

Letters to the Editor

Factors Impacting Prognosis Among Patients with Tako-tsubo Syndrome**Factores que afectan al pronóstico de pacientes con síndrome de tako-tsubo****To the Editor,**

Pérez-Castellanos et al. published an excellent analysis of the prospective RETAKO registry describing important gender disparities among patients with tako-tsubo syndrome (TTS).¹ They observed worse prognosis with higher in-hospital mortality, longer intensive care unit length of stay, and a higher prevalence of heart failure in men whereas women exhibited higher rates of functional mitral regurgitation. Dynamic left-ventricular outflow tract obstruction occurred exclusively in women.

The higher mortality rates among men with TTS could be explained by the following considerations. Men generally have a higher incidence of acute critical conditions with increased serum catecholamine concentrations, which may result in higher in-hospital mortality.² Furthermore, the lack of the direct protective effects of estrogen on the sympathetic nervous system and coronary vasoreactivity may also predispose men to the development of TTS. Estrogen improves coronary blood flow by exerting its beneficial effects on the coronary microcirculation through endothelium-dependent and independent pathways. It has been shown that the lack of estrogen replacement in postmenopausal women may be a risk factor for the development of TTS.³ Furthermore, experimental murine models have demonstrated greater left ventricular dysfunction in ovariectomized female rats than in ovariectomized rats receiving estradiol supplementation exposed to stress.⁴ Since estrogen plays a major role in the pathophysiology of TTS, most affected patients are postmenopausal women. Moreover, since estrogen has an essentially negligible role in men developing TTS, they may potentially develop at any age, mostly due to an overwhelming surge of plasma catecholamines (much higher than in women), which may potentially result in more serious short-term and long-term direct cardiotoxic effects. This may be one of the possible reasons for the higher mortality in men. In the present study, men exhibited a mortality rate of 4.4%, which is comparable to the mortality of ST-segment elevation myocardial infarction in the primary percutaneous coronary intervention era, thus making this entity particularly relevant even among men.

Traditionally thought to be a benign condition, recent studies have demonstrated that patients with TTS have higher short- and long-term mortality than previously recognized. Apart from the

impact of sex on mortality, another important factor, prognostication of TTS, also depends on the underlying trigger for TTS and thus it may be important to clinically subdivide patients into those with primary and secondary TTS forms, as we have discussed elsewhere.⁵

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Factors Impacting Prognosis Among Patients with Tako-tsubo Syndrome. Response**Factores que afectan al pronóstico de pacientes con síndrome de tako-tsubo. Respuesta****To the Editor,**

We appreciate the interest and comments of Khalid et al. regarding our article.¹ The results of the successive registries and

experimental studies add evidence to support that estrogens play an important role in the modulation of catecholaminergic discharge on the heart, thus affecting the development and outcome of tako-tsubo syndrome (TTS). It is interesting to think that this could lead in the future to design strategies for targeted treatment in patients with TTS. However, other sex-related factors probably influence this different prognosis. For instance, the number of previous pregnancies has recently been shown to be associated with a better prognosis in women with heart failure.² Also, important sex-related differences have been described in patients with acute myocardial