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Short Commentary

Lingering Morbidity, and Myocardial and Systemic Inflammation, in Patients with Takotsubo Syndrome

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Abstract

The aim of this commentary is to draw attention to a plausible interrelationship between a lingering morbidity, myocardial and systemic inflammation, and to the imaging modalities to detect and monitor such inflammation, in patients with Takotsubo Syndrome (TTS). Although TTS is portraited as a stress-related affliction, whose pathophysiology is still elusive, systemic and myocardial inflammation appears to be a prominent accompaniment.

Discussion

I find fascinating the persistence of inflammation in patients with TTS, both during the acute phase and at the 5-month follow-up testing, reported in a recent study [1]. I also concur with the authors [2,3] about the lingering phenotypic phase of TTS in some patients, characterized by mild unexplained chest pains, often of short duration, dyspnea at rest and on exertion, fatigue, and palpitations, in-spite of the normalization of the left ventricular function, and even after return of the inverted T-waves in the Electrocardiogram (ECG) to the upright position, persisting for several months after the acute TTS episode.

The above have been observed in our clinic where our patients with prior TTS have been followed; however, no systematic evaluation has been carried out regarding the frequency of this problem, the duration of these symptoms, and whether they eventually completely dissipate. Indeed, of great interest would be whether this myocardial and systemic inflammation in patients with TTS persists beyond the 5-month time point, for which data currently exist [1]. One also wonders whether this phenotype is due to lingering TTS or recurrent multiple atypical (i.e., subclinical) TTS episodes, the existence of which should be explored in the future, at least via the ECG, employing "smart-phone"-based technology, in ambulatory patients after hospital discharge following the index TTS admission [4]. Finally, one wonders whether some patients with otherwise unexplainable types of dilated cardiomyopathy and/or heart failure, have been the victims of chronic recurrent atypical subclinical bouts of TTS [5].

Scally et al [1] have provided compelling evidence of underlying myocardial and systemic inflammation, expressed as macrophage and pro-inflammatory monocyte subpopulations infiltration, and activation of serum cytokines, persisting in the form of a milder chronic inflammatory state, at least until 5 months, the time point at which the follow-up retesting of the patients was carried out. In the process the authors have uncovered evidence of left ventricular Myocardial Edema (ME), assessed with native T1 Magnetic Resonance Imaging (MRI) mapping, involving not only the myocardial territories displaying regional wall contraction abnormalities, but the entire left ventricle, thus including myocardial regions displaying a normal or hypercontractile activity during acute testing; however at 5-month retesting such T1 values were not different than the ones of the control subjects for both the previously acutely left ventricular ballooning and non-ballooning segments [1]. The authors were prudent to emphasize that this inflammatory state may represent an epiphenomenon and not necessarily the cause of TTS, and its role at least in the lingering TTS phase can be ascertained only by randomized controlled trials of anti-inflammatory interventions, which potentially may result in a dissipation of the inflammation evidence [1]. Indeed the same authors [6] have evaluated the issue of inflammation and its temporal course in a murine model of TTS, with additional limited autopsy data from 2 patients who succumbed to TTS; in both, systemic and myocardial inflammation were prominent features of TTS with some distinct differences, from what is observed in acute myocardial infarction. In addition, the authors expressed the opinion that inflammation and its mediated ME may be at the roots of the long-term persistent symptoms, that occur in some patients with TTS, and that these pathohistological consequences may merit specific modulation targeting, as a therapeutic option [6].

It has been previously reported [7] that low amplitude of the ECG QRS complexes are highly prevalent in patients with TTS, on admission, or develop in the early clinical course;

these ECG QRS amplitude attenuations are transient, as assessed by subsequent ECGs at follow-up, and are attributed to ME [7]. Indeed, not only the ECG QRS attenuation, but the inverted T-waves, and the prolonged QTc in patients with TTS have been attributed to ME. An opportunity arises in studies like the one of Scally et al [1], to correlate native T1 values for "the whole left ventricle" [1], from the acute and 5-month testing, with the corresponding ECG QRS amplitudes, as previously shown [7], employing data from patients who had repeat testing. The state of ME in the acute TTS phase, involving not only the ballooned territories, but to a lesser degree the myocardial regions displaying normal or hypercontractile function, along with the dissipation of ME at follow-up [1], may be reflected in the changes in the ECG QRS amplitudes, witnessed during the acute, subacute [7], and follow-up phase of patients with TTS. Thus, an ECG-based index of ME could become available for the serial assessment of all patients with TTS, not only for a limited number of patients (i.e., N=48), who underwent the repeat MRI analysis implemented by Scally et al [1].

Conclusion

The above suggest that systemic and myocardial inflammation, consequent ME, and lingering morbidity in some patients with TTS may be interrelated, and are worth of our attention and scrutiny, employing various currently available modalities. In addition, their elucidation may aid in deciphering the pathophysiology of this enigmatic disease, and provide specific therapies for its management, and prevention for its occasional protracted clinical course.

Disclosures

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References

1. Scally C, Abbas H, Ahearn T, Srinivasan J, Mezincescu A, et al. (2019) Myocardial and systemic inflammation in acute stress-induced (takotsubo) cardiomyopathy. Circulation. 139:1581-1592 [Crossref]
2. Scally C, Rudd A, Mezincescu A, Wilson H, Srivanasan J, et al. (2018) Persistent long-term structural, functional, and metabolic changes after stress-induced (takotsubo) cardiomyopathy. Circulation. 137:1039-1048. [Crossref]
3. Madias JE (2016) Recurrence, lingering recovery course, mild variants, and "chronic" forms, of takotsubo syndrome. Int J Cardiol. 220:70-71. [Crossref]
4. Madias JE (2015) Is there a "chronic takotsubo syndrome"? Could "smartphone"-based technology be of aid? Int J Cardiol. 186:297-298. [Crossref]
5. Madias JE (2014) Decompensated chronic heart failure > Takotsubo syndrome versus Takotsubo syndrome > decompensated chronic heart failure: two plausible inverse parallels. Int J Cardiol. 173:319. [Crossref]
6. Wilson HM, Cheyne L, Brown PAJ, Kerr K, Hannah A, et al. (2018) Characterization of the myocardial inflammatory response in acute stress-induced (takotsubo) cardiomyopathy. JACC Basic Trans Sci. 3:766-778. [Crossref]
7. Madias JE (2014) Transient attenuation of the amplitude of the QRS complexes in the diagnosis of takotsubo syndrome. Eur Heart J Acute Cardiovasc Care. 3:28-36. [Crossref]