Takotsubo Syndrome and Embolic Events

Ibrahim El-Battrawy, MD[a,b], Martin Borggrefe, MD[a,b], Ibrahim Akin, MD[a,b,*]

KEYWORDS

• Takotsubo cardiomyopathy • Thromboembolic events • Ventricular thrombus • Stroke

KEY POINTS

- Thromboembolism is a common complication of takotsubo cardiomyopathy (TTC).
- Patients present initially with symptoms such as chest pain and dyspnea.
- Close follow-up of patients with TTC is important to avoid overlooking this serious complication.
- There is a need for individualized therapy.

INTRODUCTION

Takotsubo cardiomyopathy (TTC), a well-known reversible disease predominantly affecting postmenopausal women,[1] was first described in 1990. It is usually precipitated by a transient apical ballooning of the left ventricle (LV) with wall motion abnormalities of the middistal and apical regions and is associated with a decreased ejection fraction. Additionally, the involvement of the right ventricle (RV) has also been described in up to 18.6% of patients.[2,3] The spontaneous recovery of stunned myocardial muscle in TTC, however, is generally observed within days or weeks.

Patients present initially with symptoms such as chest pain and dyspnea. This could mimic an acute coronary syndrome (ACS) and admitted patients are commonly treated as having suffered from one.

TTC has also been associated with some critical complications such as heart failure, life-threatening arrhythmias, atrial fibrillation, prolonged QT interval, thromboembolic events, recurrence of TTC, LV outflow obstruction, mitral valve regurgitation, and cardiac rupture.[4–9] Interestingly, the in-hospital mortality rate of TTC is similar to that of ACS.[10]

We sought to determine the epidemiologic as well as the clinical aspects of thromboembolic events in TTC.[4,11–16]

INCIDENCE OF THROMBOEMBOLIC EVENTS IN TAKOTSUBO CARDIOMYOPATHY

The incidence and clinical significance of thromboembolic events in TTC has not yet been established sufficiently. Data documenting these events are scarce and recent literature highlights only a few isolated case reports.[4,11–26]

An in-depth analysis of existing references, however, does reveal the common occurrence of intraventricular thrombus (**Fig. 1**), signifying potential relevance in many of the thromboembolic events. For example, cerebral ischemic stroke (**Fig. 2**), following to the development of a thrombus in a patient with TTC, has been reported recently in the literature. In rare cases, thromboembolic events may present as emboli in the peripheral arterial system, such as the radial, renal, pulmonary, and popliteal arteries. The incidence of ventricular thrombus formation and stroke varies between 2.5% and 8% and 1% and 5%, respectively.[4,10,14,16]

Conflict of Interest: None.

[a] First Department of Medicine, Medical Faculty Mannheim, University Heidelberg, Theodor-Kutzer-Ufer 1-3, Mannheim 68167, Germany; [b] DZHK (German Center for Cardiovascular Research), Partner Site, Heidelberg-Mannheim, Theodor-Kutzer-Ufer 1-3, Mannheim 68167, Germany

* Corresponding author. First Department of Medicine, University Medical Centre Mannheim, Theodor-Kutzer-Ufer 1-3, Mannheim 68167, Germany.

