American Journal of Medical Case Reports, 2019, Vol. 7, No. 6, 109-116
Available online at http://pubs.sciepub.com/ajmcr/7/6/4
Published by Science and Education Publishing
DOI:10.12691/ajmcr-7-6-4

A Case of Takotsubo Cardiomyopathy Complicated with Life Threatening Arrhythmia and Cardiogenic Shock

Philip Tulio[1], Jehad Azar[1,*], Keyvan Ravakhah[2], Randol Kennedy[1], Vasant Temull[1]

[1]Internal Medicine Resident, St. Vincent Charity Medical Center, Cleveland, USA
[2]Chairman of Internal Medicine, St. Vincent Charity Medical center, Cleveland, USA
Both Dr. Philip Tulio and Dr. Jehad Azar are first authors and contributed equally for the manuscript preparation.
*Corresponding author: jehad.azar@gmail.com

Received May 04, 2019; Revised June 07, 2019; Accepted June 11, 2019

Abstract Stress (Takotsubo) cardiomyopathy (CM) is defined as a transient regional systolic dysfunction of the left ventricle that mimics acute coronary syndrome (ACS) in the absence of significant coronary artery disease or plaque rupture. This phenomenon commonly occurs in postmenopausal females in the presence of emotional, physical and psychological stressors with excess catecholamine stimulation, resulting in diffuse microvascular spasm and subsequently myocardial stunning. Here we report a 58-year-old postmenopausal female patient with end stage renal disease (ESRD) who was presented to our hospital with a clinical picture suggesting ACS. Shortly after admission she progressed to cardiogenic shock and pulseless electrical activity (PEA) and was diagnosed retrospectively with Takotsubo cardiomyopathy. She was successfully treated with beta-blockers, IV fluids and inotropic agents. Intra-aortic balloon pump (IABP) was considered, however, the patient gradually improved to full recovery with resolution of left ventricular function back to normal.

Keywords: *Takotsubo, stress cardiomyopathy, arrhythmia, cardiogenic shock, Intra-aortic balloon pump, Left ventricular outflow tract obstruction*

Cite This Article: Philip Tulio, Jehad Azar, Keyvan Ravakhah, Randol Kennedy, and Vasant Temull, "A Case of Takotsubo Cardiomyopathy Complicated with Life Threatening Arrhythmia and Cardiogenic Shock." *American Journal of Medical Case Reports*, vol. 7, no. 6 (2019): 109-116. doi: 10.12691/ajmcr-7-6-4.

1. Introduction

Stress cardiomyopathy (CM), a life threatening cardiovascular event characterized as an acute transient left ventricular systolic dysfunction, was first observed and reported in Japan by Satoh et al. and Dote et al. [1,2] Stress CM occurs predominantly in postmenopausal females (mean 65 ± 13 years) and is triggered by exaggerated sympathetic stimulation as a result of emotional and physical stress [3]. It is also referred to as Takotsubo cardiomyopathy, with *tako-tsubo* translating to "octopus pot" in Japanese, due to its characteristic appearance of the left ventricle with a rounded bottom and narrow neck on ventriculogram. The proposed mechanism for stress CM is excess catecholamine stimulation which is believed to cause diffuse microvascular spasm with subsequent myocardial stunning. Hypokinesis most commonly occurs in the apical regions of the ventricles, which is best explained by the hypothesis that the apex of the heart has a higher adrenoceptor density. Stress CM mimics symptoms seen with ACS, including chest pain, diaphoresis and dyspnea. 1-2% of all cases suspected initially to have ACS are in fact diagnosed as Takotsubo cardiomyopathy [4]. The diagnosis is made retrospectively based on the Mayo Clinic criteria [5]. Treatment is primarily supportive with aspirin, low molecular weight heparin, ACE-inhibitors and beta blockers. Stress CM, although it is a reversible disease with generally good prognosis, can progress to a fatal disease with life-threatening arrhythmia and cardiogenic shock. Recent reports claim that the actual mortality rate related to Takotsubo CM is underreported [6]. Here, we present a patient who was first assessed as possible case of acute coronary syndrome, but was later discovered to have stress induced cardiomyopathy complicated by life threatening arrhythmia and cardiogenic shock.

2. Case Presentation

A 58-year old female with a past medical history of end stage renal disease on dialysis, asthma, diabetes mellitus type 2, hypertension and atrial fibrillation presented with chest pain. The patient records onset as 2 hours prior, and describes it as sharp and constant, substernal in location without radiation, and rates it as 9/10 in severity. She also reports associated dyspnea, diaphoresis, nausea and vomiting. Home medications include Coumadin, carvedilol,

nifedipine, calcium acetate, glipizide and Nephrocaps. Cardiac exam indicates tachycardia, but is otherwise unremarkable.

Admission labs significant for sodium 126 mEq/L (normal range 136 to 144 mEq/L), potassium > 10 mEq/L (normal range 3.7 to 5.2 mEq/L), BUN 30 mg/dL (normal range 7 to 20 mg/dL), creatinine 10 mg/dL (normal range 0.8 to 1.2 mg/dL), INR 5.74, troponin 0.119, had normal calcium, phosphorus and magnesium. Initial electrocardiogram (ECG) demonstrated tachycardia with regular rhythm and diffuse hyperacute T wave (Figure 1). Patient received calcium gluconate, kayexalate and insulin and was started on beside urgent hemodialysis. A few hours later, troponin had trended up to 4.22 and repeat ECG demonstrated a 2-mm ST-segment elevation in the lateral precordial leads and the inferior limb leads (Figure 2).

