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Letter

A protocol to ascertain whether sepsis-induced cardiomyopathy constitutes a phenotype of Takotsubo syndrome

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To the Editor,

I read with interest the review by Zhang and Liu,[1] about the typical septic cardiomyopathy (SC) and sepsis-related Takotsubo syndrome (TTS) (S-TTS). The report rekindled some thoughts, which have occupied me for the past few years, regarding the possibility that SC constitutes a phenotype of TTS, or whether it is an altogether different pathophysiological entity. Indeed, both SC [1] and S-TTS [1] occur in the setting of sepsis, and one can take the view that they are different but related nosological entities, or they are different phases of a common neurogenic (via a hyperadrenergic state)/cardiac affliction seen in patients with sepsis. The authors, who have provided a comprehensive analysis of the relevant extant literature,[1] appropriately describe SC, as usually characterized by global left ventricular (LV) systolic and/or diastolic dysfunction, with frequent right ventricular (RV) involvement, not due to coronary artery disease, which affects prognosis in afflicted patients, usually described as reversible, in contrast to the S-TTS, which is associated with "LV apical and circumferential mid-ventricular hypokinesia and basal hypercontractility,"[1] although patients with TTS have also been described with global hypokinesis, with or without RV involvement.[2,3] Also, Boissier and Aissaoui[4] in their review, focusing on the pathophysiology, definition, diagnosis, prognosis, and treatments of SC, echo their uncertainty about a precise and objective definition of SC, characterizing "myocardial dysfunction in sepsis as a poorly understood phenomenon."

I share the authors' assertion that "the precise evaluation of heart dysfunction in sepsis patients is not easy," [1] because of the multitude of circumstances and many faces under which LV and RV dysfunction in patients with sepsis confront clinicians, in different medical and surgical environments, with varying expertise in managing cardiovascular disorders. The common scenario in the management of patients with sepsis, who reveal symptoms/signs pointing to cardiovascular derangement is seeking a consultation from the cardiology service, which leads to the patients' formal evaluation, and ordering of cardiac biomarkers, electrocardiograms, and a bedside transthoracic echocardiogram (ECHO), with occasional "evaluation of global longitudinal strain, which may be more sensitive and specific for SC, than the LV ejection fraction,[4] along with occasional transfer to the intensive care unit for invasive hemodynamic monitoring under the supervision of intensivists and/or cardiologists. Perhaps the incorporation of the following actionable additions to the management protocols implemented by clinicians caring for patients with sepsis, immediately after a provisional diagnosis of sepsis has been made, may be of value in our efforts to ascertain whether SC and S-TTS are different diseases or different faces of the same coin: (1) frequent auscultation of the heart; (2) obtain consecutive troponin values; (3) obtain consecutive electrocardiograms, which occasionally may not be revealing in patients with underlying SC due to electrical cancelation stemming from the global LV involvement; (4) evaluate whether patients with SC show transient attenuation of the amplitude of the ECG QRS complexes, as noted in patients with TTS, attributed to myocardial edema,[5] which also may be present in patients with SC; and (5) since "cardiac catheterization often poses a challenge in critically ill patients,"[6] frequent ECHO examinations to evaluate whether there is LV outflow tract obstruction (LVOTO) with or without mitral regurgitation (MR), regional wall motion abnormalities, or global LV hypokinesis, via hand-held portable ECHO devices at the point-of-care (POCUS), used by many members of the caring team.[7] As emphasized by others,[4] "most ECHO parameters are dependent on loading conditions" and thus "the

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ECHO assessment should be repeated at multiple time points" during the clinical course of patients with SC.

The precise pathophysiology of SC, S-TTS, and TTS is still eluding us; the thesis presented above, i.e., of a pathophysiologic continuum, incorporating the above pathological entities may be right or wrong, but discovery is based on the testing of hypotheses that may appear, at their first articulation, wanting. I understand the concerns about the added demands imposed on the critical care units (CCU) teams caring for patients with the above afflictions, but consideration of a few additional tests or point-of-care examinations could be incorporated by physicians, nurse practitioners, nurses, physicians assistants, and ECG technicians; accordingly (1) when a patient with a provisional diagnosis of SC, or S-TTS, or TTS is cared for, one to two additional ECGs could be recorded 1 day apart; (2) three sets of cardiac enzyme biomarkers, spaced as per the CCU routine, could be ordered; (3) when the patients' blood pressure or heart rate is measured or lung auscultation is carried out, as per the CCU routine, a brief auscultation of the precordium for a murmur suggesting LVOTO or MR could be incorporated; and (4) particularly important is the frequent implementation of POCUS, and I herein refer to portable, sometimes even hand-held ECHO devices for gross assessment of LV and RV regional contraction abnormalities, LVOTO, or MR. To evaluate this, I visited our Emergency Department (ED) where I was informed that ECHO light portable machines can easily be wheeled at the patients' bedside for a cursory POCUS, and that proficiency in performing such brief ECHO assessments is part of the ED residency curriculum; the resulting image files are incorporated in the patients' electronic files, and can be reviewed by the ED team or the members of the cardiology service. Also, there is ample literature about the feasibility of imparting working POCUS skills to ED residents, and even medical students, employing a 2-h teaching session, with remarkable results in their ability to identify key diagnoses of the patients' ECHO assessment.

It is conceivable that implementing the above may reveal that SC and S-TTS are different but similar phenotypes of TTS, manifesting at different time points of the clinical course of patients with sepsis; accordingly, the global LV and RV involvement in SC may be preceded by clinical phases with LVOTO, or LV apical, mid-ventricular, basal, or focal hypokinesis/akinesis, with or without RV involvement, and regional hyperkinesis in particular LV and/or RV territories. While we engage in our explorations to differentiate SC from S-TTS or prove that SC is a phenotype of TTS, we should be cognizant of the "standard management" of SC which "includes etiological treatment, adapted fluid resuscitation, use of vasopressors, and monitoring" with the "use of inotropes remaining uncertain, and the heart rate control being an option in some patients".[4]

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Conflicts of Interest

The author declares that he has no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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