




Direct current cardioversion-triggered atypical Tako-tsubo cardiomyopathy: a case report and review of literature

Ju Young Bae ¹, Joseph Tartaglia ², Michael Chen³, and John F. Setaro ^{3*}

¹Department of Internal Medicine, Yale New-Haven Health Greenwich Hospital, 5 Perryridge Road, Greenwich, CT 06830, USA; ²Section of Cardiovascular Medicine, Yale New-Haven Health Greenwich Hospital, 5 Perryridge Road, Greenwich, CT 06830, USA; and ³Section of Cardiovascular Medicine, Yale University School of Medicine and Yale New-Haven Hospital, 333 Ceder Street, New Haven, CT 06520, USA

Received 15 July 2021; first decision 6 September 2021; accepted 19 January 2022; online publish-ahead-of-print 18 February 2022

Background

Tako-tsubo stress cardiomyopathy is a clinical syndrome marked by transient reduction of left ventricular function in the setting of emotional or physical stress and in the absence of obstructive coronary artery disease. We describe a case of an atypical variant of Tako-tsubo in a male patient following an elective direct current cardioversion (DCCV).

Case summary

A 78-year-old male whose atrial fibrillation persisted after earlier unsuccessful direct current DCCV and radiofrequency ablations presented to the emergency department for acutely worsening dyspnoea and orthopnoea 12 h following his most recent DCCV. Previously, he was known to have non-obstructive coronary artery disease. Evaluation was notable for troponin I 0.019 ng/mL (negative <0.050 ng/mL), pro-brain natriuretic peptide 2321 pg/mL (reference range 0.0–900 pg/mL). There were no acute electrocardiogram abnormalities. He required bilevel positive airway pressure but was weaned off eventually to room air. Transthoracic echocardiogram revealed newly reduced left ventricular ejection fraction of 45–50%, associated with hypokinesis of the basal anteroseptal segment, as well as akinesis of mid-inferoseptal and mid-anteroseptal segments. Apical contractility was preserved. On Day 5 of hospitalization, diagnostic left heart catheterization again revealed benign coronary anatomy, and he was discharged home the following day.

Discussion

Only five other cases of cardioversion mediated Tako-tsubo cardiomyopathy have been reported in the literature. To our knowledge, this is the first case of DCCV-induced atypical Tako-tsubo cardiomyopathy. Although overall prognosis is favourable, some have been observed to require advanced support therapy. Given risk for life-threatening complications, patients undergoing cardioversion should be educated on symptoms of congestive cardiomyopathy.

Keywords

Atypical Tako-tsubo • Atrial fibrillation • Cardioversion • Case report • Pulmonary oedema • Stress cardiomyopathy • Tako-tsubo cardiomyopathy

ESC Curriculum

5.3 Atrial fibrillation • 6.2 Heart failure with reduced ejection fraction • 6.4 Acute heart failure

Learning points

- Acute pulmonary oedema and Tako-tsubo syndrome are rare complications of cardioversion that can be life threatening.
- Variant forms of Tako-tsubo cardiomyopathy are categorized by involvement of different regions of the left ventricle including sparing of the apex.

* Corresponding author. Tel: +1 203 785 4129, Email: john.setaro@yale.edu

Handling Editor: Marta Cvijic

Peer-reviewers: Emilia D'Elia; Maria Concetta Pastore

Compliance Editor: Debbie Falconer

Supplementary Material Editor: Elhosseyn Guella

© The Author(s) 2022. Published by Oxford University Press on behalf of the European Society of Cardiology.

This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial License (<https://creativecommons.org/licenses/by-nc/4.0/>), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact journals.permissions@oup.com

Introduction

Tako-tsubo cardiomyopathy is an acute and reversible form of cardiomyopathy that mimics an acute coronary event and was first described by Sato *et al.* in 1990.¹ Preceding emotional or physical stress is a classic predisposing factor, and the syndrome is most prevalent in post-menopausal women.² A wide range of triggers has been described, yet there are only five reported cases of Tako-tsubo syndrome following direct current cardioversion (DCCV).^{3–7}

In this case report, we describe a case of an anatomically atypical variant of Tako-tsubo in a 78-year-old male following an elective DCCV for persistent atrial fibrillation. To our knowledge, this is the first case of DCCV-induced atypical Tako-tsubo cardiomyopathy.