Echocardiogram demonstrated a severely-dilated left ventricle with apical hypokinesis, estimated LVEF 20-25%, apical ballooning (Figure 3, Figure 4) and LVOT mean gradient 1 mmHg as well as peak gradient 3 mmHg. Cardiac catheterization demonstrated normal left main coronary artery, left anterior descending and left circumflex functions (Figure 5) as well as normal right coronary artery function (Figure 6). Moreover, there was evidence of a dilated left ventricle as well as severe antero-apical wall hypokinesis, basal hyperkinesia and apical ballooning (Figure 7).

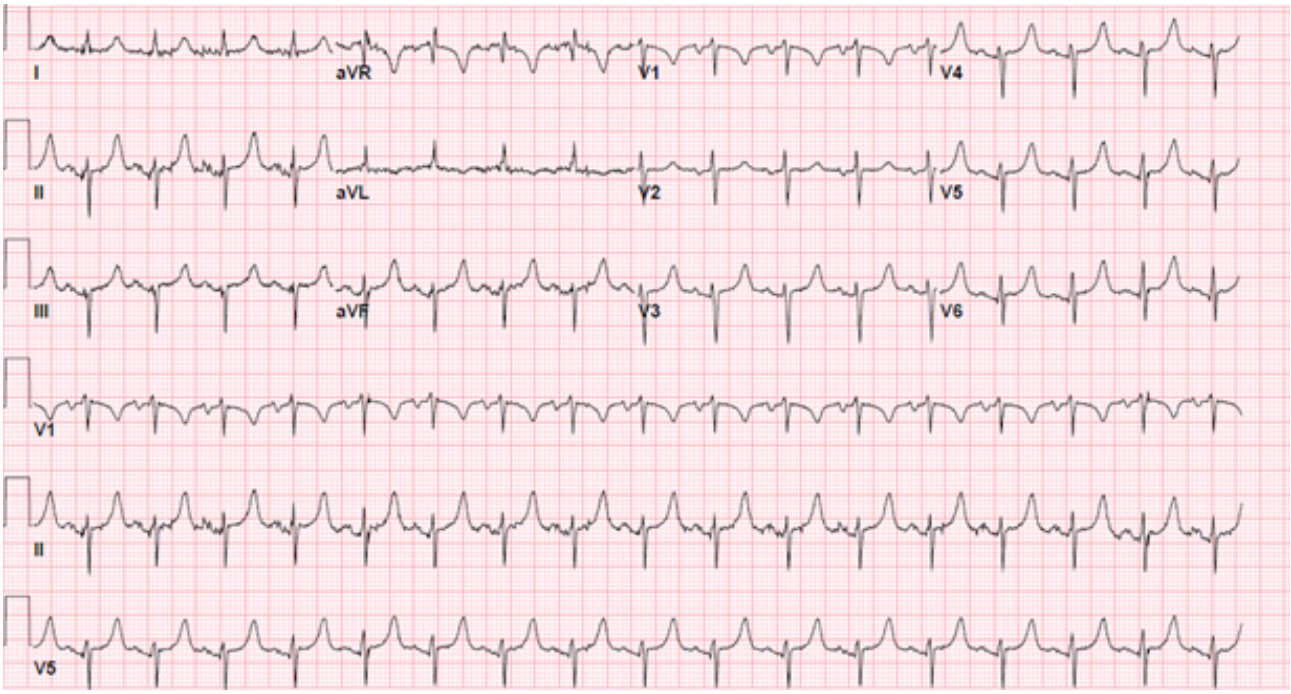

Figure 1. Initial ECG demonstrates tachycardia with regular rhythm and diffuse hyperacute T waves

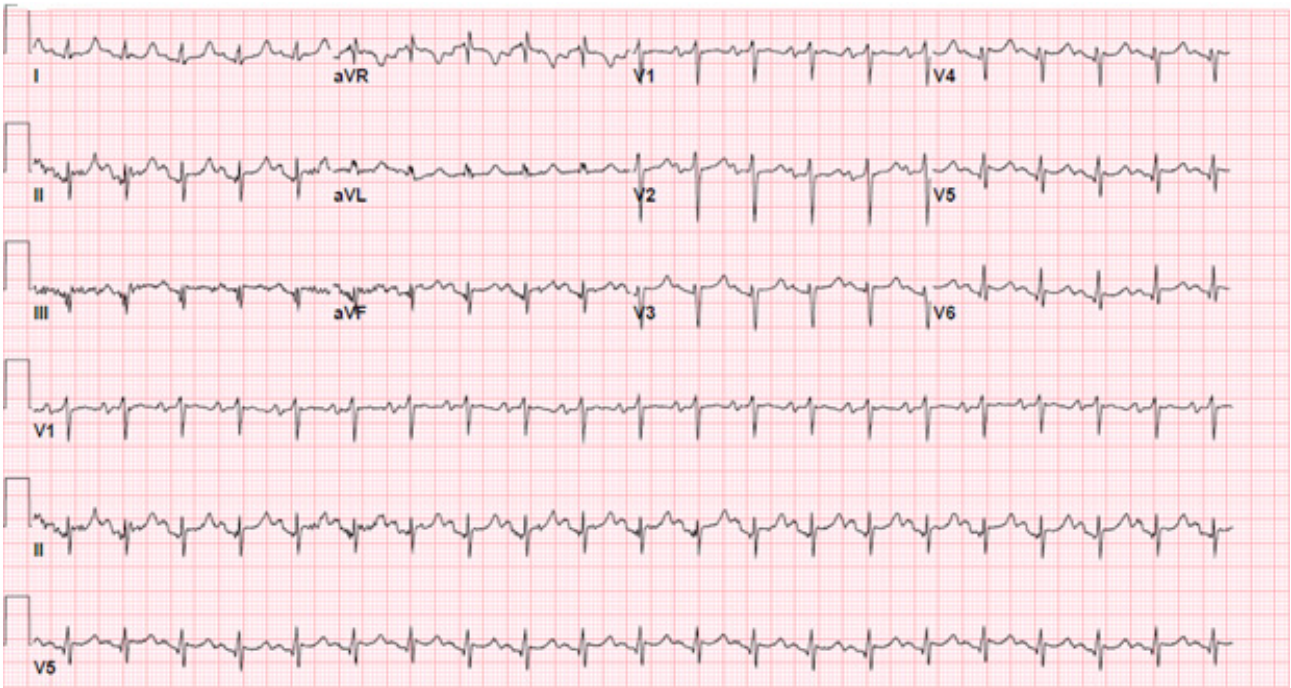

Figure 2. Repeat ECG demonstrating 2-mm ST elevations in the inferior and lateral leads

