



## LETTER TO THE EDITOR

### The assessment of coronary microvascular dysfunction: An integral part of risk-stratification in Takotsubo cardiomyopathy



### Avaliação da disfunção coronária microvascular: uma parte integrante da estratificação de risco na miocardiopatia de Takotsubo

Takotsubo cardiomyopathy (TC) is widely regarded as a reversible form of stress-induced cardiomyopathy and has a variety of suggested underlying mechanisms and prognostic factors in a clinical setting.<sup>1–3</sup> Studies to date have yielded conflicting results on the pathogenetic implications of microvascular dysfunction in TC.<sup>1,2</sup> In their recently published case report,<sup>1</sup> Bayon et al. documented coronary microvascular dysfunction, assessed using parameters such as hyperemic microvascular resistance (HMR) and coronary flow reserve (CFR), in a characteristic case of TC with apical ballooning. We would like to comment on this case and obtain further information from the authors.

Firstly, coronary slow flow (CSF) pattern, assessed using the TIMI frame count (TFC) method, have been viewed as a sign of increased coronary microvascular resistance, and are generally indicative of a severe adrenergic storm and the presence of substantial levels of associated vasoconstrictor mediators, such as neuropeptide-Y (co-released with noradrenaline) in the setting of TC.<sup>2,4–10</sup> As expected, an existing CSF in this setting might also suggest high HMR values, and vice versa. What, therefore, were the baseline TFC values in the patient's major epicardial coronary arteries? Did these values also change significantly after adenosine infusion in correlation with the HMR values? This information might shed light on whether CSF patterns and increased HMR could be used interchangeably or in a complementary fashion to determine enhanced microvascular resistance in patients with TC.

Secondly, CSF pattern in TC may not be a uniform finding, yet; a prognostic sign that might only emerge in a portion of TC cases, and might predict adverse events, including arrhythmogenesis, heart failure, etc., and in these cases,<sup>2,8–10</sup> possibly in correlation with its extent and severity. This may also hold true for increased HMR values in this setting. Did the patient with apparently very high HMR

values in two of her major coronary arteries present with an arrhythmic event or decompensated heart failure in a hospital setting? Additionally, an extreme adrenergic storm during an index TC might be a predictor of recurrent episodes<sup>6,9,10</sup> and might be evidenced by very high TFC<sup>9</sup> and/or HMR values in this setting. This would require close supervision of the patient<sup>1</sup> combined with potential preventive strategies against TC recurrence in the long-term.<sup>3,9,10</sup>

Thirdly, a significant drop in baseline HMR values in response to adenosine infusion (observed in the patient's left anterior descending artery)<sup>1</sup> might help to identify TC cases that are most likely to benefit from coronary vasodilator strategies, thus improving overall prognosis.<sup>5,9</sup> This leads us to question whether the patient received any vasodilator therapy.

And lastly, the patient<sup>1</sup> was also reported to have low CFR, which has been an underrated vascular index in patients with TC. It is important to note that acutely impaired CFR might also have adjunctive prognostic value in these patients. However, given the high predilection of syndrome-X, characterized by blunted coronary vasodilation during exercise as part of generalized endothelial dysfunction in postmenopausal women,<sup>7</sup> impaired CFR might be present as a coincidental finding in certain TC cases (which might have occurred in the present case) long before index TC progression, potentially diminishing its value as an acute prognostic marker in this setting.

In summary, the authors<sup>1</sup> should be congratulated for their enlightening case report that documents coronary function as assessed by vascular indices in a patient with classical TC. Routine assessment of these parameters during coronary angiogram might enable initial risk-stratification of TC cases at disease onset, and help tailor patient-specific management strategies (vasodilators, antiarrhythmics, etc.) to improve overall prognosis in these patients.

### Conflict of interest

The authors have no conflicts of interest to declare.

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