Timeline

Hospital day	Events
Morning prior to admission	Successful elective direct current cardioversion (DCCV) to sinus rhythm
Day 0, emergency department	Admitted to intermediate care unit due to 12 h of progressively worsening dyspnoea following elective DCCV conducted earlier that morning Electrocardiogram: sinus rhythm. No acute ST-changes. Chest X-ray: cardiomegaly and pulmonary oedema Oxygen requirements: bilevel positive airway pressure
Day 1, intermediate care unit	Transthoracic echocardiogram (TTE): left ventricular ejection fraction (LVEF) 45–50%, hypokinesis of basal anteroseptal segment, as well as akinesis of mid inferoseptal and mid anteroseptal segments New treatment: carvedilol, spironolactone Oxygen requirement: 2 L of oxygen via nasal cannula (NC)
Day 3, intermediate care unit	Lab: international normalized ratio 2.12→1.73 New treatment: intravenous heparin Oxygen requirement: 3 L of oxygen via NC
Day 4, intermediate care unit	Oxygen requirement: room air

Continued

Continued

Hospital day	Events
Day 5, intermediate care unit	Diagnostic left heart catheterization: non-obstructive coronary vessels; diagnosis of DCCV-induced Tako-tsubo syndrome established Oxygen requirement: room air
Day 6, intermediate care unit	Discharged home
2-month follow-up, outpatient	Normalization of LVEF and normal wall motion on TTE

Case presentation

A 78-year-old male with a history of persistent atrial fibrillation, hypertension, Stage 3 chronic kidney disease, non-obstructive coronary artery disease (2018), thoracic aortic aneurysm (4.5 cm), and Gilbert syndrome presented with progressively worsening dyspnoea, orthopnoea, and wheezing for 12 h following elective DCCV conducted earlier that morning. The patient had prior DCCV attempts and radiofrequency ablation that were unsuccessful on a longitudinal basis.

The patient was afebrile, and his vital signs included pulse 95 beats/minute (b.p.m.), blood pressure 177/94 mmHg, respiratory rate 34 breaths/minute, and oxygen saturation 90% on room air that improved with bilevel positive airway pressure. Physical exam was notable for reduced breath sounds throughout his thorax with visible rib cage retractions during inspiration and an inability to complete full sentences. No peripheral oedema was seen.

Initial labs were notable for white blood count of $17.9 \times 10^3/\mu\text{L}$, creatinine 1.39 mg/dL (baseline), total bilirubin 2.8 mg/dL, direct bilirubin 0.5 mg/dL, troponin I 0.019 ng/mL (reference ranges <0.050 = negative; 0.050–1.50 = indeterminate; >1.500 = positive), pro-brain natriuretic peptide 2321 pg/mL (reference range 0.0–1800 pg/mL), and international normalized ratio (INR) 3.24. Severe acute respiratory syndrome coronavirus 2 polymerase chain reaction was negative. Electrocardiogram (ECG) showed normal sinus rhythm at heart rate of 72 b.p.m. without any acute ST-changes (*Figure 1*). Chest radiograph demonstrated interval development of moderate cardiomegaly and prominent pulmonary oedema without pleural effusion (*Figure 2*). In the emergency department, he was given furosemide 40 mg intravenously.