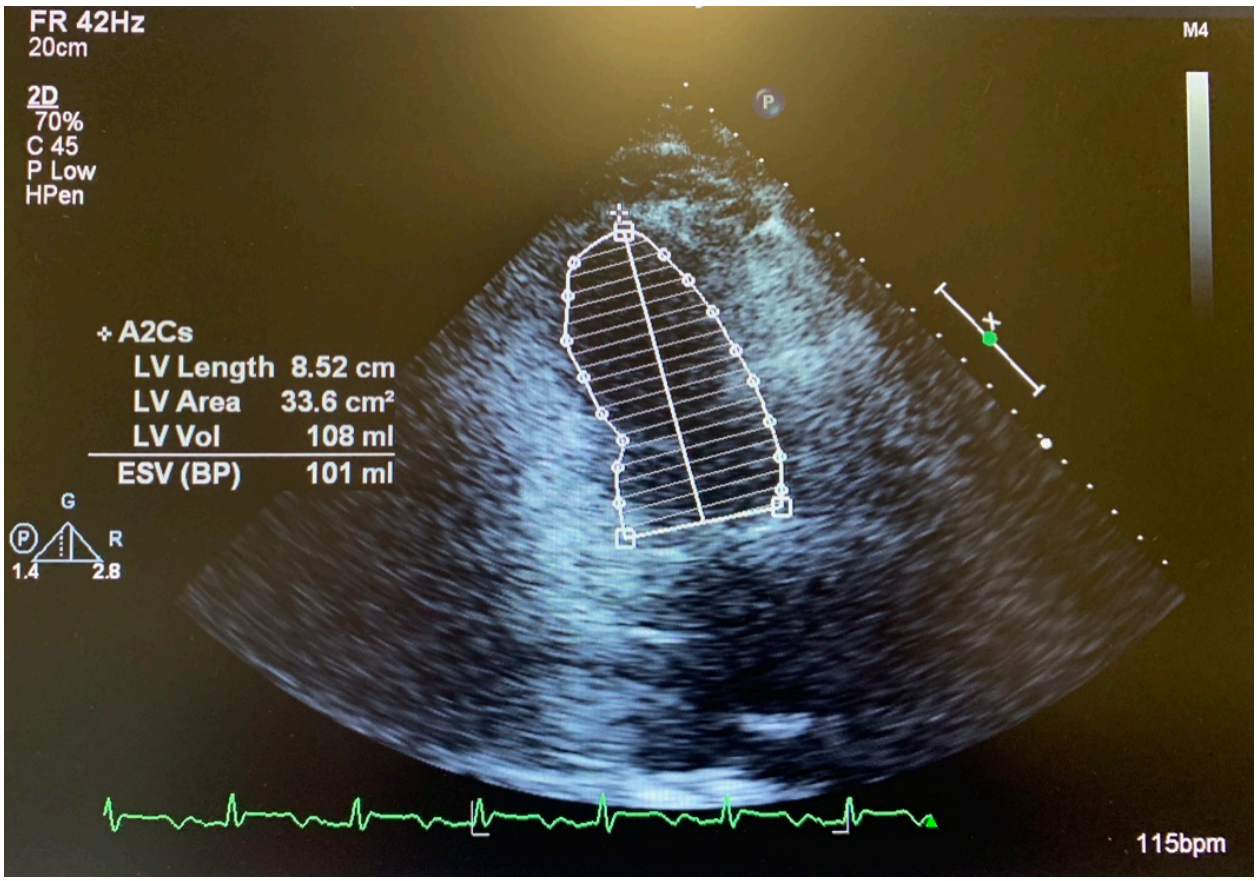

Figure 3. Apical view of the left ventricle demonstrating significant apical dilatation

