EDITORIAL

Takotsubo syndrome: lonely hearts

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by Budnik et al, see p. 25

Although the nosology of takotsubo syndrome (TTS) has shifted from an acute coronary syndrome–like condition to a heart failure phenotype, its pathology and clinical course still present many unresolved issues.[1] This gap in our knowledge has a significant impact on the various phases of clinical practice: from a challenging differential diagnosis to uncertain therapeutic management and prognosis.

In the current issue of *Polish Archives of Internal Medicine* (*Pol Arch Intern Med*), Budnik et al[2] present their experience regarding 232 patients with TTS from 2 Polish cohorts. The paper confirms the "state-of-the-art" profile of patients with TTS: mostly women, with a great burden of comorbidities, and with a non-negligible rate of in-hospital complications such as thromboembolism and life-threatening arrhythmias, as demonstrated by the current literature.[3,4]

Indeed, a major concern in TTS arises from evidence of a nonbenign course of the disease, contrary to what was initially thought.[1] In recent years, such findings have prompted a search for predictors of poor prognosis. The paper by Budnik et al[2] confirms that tools from the setting of acute coronary syndromes, such as heart rate on admission[5] or the Global Registry of Acute Coronary Events risk score, have proven utility.[6] However, once high-risk patients with TTS are identified, the choice of the best treatment strategy remains difficult, as their prognosis appears to be burdened not only by cardiovascular but also other mortality.[7]

This uncertainty in outcomes mainly stems from the unknown physiopathology of TTS. How do diverse predisposing factors, such as catecholaminergic excess, genetic polymorphisms, and comorbidities, interplay to induce TTS? How do emotional and physical stresses produce the same condition? How is it possible that TTS may present with diverse variants? Why are women mostly affected, but men have worse prognosis?

A central role of the heart–brain connection in the physiopathology of TTS has been suggested.[8] An interesting point highlighted by Budnik et al[2] is that men suffering from TTS are more likely to live alone.[2] Solitude in males has been established as a risk factor for developing cardiovascular diseases[9,10] and TTS.[11] Although we still do not know the underlying mechanism, it is appealing to speculate that extreme emotions, depression, menopause, and solitude may all damage the heart–brain axis and predispose to TTS.

In a certain way, all these conditions are characteristics of psychological frailty, and in TTS it all boils down to frailty in the end.[11] Apart from cardiac factors, a greater burden of comorbidity has been found to predict a worse prognosis in TTS,[12] and the burden of comorbidities itself is an indicator of frailty.[13] Moreover, an impaired cardiac function on presentation (ie, cardiogenic shock) has been linked to poor long-term prognosis, but with most of the events being noncardiovascular,[14] suggesting that, in TTS, worse cardiac parameters on presentation may merely be indicators of a fragile phenotype that is more prone to complications.[14,15]

In conclusion, though still poorly understood, TTS is an extremely intriguing disease and its study may potentially unravel important mechanisms which act not only at its basis but also in the whole spectrum of cardiovascular disease.

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