On hospital day (HD) 1, the patient's white blood cell count normalized to $9.7 \times 10^3/\mu\text{L}$. INR was 3.49, and troponin I peaked at 0.173 ng/mL. His respiratory status improved, and he was transitioned to 2 L of oxygen via nasal cannula. Transthoracic echocardiogram (TTE) showed newly reduced left ventricular ejection fraction (LVEF) of 45–50%, moderate concentric left ventricular (LV) hypertrophy, biatrial enlargement, hypokinesis of apical septum and basal anteroseptal segment, as well as akinesis of mid inferoseptal and mid anteroseptal segments. In contrast to the typical Tako-tsubo pattern,

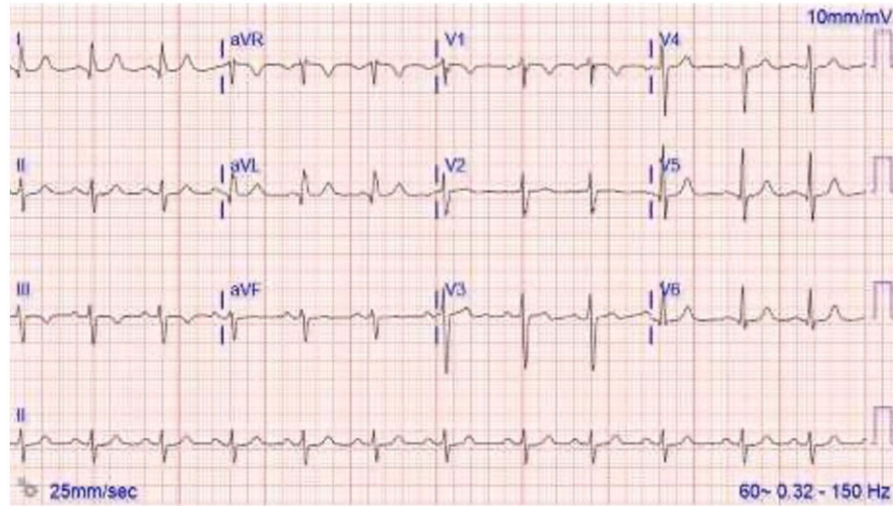


Figure 1 Admission electrocardiogram.

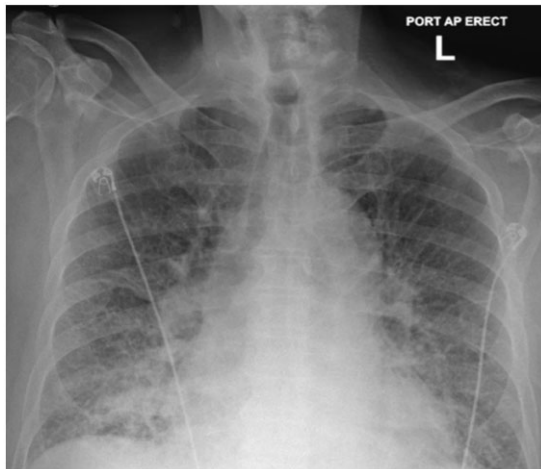
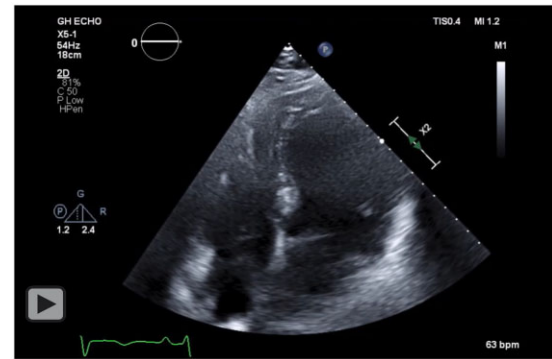


Figure 2 Admission chest X-ray.



Video 1 Admission transthoracic echocardiogram.

apical contractility was preserved ([Video 1](#), [Table 1](#)). Transthoracic echocardiogram performed 1 year prior had shown normal LVEF and no evidence of any wall motion abnormalities. He was continued on sotalolol 160 mg two times daily, diltiazem 180 mg daily as needed, losartan 25 mg daily and furosemide 40 mg daily. His home regimen had included metoprolol tartrate 50 mg two times daily, but this medication was discontinued as both spironolactone 25 mg daily and carvedilol 12.5 mg two times daily were added to his regimen. On HD 3, intravenous heparin was started because of subtherapeutic INR. The patient was weaned off supplemental oxygen, and on HD 5, diagnostic left heart catheterization demonstrated no evidence of obstructive coronary artery disease. The patient was resumed on warfarin 3 mg daily, and diltiazem 180 mg daily as needed was discontinued. The patient was discharged home on HD 6 with

scheduled outpatient cardiology follow-up. Repeat TTE at 2 months showed restoration of LVEF at 60% with no regional wall motion abnormalities ([Video 2](#), [Table 1](#)).