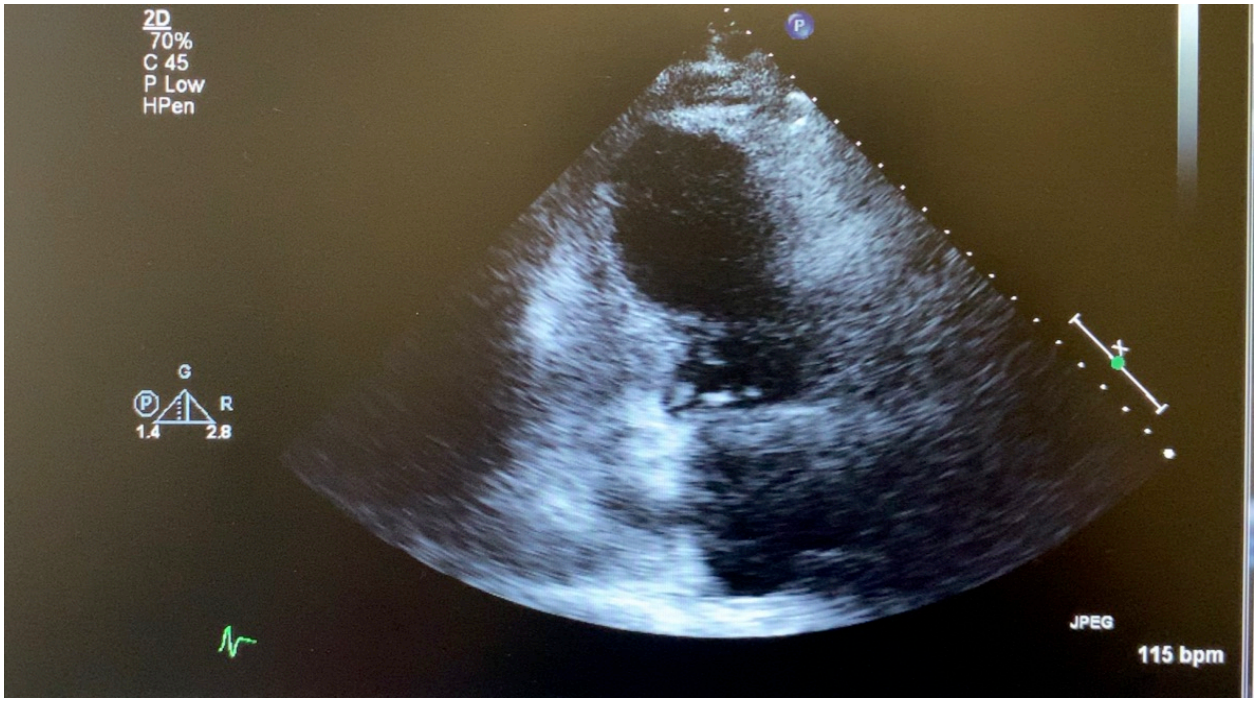

Figure 4. Apical view of the left ventricle demonstrating significant apical dilatation

The patient was given supportive management with aspirin, low-molecular weight heparin and short-term IV metoprolol 5 mg QID, that was transitioned to PO metoprolol tartrate 25 mg BID. Nevertheless, the patient progressed into cardiogenic shock despite receiving treatment. Repeat ECG demonstrated ST elevations in the inferior leads and T wave depression in the lateral leads. QT prolongation (Figure 8) also featured on the patient's ECG and was followed by PEA shortly thereafter. Subsequently, ACLS protocol was initiated and the patient was transferred to the ICU for further monitoring and treatment.

Repeat echocardiogram showed no evidence of LVOT obstruction, thus the patient was treated with IV fluid

resuscitation as well as inotropic medication. Intra-aortic balloon pump (IABP) was considered, however the patient showed gradual hemodynamic improvement on supportive care only. Inotropes were weaned off, ECG changes and troponins normalized (Figure 9). An echocardiogram 3 weeks later showed normal global left ventricular systolic function. The patient, who suffered from cardiomyopathy (Takotsubo), continued to improve and made a full recovery at time of discharge.

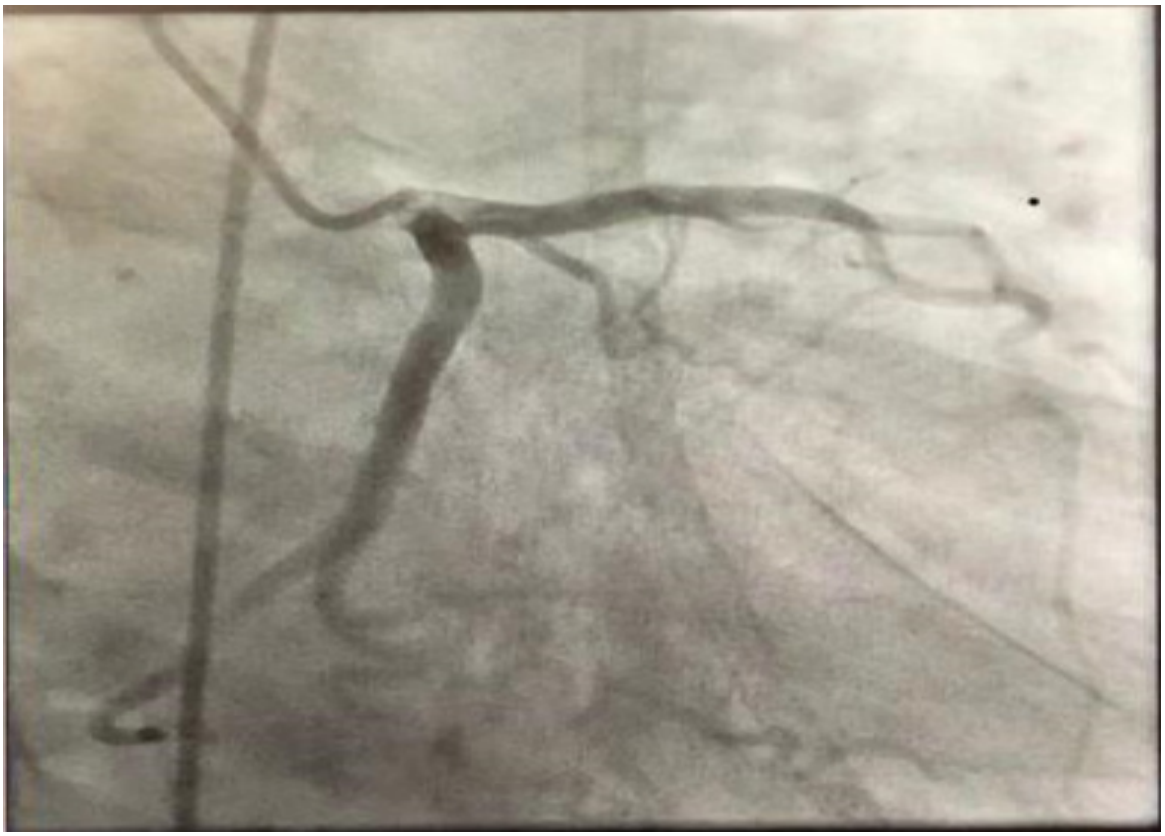

Figure 5. Coronary angiography showing normal left main, left anterior descending and left circumflex coronary arteries

