Timing of Noninvasive Studies in Patients With Secondary Takotsubo Syndrome

We read with great interest the study by Isogai et al, recently published in the Journal.[1] They have evaluated the differences in initial electrocardiographic (ECG) findings in a very selected cohort of patients with the typical apical form of Takotsubo Syndrome (TTS) who have been admitted in the Tokyo Cardiovascular Care Unit network. Patients were divided into 5 different groups and categorized by the time from symptom onset to the initial ECG. The main findings of the study suggest that the wide variation observed in initial ST-T changes in apical TTS is affected by the time from symptoms onset to ECG acquisition.[1] More specifically, isolated ST elevation was the most frequent pattern in the precordial leads in the <24-hour groups, whereas isolated T-wave inversion was the most frequent in the >24-hour group.[1] We wish to draw readers' attention on the potential pitfalls in ECG evaluation of secondary TTS in patients hospitalized for different conditions, especially neurovascular events.[2] These patients with secondary TTS require careful evaluation and monitoring, as the presence of neurologic disease as the trigger for TTS (Class IIb of the InterTAK classification) has been associated with the worst prognosis.[3] It is likely that if the patient has a stable hemodynamic condition and is unable to complain about chest discomfort because of the concurrent neurologic condition, the ECG could be obtained on a later stage.[4] Provided the time dependency of ECG changes,[1,5] in such cases the most common pattern of presentation would be T-wave inversion with QT-interval prolongation. In other words, the clinical picture would not resemble that of an acute myocardial infarction requiring emergency coronary angiography. We underline the role of computed tomography coronary angiography in such cases of delayed cardiologic observation of secondary TTS or for any case of retrospective evaluation of a patient with the typical history of TTS in the previous weeks or months: indeed, it remains essential to rule out coronary occlusion and significant coronary stenosis, even if with a noninvasive study.[6]

In conclusion, the authors should be congratulated for this detailed overview of ECG patterns of presentation in patients with typical primary TTS and who underwent coronary angiography in a timely fashion, according to the clinical workup of patients with acute coronary syndrome. However, the pathophysiologic condition is different than that of coronary atherosclerosis and bystander coronary disease may be present as well. Thus, the most suitable risk stratification and management of TTS patients necessarily requires a comprehensive evaluation in which all noninvasive studies, beyond timing of ECG, play a crucial role.

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8 October 2018

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https://doi.org/10.1016/j.amjcard.2018.10.001

Questionable Study Inclusion in Meta-Analysis

To the Editor,—

Elgendy et al performed an elegant meta-analysis of randomized clinical trials that compared catheter ablation with medical management in patients with heart failure and atrial fibrillation.[1] They concluded that catheter ablation was associated with significant improvements in important clinical variables including survival and heart failure hospitalizations. In my view, however, it is questionable if the latest and largest CASTLE-AF trial[2] should have been included in the meta-analysis.

As we have recently pointed out, the trial design of CASTLE-AF had structural bias that clearly favored catheter ablation.[3] Patients were enrolled only if they had no previous response to or had unacceptable side effects from antiarrhythmic drugs, or if they were not willing to take such drugs. These were important and enforced criteria as 210 patients were excluded from randomization specifically for not fulfilling the antiarrhythmic drug failure requirement [Ref. 2, Supplementary Appendix]. Nonetheless, per protocol, patients assigned to medical therapy were still encouraged to proceed with pharmacologic rhythm control. Such a strategy essentially predetermined a superior outcome with ablation: by randomizing only antiarrhythmic drug failures to catheter ablation versus medical management that included antiarrhythmic drug therapy, it was to be expected that catheter ablation would become the "winner." Appropriate and easily achievable approaches would have been to enroll patients regardless of results of previous antiarrhythmic treatment, or to randomize antiarrhythmic drug failures to catheter ablation versus