Discussion

This is the first reported case of an atypical variant Tako-tsubo stress cardiomyopathy diagnosed after DCCV, and the second reported case of post-DCCV stress cardiomyopathy in a male patient. Based on review of the cardiovascular literature, the typical variant of Tako-tsubo with apical impairment has been observed in 75–80% of all Tako-tsubo cases.⁸ It typically manifests as transient LV dysfunction associated with ECG changes such as ST-segment elevation or depression, T-wave inversion, or QTc prolongation, and moderately elevated levels of cardiac biomarkers. Diagnosis of Tako-tsubo may be challenging especially with rare or atypical presentations. In order to improve specificity of Tako-tsubo cardiomyopathy diagnosis, new

international diagnostic criteria (InterkTAK Diagnostic Criteria) has been introduced with score of greater than 50 specific for Tako-tsubo diagnosis.⁹ Our patient's score was 25.

The pathophysiology of Tako-tsubo syndrome after DCCV is not well established, but proposed hypotheses include (i) acute myocardial injury or myocardial stunning arising from catecholamine release¹⁰; (ii) ischaemia-induced myocardial stunning secondary to microvascular or multi-vessel vasospasm¹¹; and (iii) direct injury of the myocardium by the shock current.¹² An animal study modelling Tako-tsubo demonstrated high serum epinephrine levels with apical-basal gradient in pleiotropic β 2-adrenoreceptors in the setting of apical myocardial depression, which is consistent with the typical echocardiogram findings in Tako-tsubo syndrome.¹³

We reviewed characteristics of all six reported cases of DCCV-induced Tako-tsubo syndrome to identify potential associations (Table 2). Consistent with the known female predominance, 66% (4 of 6) were women with mean age of 77 years (age range 67–87). Underlying rhythm was most commonly atrial fibrillation (5 of 6), and mean troponin I was 1.49 ng/mL (range 0.173–3.39 ng/mL). Time to presentation at the emergency department post-DCCV ranged from immediately after the procedure to 36 h (mean of 14.5 h). Interestingly, all six patients had other underlying cardiac conditions in addition to atrial fibrillation. Despite their advanced age, all patients

survived to hospital discharge with eventual restoration of LV function.

Acute pulmonary oedema is a rare complication seen after DCCV with only 30 cases reported in the medical literature.¹¹ In addition to pulmonary oedema, our patient demonstrated atypical features of Tako-tsubo syndrome including male gender, absence of significant troponaemia, absence of ischaemic ECG changes, and presence of multiple regional wall motion abnormalities with apical sparing, which posed a challenge in determining the diagnosis. Myocarditis was considered as an alternative diagnosis but was deemed unlikely due to the absence of ECG changes, lack of infectious prodrome, insignificant troponaemia, presence of regional wall motion abnormalities, the rapid onset of symptoms after DCCV, and similarly quick improvement in symptoms without the use of anti-inflammatory therapies. Interestingly, all previously reported cases of Tako-tsubo syndrome post-DCCV required either pressor support, mechanical ventilation, or both, yet our patient did not require advanced supportive therapy.