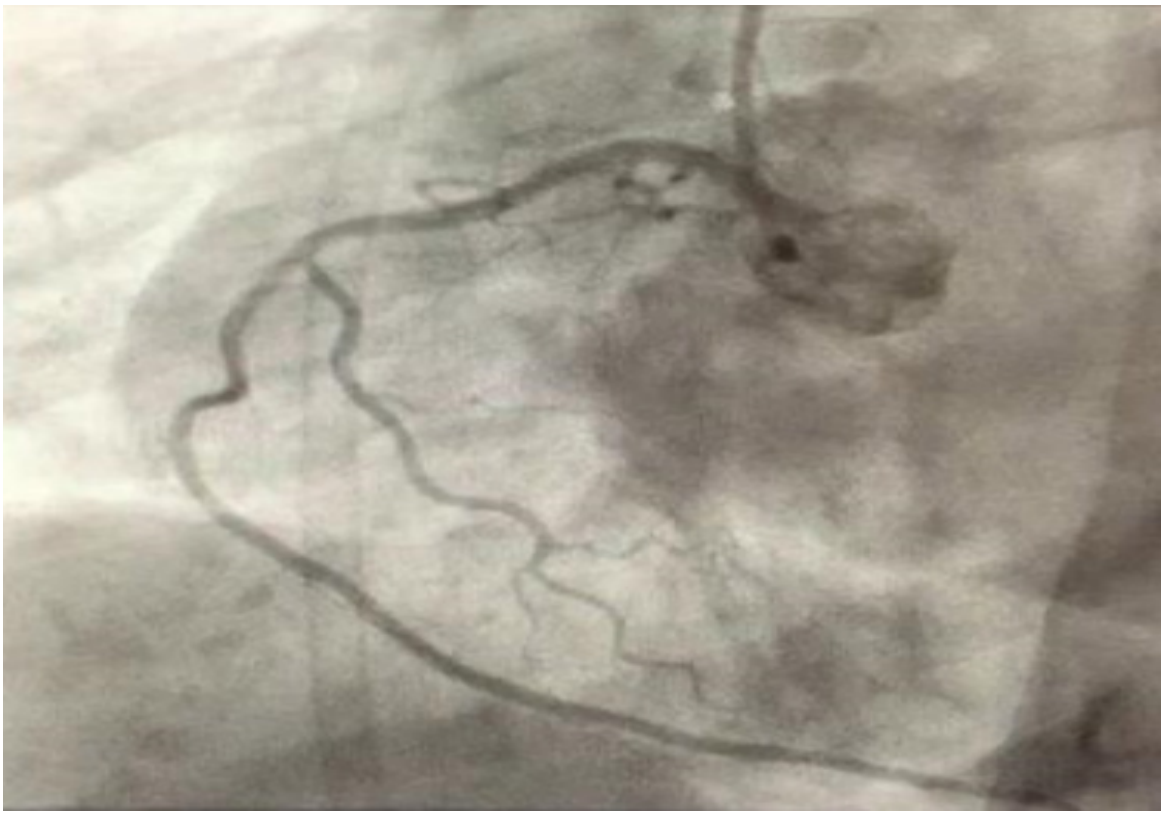

Figure 6. Coronary angiography showing normal right coronary artery

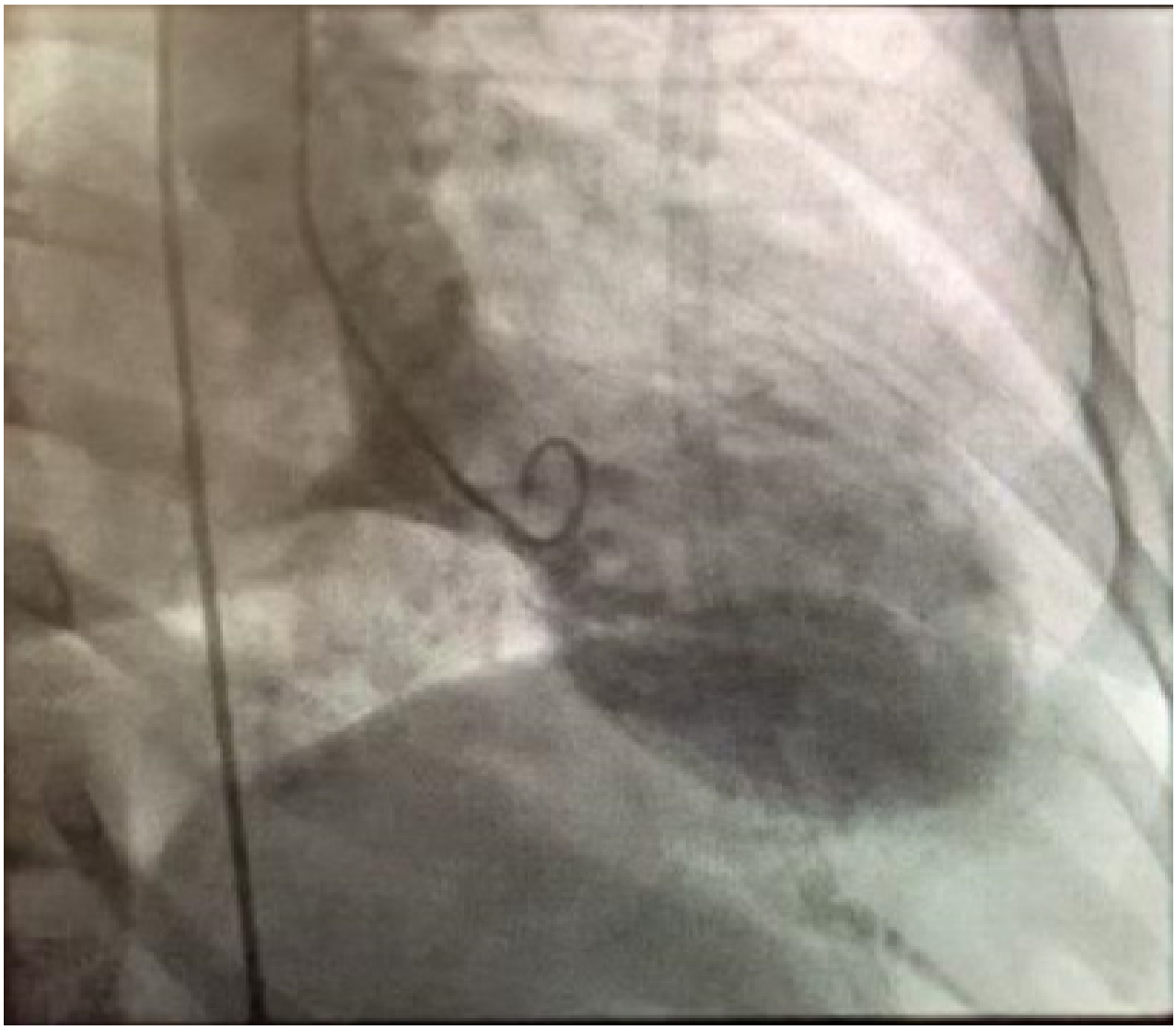

Figure 7. Left ventriculogram: morphology of the left ventricle with apical ballooning

