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Letters

TO THE EDITOR

What Is the Prevalence of Diabetes Mellitus in Patients With Principal and Secondary Takotsubo Syndrome?

I read with great interest the report by Murugiah et al. (1) and the accompanying editorial by Sharkey (2), published in *JACC: Heart Failure*, about the prevalence of Takotsubo syndrome (TTS) and some relevant particulars of patients in the United States, derived from the 2007 to 2012 Centers for Medicare & Medicaid Services dataset. The authors and the editorialist (1,2) refer to the important issue of the "2 clinical scenarios" of TTS "either as a principal event (P-TTS) or as a secondary event (S-TTS) in the context of a co-existing major illness" (1,2), and the authors report separately on the patient characteristics and outcome in these 2 subcategories of TTS patients. Curiously, the authors refer to the "principal diagnoses of TTS" as "more likely representing primary coronary presentations of TTS" (1), as if it had been already established that TTS is due to some pathological/functional alterations of the coronary arteries, which is not the case. They analyzed data for the years 2007, 2009, and 2011, and in patients with both P-TTS and S-TTS, they found that their mean age was 76.0 versus 76.4 years, respectively, and the prevalence of hypertension (67.4% vs. 63.1%), diabetes mellitus (18.5% vs. 20.1%), and previous diagnosis of atherosclerotic disease (46.1% vs. 47.5%) were similar (1).

In another study of patients of similar mean age (74.6 years old), on the basis of individually reported single cases, the prevalence of hypertension was 52.2% and that of diabetes mellitus was 12.5% (3), but this cohort did not have a history of atherosclerotic disease (3), in contrast to the patients with P-TTS and S-TTS of the present study, with prevalence of atherosclerotic disease in >46% of the patients (1). Both the present study (1) and that based on individual cases from the literature (3) comprised patients of the same mean age who underwent "coronary angiography without revascularization therapy" (1), but they seem to have a different risk factors burden. Of course, the former examines patients residing in the United States, whereas the latter represent populations from the entire world. One wonders whether the latter populations are more suitable for studying the pure Takotsubo phenotype (i.e., P-TTS), in terms of disease pathophysiology, because they bare "less contamination" by "atherosclerotic disease." However, this does not detract from the importance of studying patients with TTS residing in the United States, and learning how to best take care of them. Both approaches have merit, scientifically and in terms of applied science, but we should evaluate whether these 2 (local or national patient databases, generated by practicing physicians versus pooled literature case reports produced by physicians with a specific focus on the underlying pathology) represent different (albeit complementary) slices of reality. I will greatly appreciate the response of the authors on the above.

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Please note: Dr. Madias has reported that he has no relationships relevant to the contents of this paper to disclose.

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REPLY: What Is the Prevalence of Diabetes Mellitus in Patients With Principal and Secondary Takotsubo Syndrome?

We thank Dr. Madias for his interest in our paper and for his comments. With regard to the first comment concerning the cohort with a principal diagnosis of Takotsubo cardiomyopathy (TTC), we would like to

clarify that by "coronary presentations of TTC," we mean patients presenting with symptoms suggestive of an acute coronary syndrome, as opposed to those being admitted with infective symptoms (e.g., sepsis) or neurological symptoms, as in a stroke, etc. We are not suggesting that the causal mechanism for TTC among principal TTC patients involves a pathological or functional alteration of the coronaries.

With his second comment, Dr. Madias makes an important observation about differences in cardiac risk factor burden. There is likely to be important heterogeneity between U.S. and international studies of TTC in terms of risk factor and coronary artery disease (CAD) burden, and we are not surprised by this finding. We know this to be true in terms of the prevalence of comorbidities, health care delivery, and socioeconomics and other contextual factors between different global populations in general (1), factors that are likely also relevant in TTC.

With regard to CAD and TTC, CAD is frequently encountered in patients with TTC, and we don't think it must be regarded as a "contamination" of a true phenotype of TTC. A recently published report from the International Takotsubo Registry showed that patients with TTC had a 15.3% prevalence of coexistent CAD (2). Other studies reporting angiographic findings in patients with TTC have reported a 40% to 80% prevalence of CAD (3,4). The Mayo criteria for establishing a diagnosis of TTC require the absence of "obstructive" CAD or evidence of acute plaque disruption (5). If CAD is found but the wall motion abnormalities are not in the distribution of the stenosis, the diagnosis of TTC can still be made. However, the role of CAD or coronary artery dysfunction in the pathogenesis of TTC, as Dr. Madias points out, is unclear.

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