Medical therapy for Tako-tsubo cardiomyopathy is based on the presence or absence of haemodynamic stability and other complications. Patients who like our case have complications such as acute heart failure without LV outflow tract obstruction should receive diuretics, angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor blocker, and beta-blockers. However, in comparison to the mortality benefit seen in other types of heart failure, therapy with beta-blockers and ACE inhibitors do not confer significant survival benefit in patients with Tako-tsubo cardiomyopathy.^{14,15} In addition, only ACE inhibitors were shown to help prevent the recurrence of Tako-tsubo induced cardiomyopathy.¹⁶ The role of aldosterone antagonists have not been well-established, but they have been hypothesized to be potentially cardioprotective due to anti-catecholamine effects.¹⁷ Guidelines on the duration of treatment are lacking, but patients are typically treated for 4 weeks until improvement of LVEF is seen. There are no studies that have evaluated the role of goal-directed medical therapy on atypical variant Tako-tsubo. Our patient was transitioned to carvedilol for additional blood pressure control, diuretics for optimization of fluid status and symptomatic relief, and spironolactone for anti-catecholamine effect. He was continued on this regimen for 2 months with restoration of LVEF



Video 2 Transthoracic echocardiogram 3 months post discharge.

Table 1 Comparison of transthoracic echocardiogram parameters on initial admission and at 3-month follow-up

	Initial TTE	TTE 3 months post-discharge
LVEDV	160	103
Normal reference range for male (62–150 mL)		
LVESV	68	22
Normal reference range for male (21–61 mL)		
LVEF (%)	45–50	60
Wall motion abnormalities	Akinesis of mid inferoseptal and mid anteroseptal segments. Apical sparing	None

LVEDV, left ventricular end-diastolic volume; LVEF, left ventricular ejection fraction; LVESV, left ventricular end-systolic volume; TTE, transthoracic echocardiogram.

Table 2 Comparison of characteristics and outcomes of six reported patients with direct current cardioversion-induced Tako-tsubo cardiomyopathy

Case	Age	Gender	Past medical history	Underlying rhythm prior to DCCV	Symptoms/signs	Peak troponin I (ng/mL)	ECG on admission	Hour to ED presentation post-DCCV	Trans-thoracic echocardiogram	Coronary angiography	Treatment	Complications and outcome	Reference
1	81	Female	Hypertension, hyperlipidaemia	Atrial fibrillation	Chest pain, dyspnoea, transient aphasia and left arm/leg weakness Pulmonary and hepatojugal congestion; Grade 3/6 systolic murmur	1.14	SR with prominent TWI V2-V6	Approximately 24h	New LVEF 20%, akinesia of apical LV and mid-ventricular segments; hyperdynamic basal segments and severe MR. PAP 50 mmHg	Absence of coronary disease	Lasix gtt, heparin gtt, antiplatelet medication, dobutamine, and dopamine gtt. BIPAP	Atrial fibrillation, Day 7 TTE showed LVEF 50%	Vizzardi et al. ³
2	76	Female	Hypertension, hyperlipidaemia	Atrial fibrillation	Dyspnoea and orthopnoea	0.2	SR, LAFB, and bifid T wave in anteroseptal leads. QTc 537 ms	10 h	New EF 45%. Apical and mid segment akinesia with hyperdynamic basal segments	30% mid-LAD and 30% mid RCA lesions	Aspirin, furosemide, and topical GTN	Systemic hypotension, oliguria, atrial fibrillation, QTc prolongation Day 6 TTE normal LVEF and no WMA	Eggleton et al. ⁴
3	67	Female	Hypertension	Atrial fibrillation	Dizziness, diaphoresis, near-syncope	3.39	Atrial fibrillation, HR 126 b.p.m., low voltage. QTc prolonged	Immediate	New LVEF 15%. Contraction only on basal segments with ballooning appearance	None. CT angiogram 2 years prior was normal	DC cardioversion (200 J), Furosemide	Sinus bradycardia, cardiogenic shock, mechanical ventilation Day 11 TTE EF 35-40%, day 14 EF normal	Siegrfried et al. ⁷
4	73	Male	Hypertension, hyperlipidaemia	Atrial flutter	Chest pain, shortness of breath, severe respiratory failure	1.3	Sinus tachycardia (HR 105) QTc prolonged	5 h	New LVEF 25%, severe hypokinesia and ballooning of the apex with hyperdynamic basal segments	Non-obstructive	Furosemide	Atrial fibrillation, mechanical ventilation Day 3 TEE normalization of LVEF 60% and no WMA	Zaghlool et al. ⁵
5	87	Female	Hypertension, hyperlipidaemia, asthma, CKD	Atrial fibrillation	Pulmonary oedema	2.79	New LBBB	Approximately 36h	New antero-apical akinesia	Non-obstructive	Anticoagulation, beta-blockers	Mechanical ventilation, atrial fibrillation	McCurcheon et al. ⁶
6	78	Male	Hypertension, hyperlipidaemia, coronary artery disease, thoracic aortic aneurysm	Atrial fibrillation	Dyspnoea, orthopnoea, wheezing	0.173	Normal sinus rhythm, LAD	12 h	New LVEF 45-50%. LVH, hypokinesia of the basal antero-septal segment, as well as akinesia of mid-inferoseptal and mid-antero-septal segments	Non-obstructive	Lasix, nitroglycerine, beta blocker, ACE-inhibitor	None Discharged on day 6, LVEF 60% at 2 months	Author's case

