The Role of Arrhythmias in Defining Cardiac Dysfunction during Sepsis

To the Editor:

We read with interest the article by Takasu and colleagues investigating cardiac and renal pathologic changes in patients who died with sepsis (1). We have two comments and two questions for the authors:

The authors correctly point out that it is "difficult to know the extent of sepsis-induced myocardial depression" among their study subjects, who on average had normal ejection fractions and among whom only 13/38 (34%) required potent β-agonists (e.g., dobutamine or epinephrine). Circulatory failure from distributive shock requiring vasopressors may or may not occur in the setting of cardiac dysfunction. The study by Takasu and colleagues highlights the need for more clear definitions of "cardiac dysfunction" during sepsis.

New-onset arrhythmias [particularly atrial fibrillation (AF)] during sepsis traditionally have not been considered signs of "cardiac dysfunction." However, epidemiologic evidence suggests that new-onset AF represents an additional "organ failure" in patients with severe sepsis. For example, hospital mortality rates of patients with new-onset AF during sepsis are similar to patients without new-onset AF, but with one additional organ failure (2). We propose that future studies include dysfunction of the cardiac electrical system as evidence of "cardiac dysfunction during sepsis," that is, serious arrhythmias such as AF, atrial flutter, ventricular tachycardia, or ventricular fibrillation.

In regards specifically to the study by Takasu and colleagues, data from Table E4 in their online supplement shows that 6/38 (16%) of patients with sepsis had pre-existing AF and 1/38 (2.6%) developed new-onset AF. Was AF systematically ascertained by the investigators? The proportions of patients identified with AF during sepsis are much lower than previous reports.

Finally, genomic and transcriptomic variation in connexin-43 previously has been demonstrated in patients and experimental models of AF (3). Although the tissue under examination in the present study was ventricular, rather than atrial, was there overlap between the seven patients with sepsis with connexin-43 abnormalities and the seven patients who had AF during sepsis? Specifically, might AF represent an alternative mechanism for the association between sepsis and connexin-43 abnormalities? Alternatively, could connexin-43 perturbations in sepsis be a mechanism predisposing susceptible patients to AF?

Author disclosures are available with the text of this letter at www.atsjournals.org.

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Reply

From the Authors:

We appreciate the insightful comments of Dr. Walkey and colleagues regarding the work described in our article (1). Dr. Walkey and colleagues are correct when they postulate that the 2.6% incidence of new onset atrial fibrillation cited in our manuscript is likely an underestimation of the actual incidence of new onset atrial fibrillation in the septic patients. Although we have not systematically reviewed all the electrocardiogram monitor tracings in septic and critically ill nonseptic patients, we do believe that the actual incidence of atrial fibrillation is much higher in this population. If brief periods of atrial fibrillation occur, they are often not recorded. Usually, only persistent atrial fibrillation is noted in the patients' clinical records.

We also agree with Dr. Walkey and associates that new onset atrial and ventricular arrhythmias in the setting of sepsis likely represent a serious adverse effect of the disorder on the cardiac electrical apparatus and could rightly be considered an additional "organ" failure. Finally, regarding the association of atrial fibrillation with connexin-43 translocation, there was no statistically significant association but there is insufficient power to make any conclusions.

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The Effect of Etanercept on Lung Leukocyte Margination and Fibrin Deposition after Cardiac Surgery

To the Editor:

Acute lung injury (ALI) remains a major cause of death and long-term disability and an effective treatment is yet to be established. Conditions causing ALI include pneumonia, sepsis,