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Short Communication

Takotsubo cardiomyopathy and acute coronary syndromes: Are they always mutually exclusive?

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In clinical practice, takotsubo cardiomyopathy (TTC) and acute coronary syndromes (ACS) may not always appear to be mutually exclusive potentially denoting a co-existence of these two conditions in a portion of suspected ACS admissions.[1,2] Within this context, absence of critical coronary lesions through coronary imaging might, to a large extent, be suggestive of TTC in isolation in patients with suspected ACS. Conversely, an ACS with a critical or total occlusion on coronary imaging may not definitely exclude an accompanying TTC in these patients. On the other hand, the presence of significant coronary artery stenosis (≥50%) in patients with a final diagnosis of TTC was not a rare finding (as was previously considered) in some TTC series.[3] However, coronary artery disease (CAD) in the setting of TTC has been generally regarded only as a silent bystander, and not a co-existing acute clinical phenomenon that might contribute to the clinical presentation in the acute setting. Therefore, previous reports on TTC, despite their particular emphasis on co-existing CAD in certain settings,[3] did not specifically highlight TTC-ACS co-existence and its clinical implications in a detailed manner so far. Accordingly, we would like to comment on potential predictors and clinical relevance of this co-existence in the clinical setting:

Firstly, spontaneous coronary artery dissection (SCAD) has emerged as a distinct phenomenon mostly presenting with an ACS in clinical practice.[1] More importantly, there may exist a subtle relation between SCAD and TTC largely owing to the common origin of these conditions (excessive endogenous stress with adrenergic hyperactivation).[1] Furthermore, an ACS associated with SCAD may serve as a substantial trigger of TTC during its course.[1] Therefore, it should be borne in mind that an ACS presentation with an existing SCAD appearance on CAG might be suggestive of an accompanying TTC necessitating further investigation of the patient.

Secondly; systemic inflammation on top of sympathetic hyperactivation, was previously suggested to contribute to the evolution of TTC through enhanced adrenoceptor hypersensitivity particularly in the setting of serious conditions including cancer.[4] On the other hand, there also exists a well-known association of systemic inflammation with atherosclerotic plaque instability along with its particular impact on ACS evolution. Therefore; excessive levels of systemic inflammation response might also account for the co-occurence of ACS and TTC largely due to the detrimental effects of certain mediators (including cytokines, etc.) both on myocardium[4] and atherosclerotic plaque stability.

Thirdly; since acute or chronic physical stressors are associated with a more substantial adrenergic activation and systemic inflammation response in comparison to emotional ones,[4,5] a history of such stressors might be suggestive of a TTC— ACS co-existence as well. However, this may only apply to the setting of extraordinary and excessive physical triggers including severe strenuous excercise, chronic debilitating disease, etc. and might possibly be confined to a small portion of ACS cases in clinical practice.

Fourthly; certain patient and ACS characteristics might also predispose to this co-existence: very old age (85 years and over) and frailty in the setting of ACS might be regarded as enhanced vulnerability to internal or external stressors due to a substantial decline in physiological reserve[6] potentially increasing the risk of ACS-TTC co-existence. Similarly, certain ACS characteristics might also signify this co-existence: for instance; an extensive myocardial infarction with hemodynamic compromise or with an intractable chest pain might be more likely to trigger a TTC attack largely due to the excessive sympathetic discharge associated with these settings. Accordingly, TTC arising as a complication of ACS has been very rarely reported in the literature.[2] Potential risk

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Table 1
Potential risk factors (and hence predictors) (1–6) for ACS-TTC co-existence in the clinical setting.

SCAD on coronary imaging
History of excessive physical stressors
Severe systemic inflammation on admission [a]
Very old age (85 years and over)
Frailty
Extensive myocardial infarction or mechanical complications in the setting of ACS[b]
Severe and intractable chest pain

ACS; acute coronary syndrome, TTC; takotsubo cardiomyopathy, SCAD; spontaneous coronary artery dissection.
[a] Presenting with substantial levels of inflammation markers.
[b] Particularly presenting with hemodynamic compromise.

factors (and hence predictors) for ACS-TTC co-existence are summarized in Table 1.

On the other hand, despite the guidance of these potential risk factors, definitive diagnosis of an accompanying TTC on top of ACS might not be so easy through basic diagnostic modalities (echocardiogram, etc.) particularly when these two conditions involve the same or largely intersecting myocardial territories. Since transient wall motion abnormalities (WMA) in patients with ACS are generally attributed to myocardial stunning associated with reperfusion, etc., TTC mostly go undetected in these patients. However, it should be borne in mind that a portion of transient WMAs in the setting of ACS might be due to a co-existing TTC particularly when they emerge remote from the infarct or ischemia-related territory. On the other hand, cardiac magnetic resonance imaging (MRI) might work much better to define myocardial tissue characteristics (including edema, etc.),[7] and hence; to confirm the final diagnosis of TTC in suspected cases. However, majority of clinicians may feel reluctant to perform MRI in ACS patients managed with coronary stenting (despite its reported safety in this setting) just to diagnose an accompanying TTC.

Lastly; co-existence of ACS and TTC might be associated with a variety of adverse outcomes including acute heart failure, mechanical complications as well as arrhythmogenesis and sudden cardiac death (SCD) (as compared with ACS in isolation).[1] However, the evolution and magnitude of these complications largely depend on the intensity of the common trigger (inflammation, etc.) as well as the extent and location of the emerging myocardial injury and stunning. Clinical suspicion or confirmation of such a co-existence may warrant strict management strategies including close monitoring and intensive therapeutic regimens (higher doses of agents with proven mortality benefit, prophylactic antarrhythmics?, mechanical support in certain settings, etc.) for the prevention as well as timely management of these complications.

In conclusion, co-existence of ACS and TTC may be more prevalent than expected in clinical practice, and more importantly; it might not always be feasible to exclude TTC even after coronary imaging in ACS admissions. These notions appear to be in line with the recent literature demonstrating the presence of significant CAD in a portion of patients with a final diagnosis of TTC.[3] However, an existing severe CAD might not always signify an accompanying ACS, and might also appear only as a silent bystander in the setting of TTC. Accordingly, a variety of risk factors[1–6] may potentially aid in the identification of patients with a potential ACS-TTC co-existence in clinical practice. However, despite the guidance of these risk factors, definitive diagnosis of such a co-existence may be quite challenging through basic modalities particularly when these two conditions involve the same or largely intersecting myocardial territories. As ACS-TTC co-existence potentially harbors diagnostic and prognostic implications,[1,2] future studies are still warranted to investigate the clinical relevance, and more importantly; absolute predictors of such a co-existence (along with a simple risk score) in the clinical setting.

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