CT, contrast tomography; GTN, nitroglycerine; HR, heart rate; LAD, left axis deviation; LAFB, left anterior fascicular block; LBBB, left bundle branch block; LVEF, left ventricular ejection fraction; LVH, left ventricular hypertrophy; QTc, corrected QT; SR, sinus rhythm; TTE, transthoracic echocardiogram; TWI, T-wave inversion; WMA, wall motion abnormality.

seen on follow-up TTE. Spironolactone and sotalol were discontinued.

Patients with Tako-tsubo syndrome generally have a good prognosis. An outcomes study assessing trends of hospitalized patients with Tako-tsubo cardiomyopathy demonstrated in-hospital mortality rate of 1.3% [95% confidence interval (CI) 1.1–1.6], hospital discharge rate to home of 73.6% (95% CI 72.7–74.6), and 1-year mortality of 6.9% (95% CI 6.4–7.5).¹⁸ Consistent with the prior case experiences of post-DCCV Tako-tsubo syndrome, our patient survived hospitalization and was discharged home without the need for post-acute care services. Repeat TTE at 2 months showed complete global and regional restoration of LV function.

Conclusion

Given the potential need for inpatient care, patients undergoing DCCV should be taught to recognize symptoms of acute pulmonary oedema to allow for earlier detection of rare but serious complications of cardiomyopathy. Clinicians should be aware of atypical presentations of Tako-tsubo and consider them when using InterTAK Diagnostic Criteria as those criteria have not been validated on atypical variant Tako-tsubo syndrome. We propose future study into whether variants of Tako-tsubo differ in severity of disease when compared against typical Tako-tsubo; further studies should be sought to evaluate mortality benefit of standard heart failure medications in atypical variant Tako-tsubo cardiomyopathy. A better understanding of the potential benefit of medical therapy would allow clinicians to accurately weigh the relative benefits and risks of procedural interventions.

Lead author biography



Ju Young Bae, MD is a third-year internal medicine resident at Yale-New Haven Health Greenwich Hospital in Connecticut. She will be pursuing fellowship training in cardiovascular medicine at Yale University/Bridgeport Hospital.

Supplementary material

Supplementary material is available at *European Heart Journal - Case Reports* online.

Acknowledgements

The authors thank Donna Belcinski, Greenwich Hospital medical librarian for providing assistance for literature review and article acquisition.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as [Supplementary data](#).

Consent: The authors confirm that written consent for submission and publication of this case report including images and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: None declared.

Funding: None declared.

