KARDIOLOGIA POLSKA
Polish Heart Journal
The Official Peer-reviewed Journal of the Polish Cardiac Society since 1957
Online first
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ISSN 0022–9032 e-ISSN 1897–4279

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Article type: Letter to the Editor

Received: July 17, 2023

Accepted: July 21, 2023

Early publication date: July 26, 2023

Left ventricular aneurysm formation in patients with Takotsubo syndrome: A peculiar phenomenon with subtle implications. Author's reply

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We would like to sincerely thank Yalta and colleagues for their detailed observations regarding our clinical vignette [1]. We agree with our commenters that Takotsubo syndrome (TTS) is a heterogeneous and often challenging clinical diagnosis. Yalta et al. [1] provide a rationale that transient apical ballooning (TAB) during the TTS presentation might just be an epiphenomenon, or secondary phenomenon, that is caused by the presence of a left ventricular apical aneurysm (LVAA). The authors postulate that mechanical factors, such as chronic exposure to severe midventricular and intraventricular pressure gradients arising from hypertensive heart disease or hypertrophic cardiomyopathy, might have led to the progressive formation of LVAA [2]. Our colleagues suggest that in the case of a TTS presentation, it might be useful to distinguish whether the apical ballooning silhouette we typically visualize on ventriculography is indeed TAB or perhaps a preexisting LVAA. Similarly, they note that patients with LVAA rather than TAB during a presumed TTS episode might have no obvious stressors identified. They go on to suggest that cardiac magnetic resonance (CMR) imaging is an excellent method of choice to distinguish these two entities.

It is possible that the patient had a preexisting LVAA and that TAB was superimposed phenomenon. Factors that support this scenario include: (1) the lack of regression of the LVAA on the follow-up imaging; (2) the presence of concomitant inferoapical mural thrombus on initial imaging, which made the differential diagnosis challenging; (3) pronounced wall thinning of the apex; (4) the presence of late gadolinium enhancement on CMR; and (5) the patient's history of arterial hypertension. On the other hand, the patient did have a clear precipitating emotional stressor that provoked the acute decompensation episode. The acute catecholamine surge may have exacerbated the *locus minoris resistentiae* of preexisting LVAA, making it vulnerable and prone to transforming into a pseudoaneurysm. It is important to note that the CMR was performed only during the second hospitalization when we identified pseudoaneurysm. Therefore, we lack CMR data at the index presentation. However, the second transthoracic echocardiogram, performed eight weeks after the TTS episode, showed dissolution of the mural thrombus and revealed LVAA. This would favor the notion that the true LVAA might have been pathomorphological substrate for the later development of the large pseudoaneurysm.

We appreciate the comment regarding the possibility of coexisting myocardial infarction with non-obstructive coronary arteries (MINOCA), which could give rise to LVAA formation within the clinical picture of TTS. However, we performed invasive coronary angiography both during the index TTS event and several months later at the second presentation. The results showed patent epicardial coronary circulation with minimal atherosclerotic disease and no „slow-flow“ phenomenon.

It could be hypothesized that a coronary embolism originating from the mural thrombus might have caused regional ischemia in the apex of the myocardium and supported the formation of LVAA. Of note, our patient had diffuse ST segment elevations in inferior and anteroseptal leads and marked elevation of high-sensitivity troponin I levels at index presentation. The acute coronary syndrome had to be clinically excluded, while female sex, the presence of the stressful event preceding clinical presentation, regional systolic contractile dysfunction, and no obstructive epicardial coronary lesions on angiography suggested TTS as our first diagnosis [3].

It should be noted that coronary vasomotion abnormalities likely play an important role in TTS, and the key might be in the coronary microcirculation. For example, coronary microvascular dysfunction (CMD) was associated with decreased myocardial blood flow in the apex compared to the base of the heart in the experimental model of hemodynamic stress-induced TTS [4]. Additionally, the prevalence of CMD is higher in patients with TTS than with

MINOCA and more severely affects apical compared to midventricular segments. CMD also significantly affects left ventricular contractility, but it does not appear to be related to the degree of coronary atherosclerosis [5]. These clinical findings validate those observed in preclinical models, thus establishing CMD as an important pathophysiological driver in TTS. While our patient had a patent epicardial coronary circulation, this does not rule out the possibility of impaired coronary microcirculation.

Finally, we believe that the points raised by Yalta and colleagues are valuable additions to the discussion of this complex clinical conundrum. Regardless of the many intricacies and facets of TTS, the key approach that we must maintain is the initiation of cardioprotective therapies and aggressive mitigation of comorbidities that may be responsible for the clinical exacerbation. This includes the initiation and/or uptitration of agents such as ACE inhibitors, mineralocorticoid receptor antagonists, beta-blockers, high-potency statins, and antithrombotic agents.

Article information

Conflict of interest: None declared.

Funding: None.

REFERENCES

1. Yalta K, Kaya C, Yalta T. Left ventricular aneurysm formation in patients with Takotsubo syndrome: A peculiar phenomenon with subtle implications. Kardiol Pol. Kardiol Pol. 2023; epub ahead of print.
2. Yalta K, Yilmaztepe M, Zorkun C. Left ventricular dysfunction in the setting of Takotsubo cardiomyopathy: a review of clinical patterns and practical implications. Card Fail Rev. 2018; 4(1): 14–20, doi: 10.15420/cfr.2018:24:2, indexed in Pubmed: 29892470.

3. Scantlebury DC, Prasad A. Diagnosis of Takotsubo cardiomyopathy. Circ J. 2014; 78(9): 2129–2139, doi: 10.1253/circj.cj-14-0859, indexed in Pubmed: 25131525.

4. Dong F, Yin L, Sisakian H, et al. Takotsubo syndrome is a coronary microvascular disease: experimental evidence. Eur Heart J. 2023; 44(24): 2244–2253, doi: 10.1093/eurheartj/ehad274, indexed in Pubmed: 37170610.

5. Ekenbäck C, Nickander J, Jokhaji F, et al. Coronary microvascular dysfunction in Takotsubo syndrome and associations with left ventricular function. ESC Heart Fail. 2023 [Epub ahead of print], doi: 10.1002/ehf2.14394, indexed in Pubmed: 37218383.