E-mail address: Ibrahim.Akin@UMM.de

Heart Failure Clin 12 (2016) 543–550

http://dx.doi.org/10.1016/j.hfc.2016.06.011

1551-7136/16/$ – see front matter

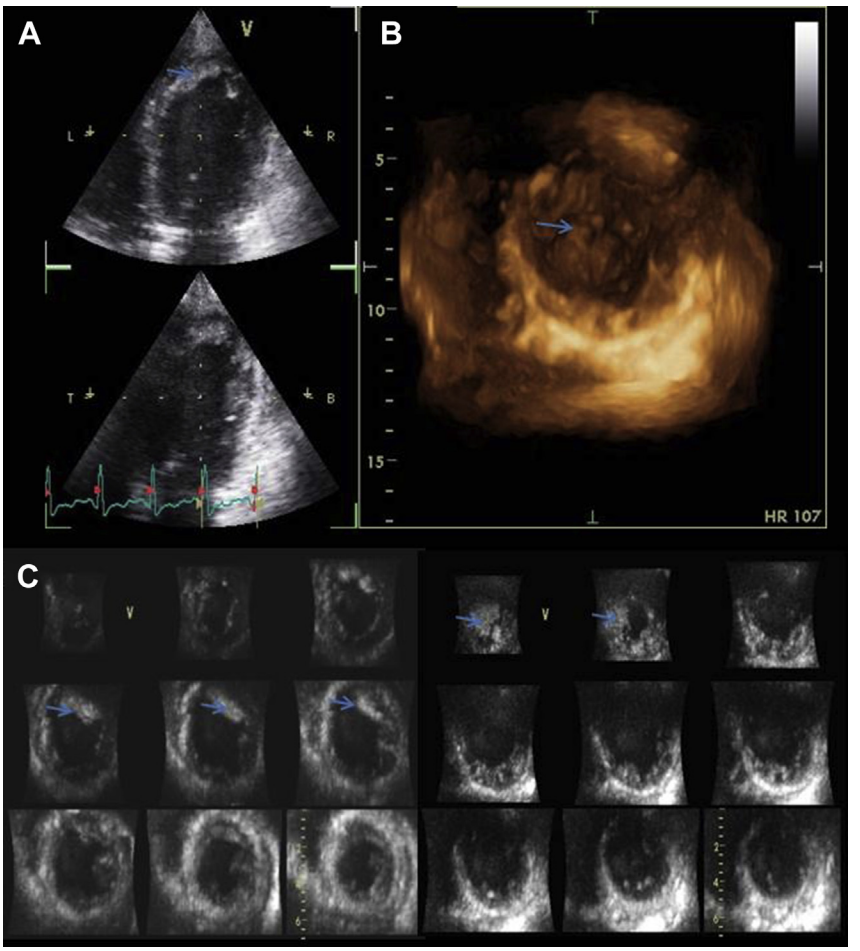

Fig. 1. (*A, B*) Echocardiography of patients with apical takotsubo cardiomyopathy showing a left ventricular thrombus formation. (*C*) A 4-dimensional full-volume dataset was used to slice the left ventricle into 9 equidistant short-axis views.

PATHOPHYSIOLOGY OF TAKOTSUBO CARDIOMYOPATHY AND RELATED EMBOLIC EVENTS

TTC occurs predominantly in postmenopausal women and the disease is usually provoked by emotional or physical stress.[1–3,27] An enhanced sympathetic activity with an elevation of catecholamine levels has been documented in these patients.[28] Furthermore, coronary vasospasm and widespread coronary microvascular dysfunction might be a contributing factor to the pathophysiologic mechanism of TTC.[29,30] Nevertheless, a defining explanation to its underlying pathogenesis remains unresolved. In general, ventricular thrombus can occur in the setting of ventricular dysfunction, especially in the acute stage after myocardial infarction,[31,32] noncompaction cardiomyopathy, dilated cardiomyopathy,[33,34] antiphospholipid antibody syndrome, hypereosinophilic syndrome, and autoimmune disorders like Adamantiadis-Behcet's disease and lupus erythematosus.[35–38] In TTC, the development of an acute ventricular thrombus is presumably explained by the triad of Virchow, outlining as cause in this scenario the low blood flow in the ventricle. The improvement of wall motion abnormality in TTC might promote discharge of this intraventricular thrombus into the peripheral bloodstream, thus initiating an embolic event.[24] Another hypothesis involving the coagulation cascade has also been proposed recently as the underlying mechanism contributing to the development of thromboemboli in patients with TTC.[39] Several endothelial markers and clotting activation biomarkers (von Willebrand factor and plasminogen) as well as lipoprotein A levels were higher in patients with TTC compared with the healthy population suggesting a role of endothelial dysfunction and similar pathologies contributing to the hyperviscosity of blood flow in TTC.[40]