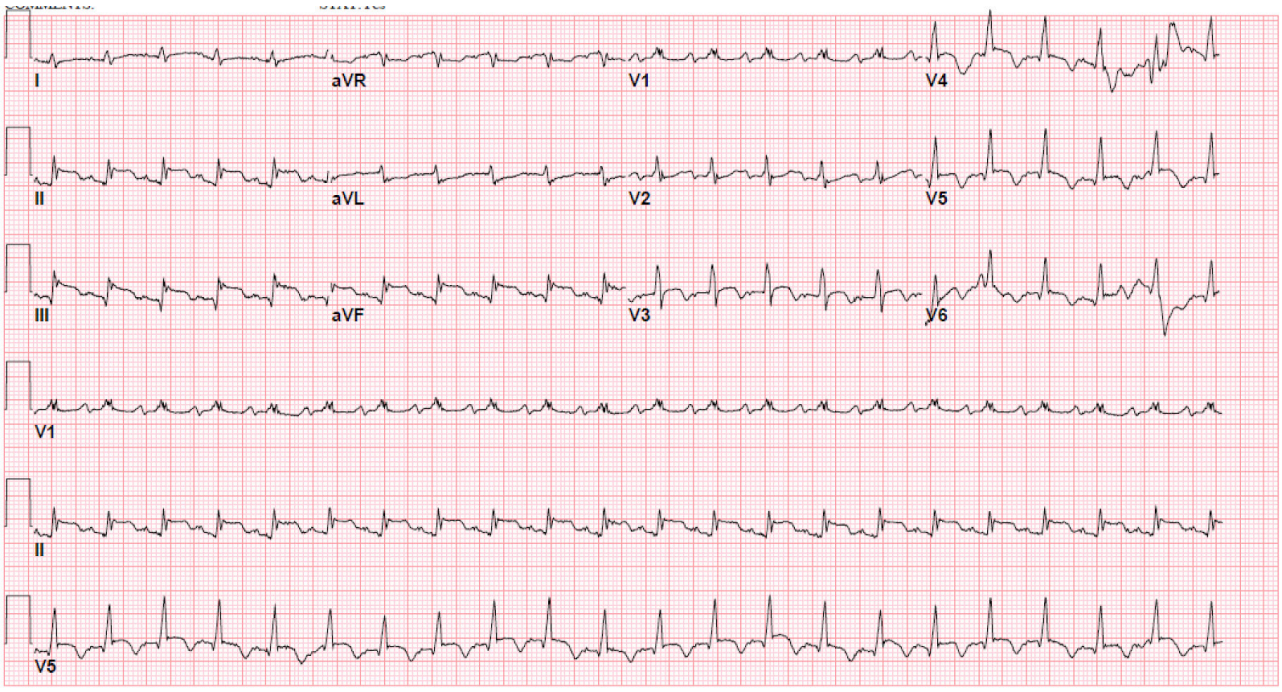

Figure 8. ECG one day after admission, demonstrating ST elevations in the inferior leads, T wave depression in lateral leads, and QT prolongation

