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 their comments that takotsubo syndrome (TTS) is a heterogeneous and often challenging clinical diagnosis. Yalta et al. [1] provide an explanation why transient apical ballooning (TAB) during the TTS presentation might just have been an epiphenomenon, or secondary phenomenon, 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 the 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 during a presumed TTS episode patients with an LVAA rather than TAB might have no obvious stressors identified. They go on to suggest that cardiac magnetic resonance (CMR) imaging is an excellent method to distinguish these two entities.

It is possible that the patient had a preexisting LVAA and that TAB was a superimposed phenomenon. Factors that support this scenario include (1) the lack of LVAA regression on the follow-up imaging; (2) presence of concomitant inferoapical mural thrombus on initial imaging, which made the differential diagnosis challenging; (3) pronounced wall thinning of the apex; (4) 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 the preexisting LVAA, making it vulnerable and prone to transforming into a pseudoaneurysm. It is important to note that 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 the dissolution of the mural thrombus and revealed the LVAA. This would favor the hypothesis that the true LVAA might have been a 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 epi-

cardial 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 heart and supported the formation of the LVAA. Notably, our patient had diffuse ST-segment elevations in the inferior and anteroseptal leads and marked elevation of high-sensitivity troponin I levels at index presentation. Acute coronary syndrome had to be clinically excluded, while female sex, 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 segments 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 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 clinical exacerbations. This includes the initiation and/or up-titration of agents such as ACE inhibitors, mineralocorticoid receptor antagonists, beta-blockers, high-potency statins, and antithrombotic agents.

Article information

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