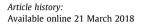
Editorial

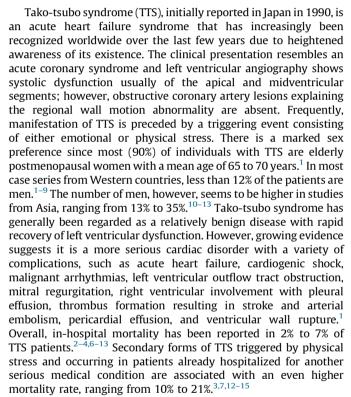
Do Male Hearts Break Differently?

¿Cómo se les rompe el corazón a los hombres?

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One still poorly understood aspect of TTS is the obvious female preponderance. Besides pathophysiological differences in the cardiovascular system, such as the higher prevalence of microvascular abnormalities predisposing women to develop TTS, it is currently unclear whether underdiagnosis or misdiagnosis may contribute to the apparently lower prevalence of TTS in men. Another reason for underestimating the prevalence of TTS in men could be that they more often die suddenly in the early phase of TTS and the diagnosis cannot be established because the typical course of this syndrome with rapid resolution of the wall abnormality cannot be documented. The fact that men more

frequently arrive at hospital after resuscitation indicates a greater electrical vulnerability in the early phase of TTS. ^{4,6}

In this context, a recent article published in Revista Española de Cardiología by Pérez-Castellanos et al. evaluated sex differences in the RETAKO registry, focusing mainly on complications and prognosis. Between 2003 and 2015, 562 patients from 32 Spanish hospitals with a diagnosis of TTS according to the modified Mayo criteria had been included in the registry.9 The mean age was 69.5 ± 14.5 years, and 493 patients (87.7%) were women. Chest pain as the presenting symptom was significantly more frequent in women and syncope was more frequent in men, and more men were current smokers. These findings are well in accordance with previous studies in other Western countries. 4,6,15 Regarding age, additional cardiovascular risk factors, baseline functional class, electrocardiogram findings, and left ventricular ejection fraction, no significant differences were found between the sexes. During the clinical course. left ventricular outflow tract obstruction and mitral regurgitation of moderate to severe degree, in part due to systolic anterior motion of the mitral leaflet, was seen more frequently in women. This contrasts with the results of 3 studies from Germany and Japan, where the frequency of left ventricular outflow tract obstruction was similar in male and female patients. 4,10,11 Possibly, these findings may have been influenced by other factors, such as the use of inotropic drugs, nitrates, or different premedication with diuretics, angiotensin-converting enzyme inhibitors, and beta-blockers. In the RETAKO registry, other complications such as severe heart failure and cardiogenic shock occurred significantly more often in men and resulted in a longer stay in the intensive care unit. In the literature, there are conflicting results, since some studies found no significant sex difference regarding cardiogenic shock, 4,6,8 whereas others reported a significantly higher prevalence in men.^{3,11} Overall, in-hospital mortality in the RETAKO registry was low (0.7%) but was higher in men than in women (4.4% vs 0.2%, P < .01). However, secondary TTS, known to be associated with a worse prognosis, was significantly more frequent in male patients and may in part be responsible for the higher mortality rate in men. Similarly, a metaanalysis of 37 studies¹¹ and evaluation of the United States National Inpatient Database³ found significantly higher in-hospital mortality in men. In these studies, the presence of underlying critical illness was

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the main driver of mortality and most likely explained the higher mortality rate among men. The InterTAK registry⁶ also reported significantly higher mortality in men. However, in a multivariate analysis including a physical trigger as a covariate, sex was no longer a significant predictor of worse outcome. Moreover, multivariate analysis in a study of 3719 patients with TTS from the Diagnosis Procedure Combination database in Japan showed that secondary TTS and old age but not male sex was associated with an increase in inhospital mortality.¹² In addition, male patients with TTS not only suffer from acute medical illnesses more frequently than women, but they also have more chronic comorbidities such as cancer, ^{8,13} chronic obstructive pulmonary disease, ^{6,8,13} and bystander coronary artery disease, ^{6,8,12} which is *per se* associated with a worse prognosis. ¹⁶

Do male hearts break differently? Overall, male patients with TTS seem to have a more severe clinical background with a higher frequency of both chronic comorbidities and acute illnesses, which determine clinical outcome. Whether "lone" TTS has indeed a worse prognosis in men than in women remains to be determined in a large prospective study.

CONFLICTS OF INTEREST

None declared.

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