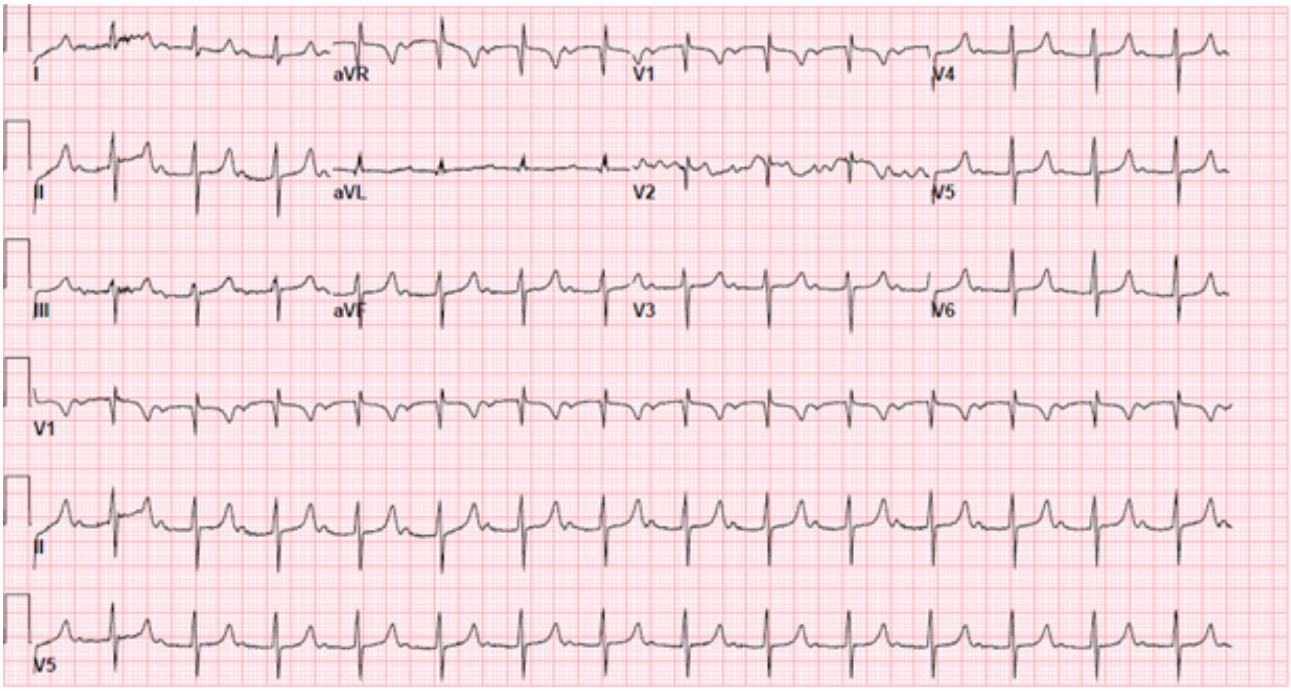

Figure 9. ECG at three-weeks follow-up, demonstrating resolution of ST elevations and T-wave inversions

3. Discussion

Stress cardiomyopathy was first described in 1990 in Japan and has since been increasingly recognized worldwide [1,2]. It is more common in women than men and occurs predominantly in older adults. The incidence of stress CM among individuals exposed to physical or emotional stress is not known. Stress cardiomyopathy commonly presents as a case of ACS. ECG typically shows ST-segment elevation and T-wave inversions that usually extend beyond the distribution of one coronary artery. QT prolongation and T wave inversions are not uncommon, cardiac biomarkers are minimally elevated relative to the extent of left ventricular akinesis. Both echocardiography and left ventriculography often show a pathognomonic apical ballooning as a result of a hypercontractile base of the heart relative to hypokinetic or even akinetic apex and mid left ventricular myocardium.

The pathogenesis of myocardial stunning in the presence of excess catecholamines is poorly understood. One postulation is that epinephrine at high levels has a cardioprotective negative inotropic effect via switching its molecular action from $\beta 2$ receptors G stimulatory (Gs) protein ligand to G inhibitory (Gi) protein signaling pathway [7]. This prevents catecholamine induced myocardial injury. $\beta 2$ adrenergic innervation is more dominant at the apex compared to the basal region, which explains the disproportionate regional contractility of the left ventricle with subsequent apical ballooning [7]. Further evidence to support the catecholamine hypothesis is the observation of similar reversible cardiomyopathy patients with pheochromocytoma and in the setting of acute brain injury [8,9]. Another proposed hypothesis is diffuse coronary arterial spasm [10]. However, the absence of angiographic evidence of coronary arterial spasms can suggest the presence of microvascular spasms [11]. Endomyocardial biopsy of akinetic tissue demonstrates contraction band necrosis, a finding shared in other states of catecholamine excess (i.e., pheochromocytoma, subarachnoid hemorrhage, exogenous catecholamine use, etc.), which suggests a correlation between catecholamine stimulation and myocardial injury.

Diagnosis of stress CM can be made according to the Mayo Clinic Diagnostic Criteria. Patients must meet all four of the following criteria for diagnosis: 1) transient LV systolic dysfunction, 2) absence of obstructive coronary disease or angiographic evidence of acute plaque rupture, 3) new ECG abnormalities or modest troponin elevations, and 4) absence of pheochromocytoma or myocarditis. Our patient presented with chest pain, dyspnea, palpitations and diaphoresis. ECG (Figure 2) demonstrated a 2-mm ST-segment elevation in the lateral precordial leads and the inferior limb leads, along with elevation in cardiac biomarkers. Initially, she was managed as a case of ST segment elevation myocardial infarction (STEMI), and then the diagnosis of stress CM was made after she fulfilled all four of the diagnostic criteria. No evidence of LVOT obstruction was seen on the echocardiogram (LVOT mean gradient 1 mmHg, LVOT peak gradient 3 mmHg).

