Recurrence of Takotsubo Cardiomyopathy

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Abstract

Takotsubo cardiomyopathy (TC) is transient systolic dysfunction of the left ventricle (LV) occurring mainly in post-menopausal women after a stressful event. It is associated with characteristic LV contraction patterns. While the prognosis for TC patients is generally favorable, some patients experience recurrence of TC, once or sometimes multiple times. This review summarizes current knowledge of recurrence of TC. Recurrence rate of TC has ranged from 0 to 10%. Although clinical correlates determining recurrence of TC have not been identified, the recurrence rate is higher in patients with severe LV dysfunction during initial TC event or younger female patients. Preventive therapy for recurrent TC has not been established. β-blockers are commonly used in the prevention of TC recurrence but no evidence to date supports their efficacy. Angiotensin converting enzyme inhibitors and angiotensin receptor blockers may have a role to prevent recurrence of TC. In patients with multiple recurrent TC triggered by emotional stress or suffering from anxiety disorder, psychological counseling or antianxiety drugs may be beneficial for preventing recurrence of TC.

Keywords: Takotsubo Cardiomyopathy; Recurrence

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Introduction

Takotsubo cardiomyopathy (TC) is transient systolic dysfunction of the left ventricle (LV) occurring mainly in post-menopausal women after a stressful event. It is associated with characteristic LV contraction patterns, typically apical dyskinesia and basal hyperkinesia. The exact pathophysiology of TC is still unclear, although several hypotheses, such as multivesSEL coronary spasm, microvascular impairment, and direct catecholamine-mediated myocardial stunning, have been proposed. While the prognosis for TC patients is generally favorable, with complete recovery from LV wall motion abnormality, some patients experience recurrence of TC, once or sometimes multiple times. There is little information about the efficacy of chronic pharmacological therapy for preventing TC recurrence. This review summarizes current knowledge of TC recurrence.

Recurrence rate of takotsubo cardiomyopathy

The reported recurrence rate of TC has ranged from 0 to 10% (Table 1). Elesber et al. reported the highest recurrence rate within the first 4 years at 2.9% per year and subsequently it decreased at 1.3% per year. Singh et al. performed meta-analysis from 31 cohorts (1,664 TC patients) and reported that the annual incidence of recurrence was 1.5% and the cumulative recurrence rate increased from 1.2% at 6 months to nearly 5% at 6 years. Several cases of multiple recurrences have also been reported.

Factors predicting recurrence of takotsubo cardiomyopathy:

Clinical or demographic features determining TC recurrence have not been clearly identified. Singh et al. demonstrated that the average LV ejection fraction during the first episode was significantly lower in patients with than without TC recurrence. It may be interpreted that severe LV dysfunction reflects increased susceptibility to stressful events. Patel et al. reported that the recurrence rate was 5-fold higher in female patients <50 years of age than in those aged 50 years old or more. The reason for higher recurrence rate in younger females is unknown. The recurrence of TC is more frequent in women but no statistically significant difference has shown between men and women, probably because of the low numbers of recurrence.

Morphology and pathophysiology

Most cases of recurrent TC have the same ballooning pattern compared to that of the initial event. However, some case reports have documented recurrent TC with different ballooning patterns (i.e., apical ballooning to mid-ventricular ballooning, mid-ventricular ballooning to apical ballooning, and apical ballooning to basal ballooning). These observations are inconsistent with the currently proposed mechanisms of TC such as anatomic variations in sympathetic innervation and adrenergic receptor density. The exact pathophysiology of TC and its recurrence is unknown. Dynamic variation in the sensitivity of the cardiac adrenergic receptors or differences in the degree of stress and the subsequent level of catecholamine...
release may be responsible for different morphologic patterns between the initial and recurrent event.\textsuperscript{14} Other possible mechanisms are aging on adrenergic receptor location or density\textsuperscript{13} and a phenomenon analogous to regional ischemic preconditioning during the initial event.\textsuperscript{12}

### Prevention therapy

Prevention therapy for recurrence of TC has not been established. \( \beta \)-blockers are intuitively the most logical pharmacological prevention therapy. They may protect against stressful triggers and catecholamine surges. In fact, \( \beta \)-blockers are the most common discharge medication in patients with TC. However, two meta-analyses failed to show benefit of \( \beta \)-blockers for preventing recurrence of TC.\textsuperscript{4,17} It is postulated that the pathogenesis of TC is related to stimulation of \( \beta_2 \)- rather than \( \beta_1 \)-adrenergic receptors. \( \beta_1 \)-selective antagonists may be ineffective for preventing recurrence of TC. \( \beta \)-blockers might be useful for preventing recurrence of TC in selected patients especially with persistent anxiety and elevated sympathetic tone.

Singh et al. reported that there was a negative correlation between use of angiotensin converting enzyme inhibitors or angiotensin receptor blockers and recurrence of TC. Reduction of sympathetic activity through the renin-angiotensin system or the anti-inflammatory effect on myocardium may explain these results. In patients with multiple recurrent TC triggered by emotional stress or suffering from anxiety disorder, the psychological response to emotionally stressful triggers may be a therapeutic target. Psychological counseling or antianxiety drugs may be beneficial for preventing recurrence of TC.

### Summary

Recurrence rate of TC has ranged from 0 to 10%. Although clinical correlates determining recurrence of TC have not been identified, patients with severe LV dysfunction during initial TC event or younger women should be followed up more carefully. Preventive therapy for recurrence of TC has not been established. \( \beta \)-blockers are commonly used in the prevention of TC recurrence but no evidence to date supports their efficacy. Angiotensin converting enzyme inhibitors or angiotensin receptor blockers and psychological counseling and/or antianxiety drugs may have a role to prevent recurrence of TC.

### Declarations of Interest

The authors declare no conflicts of interest.

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### References


