilippo and colleagues for their comments on our review summarizing the current understanding of molecular mechanisms and clinical implications of septic cardiomyopathy.[1] We fully agree with the authors that one of the main challenges in the definition of septic cardiomyopathy is the evaluation of cardiac function in the setting of highly variable preload and afterload conditions, as well as the lack of longitudinal echocardiography data starting from premorbid heart function.

Geri et al[2] recently published a clustering approach that included clinical and echocardiographic parameters in patients with septic shock. Five different hemodynamic phenotypes were identified in 360 patients with septic shock: left ventricular systolic, dysfunction, left ventricular hyperkinesia, still hypovolemia, right ventricular failure, and well-resuscitated phenotype. Overall, 17.7% of the patients had left ventricular systolic dysfunction. These patients had high lactate levels and required a high dose of norepinephrine, although they were not fluid responsive. Of note, both central venous oxygen saturation and left ventricular filling pressure as reflected by E/E′ remained nonelevated despite distinct cardiac failure. These results are in line with earlier data indicating that the absence of elevation of left ventricular filling pressure might be a specific characteristic of this hemodynamic profile, not only when evaluated according to the E/E′ but also by pulmonary artery catheter.[3-5] We fully agree, however, with Dr Sanfilippo and colleagues that there are currently not enough data to support a precise definition of septic cardiomyopathy.

We also agree with Dr Sanfilippo and colleagues that, in the context of septic shock (as mentioned in our article[1]), it is very important to clearly differentiate between left ventricular systolic and left ventricular diastolic dysfunction, keeping in mind that guidelines for grading diastolic dysfunction from the American Society of Echocardiography only poorly categorize patients who have sepsis.[6] Ehrman et al[7] recently stated that global longitudinal strain is the preferred modality for investigating the relation between left ventricular systolic function and outcomes in patients with septic cardiomyopathy. We endorse this statement and highlight that existing primary studies are limited by substantial biases and clinical heterogeneity. In line with Dr Sanfilippo and colleagues, as well as Ehrman et al, we strongly recommend performing a large-scale prospective international study to provide a definitive answer to the question regarding the relation between left ventricular systolic function and outcomes in patients with septic cardiomyopathy.

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