References

- Sato H, Tateishi H, Uchida T. Takotsubo-type cardiomyopathy due to multi-vessel spasm. In: K Kodama, K Haze, M Hon, eds. *Clinical Aspect of Myocardial Injury: From Ischemia to Heart Failure*. Tokyo, Japan: Kagakuhyouronsha, 1990, 56–64.
- Ghadri JR, Wittstein IS, Prasad A, Sharkey S, Dote K, Akashi YJ et al. International Expert Consensus Document on Takotsubo Syndrome (Part I): clinical characteristics, diagnostic criteria, and pathophysiology. *Eur Heart J* 2018; **39**:2032–2046.
- Vizzardi E, Rovetta R, Bonadei I, Quinzani F, D'Aloia A, Salghetti F et al. A case of Tako-Tsubo cardiomyopathy after electrical cardioversion. *Minerva Med* 2013; **104**:115–117.
- Eggleston S, Mathur G, Lambros J. An unusual precipitant of tako-tsubo cardiomyopathy. *Heart Lung Circ* 2008; **17**:512–514.
- Zaghlol R, Hritani R, O'Donoghue S. Shock begets shock: a case of direct current cardioversion-induced takotsubo cardiomyopathy. *HeartRhythm Case Rep* 2019; **5**: 310–313.
- McCutcheon K, Butler I, Vachiat A, Manga P. Takotsubo syndrome in an elderly woman due to electrical cardioversion. *Int J Cardiol* 2016; **224**:69–71.
- Siegfried JS, Bhusri S, Guttenplan N, Coplan NL. Takotsubo cardiomyopathy as a sequela of elective direct-current cardioversion for atrial fibrillation. *Tex Heart Inst J* 2014; **41**:184–187.
- Lyon AR, Bossone E, Schneider B, Sechtem U, Citro R, Underwood SR et al. Current state of knowledge on Takotsubo syndrome: a Position Statement from the Taskforce on Takotsubo Syndrome of the Heart Failure Association of the European Society of Cardiology. *Eur J Heart Fail* 2016; **18**:8–27.
- Citro R, Okura H, Ghadri JR, Izumi C, Meimoun P, Izumo M et al. Multimodality imaging in takotsubo syndrome: a joint consensus document of the European Association of Cardiovascular Imaging (EACVI) and the Japanese Society of Echocardiography (JSE) [published correction appears in *J Echocardiogr* 2020 Nov 10]. *J Echocardiogr* 2020; **18**:199–224.
- Wittstein IS, Thiemann DR, Lima JA, Baughman KL, Schulman SP, Gerstenblith G et al. Neurohumoral features of myocardial stunning due to sudden emotional stress. *N Engl J Med* 2005; **352**:539–548.
- Gowda RM, Misra D, Khan IA, Schweitzer P. Acute pulmonary edema after cardioversion of cardiac arrhythmias. *Int J Cardiol* 2003; **92**:271–274.
- Kugelberg J. Pulmonary oedema after defibrillation. *Lancet* 1965; **2**:740–741.
- Paur H, Wright PT, Sikkil MB, Tranter MH, Mansfield C, O'Gara P et al. High levels of circulating epinephrine trigger apical cardiodepression in a β 2-adrenergic receptor/Gi-dependent manner: a new model of Takotsubo cardiomyopathy. *Circulation* 2012; **126**:697–706.
- Isogai T, Matsui H, Tanaka H, Fushimi K, Yasunaga H. Early β -blocker use and in-hospital mortality in patients with Takotsubo cardiomyopathy. *Heart* 2016; **102**: 1029–1035.
- Kim H, Senecal C, Lewis B, Prasad A, Rajiv G, Lerman LO et al. Natural history and predictors of mortality of patients with Takotsubo syndrome. *Int J Cardiol* 2018; **267**:22–27.
- Singh K, Carson K, Usmani Z, Sawhney G, Shah R, Horowitz J. Systematic review and meta-analysis of incidence and correlates of recurrence of takotsubo cardiomyopathy. *Int J Cardiol* 2014; **174**:696–701.
- Chams S, El Sayegh S, Hamdon M, Kumar S, Kulairi Z. Zumba-induced Takotsubo cardiomyopathy: a case report. *J Med Case Rep* 2018; **12**:160.
- Murugiah K, Wang Y, Desai NR, Spatz ES, Nuti SV, Dreyer RP et al. Trends in short- and long-term outcomes for takotsubo cardiomyopathy among medicare fee-for-service beneficiaries, 2007 to 2012. *JACC Heart Fail* 2016; **4**: 197–205.