Stress CM can be distinguished from CAD with coronary angiogram, which will demonstrate no significant obstructive lesions or mild to moderate atherosclerosis in the former. If the wall motion abnormalities are inconsistent with the distribution of coronary disease further distinction can be made. Echocardiogram should be ordered for serial evaluation of left ventricular function. Findings include reduced overall left ventricular function, apical akinesis/hypokinesis and apical ballooning with abnormal wall motion of the mid and distal left ventricle. The presence of left ventricle outflow tract (LVOT) obstruction (i.e., LVOT gradient equal to or greater than 30 mm Hg) should be evaluated, as this would influence the management in the event of cardiogenic shock. LVOT obstruction occurs as a result of left ventricular basal hyperkinesis and produces a late

peaking systolic murmur. It can lead to the development of cardiogenic shock and cause severe mitral regurgitation. Thus, its presence has major implications in the modality of treatment selected [12]. In our patient, pertinent findings on ECG demonstrated ST elevations in the inferior and lateral precordial leads (Figure 2) that became more prominent after the patient sustained PEA with new development of QT prolongation (Figure 8). Echocardiogram findings demonstrated severe left ventricle dilatation with apical ballooning, anteroapical wall hypokinesis and basal hyperkinesia (Figure 3, Figure 4) along with a reduced EF of 25% and a normal LVOT gradient. Coronary angiogram demonstrated no significant obstructive coronary lesions (Figure 5, Figure 6) but characteristic apical ballooning during systole (Figure 7).

Whether the patient has either stress CM or ACS, the initial management is similar in the sense that patients should be started on aspirin, low-molecular weight heparin, ACE-inhibitors, a statin, and dual-antiplatelet therapy. The differential of stress CM should not be a reason to postpone fibrinolytic therapy in patients with ST elevations meeting criteria for reperfusion therapy. Once stress CM is confirmed through normal coronary angiogram and echocardiogram, the treatment regimen should be de-escalated to supportive therapy with beta-blockers and fluid resuscitation [13,14]. Patients should also be closely monitored for any complications, especially for cardiogenic shock. Complication rates in patients with stress CM are similar to that of patients presenting with ACS [15]. However, recent reports claim that the actual mortality rate related to Takotsubo is underreported [6].

Management of cardiogenic shock depends on the presence of LVOT obstruction. In the absence of LVOT obstruction, patients can be managed with fluid resuscitation and inotropic therapy. In the presence of significant LVOT obstruction, however, the treatment is similar to that of patients with hypertrophic cardiomyopathy with LVOT obstruction and hemodynamic collapse. Due to its negative inotropic effects, beta-blockers are considered the initial treatment, followed by increasing the preload by leg elevation and fluids resuscitation. Pure alpha adrenergic agonists, like phenylephrine, may be helpful in refractory cases by reducing LVOT gradient through increasing afterload. Patients started on these agents should receive strict clinical monitoring due to the risk of coronary vasospasm. In contrast to cardiogenic shock due to pump failure, inotropes should be avoided as they can worsen the degree of obstruction. Nitrates and volume depletion can also worsen LVOT obstruction by decreasing preload and causing reflex tachycardia. Intra-aortic balloon pump (IABP) is indicated in patients with LVOT obstruction and severe hypotension that is refractory to initial medical therapy and volume resuscitation. However, it carries a minimal risk of reducing the afterload that can worsen the degree of obstruction.

There is no definitive data for venous thromboembolism (VTE) prophylaxis in patients with stress CM. Current recommendations advocate the use of warfarin for 3 months or until the akinesis resolves for the following: presence of left ventricle thrombus, or LVEF < 30% with low bleeding risk. Anticoagulation was not provided to our patient due to supratherapeutic INR (5.74). No fibrinolytic therapy was provided, as she was managed at a hospital where angiogram was available. Coronary angiogram demonstrated no significant obstructive coronary lesion (Figure 5, Figure 6). She was started on metoprolol and IV fluids to reduce myocardial contractility and to increase preload, respectively. Nevertheless, she developed cardiogenic shock without LVOT obstruction, so she was started on pressor support. Within two weeks, the patient subjectively improved. Inotropes were weaned off, ECG changes and troponins normalized. Repeated echocardiogram was performed prior to discharge demonstrated return of normal systolic function and contractility.

Prognosis is generally good, as left ventricular function recovers within 3 to 9 days. Complete recovery is expected to be within 2 to 4 weeks [16]. Recurrence risk is reported to be 1.8% per patient year [15]. According to the International Takotsubo Registry study, the composite rate of major adverse cardiac and cerebrovascular events during the first 30 days after admission was 7.1% [15]. However, recent reports suggest a higher rate of complications and mortality rate following the acute phase of the disease, with a death rate per patient-year of 5.6% and a cerebrovascular accident rate of 1.7% per patient-year [17].

4. Conclusion

Stress cardiomyopathy should be considered in the differential when evaluating for suspected ACS in postmenopausal women.

Dynamic left ventricular outflow tract obstruction should be routinely evaluated on echocardiogram in patient with stress cardiomyopathy since it poses a major therapeutic challenge.

Despite the overall favorable prognosis and the transient systolic dysfunction, patients with suspected stress CM should be monitored for possible life threatening arrhythmias and cardiogenic shock, considering the recent reports stating that the mortality and the complication rates related to stress CM are underreported [6].

Acknowledgements

Our sincere thanks and appreciation to Dr. Keyvan Ravakhah, MD, MBA, FACP, Chairman, Department of Medicine and Research Director at St. Vincent Charity Medical Center for providing his insight and expertise that greatly assisted the research.

References

[1] H Satoh, H Tateishi, T Uchida, *et al.*Takotsubo-type cardiomyopathy due to multivessel spasm. In: K Kodama, K Haze, M Hon, eds. *Clinical Aspect of Myocardial Injury: From Ischemia to Heart Failure* (*in Japanese*). Tokyo: Kagakuhyouronsya Publishing Co; 1990: 56-64.

[2] K Dote, H Sato, H Tateishi, *et al.*Myocardial stunning due to simultaneous multivessel spasms: a review of five cases (in Japanese with English abstract) *J Cardiol*, 21 (1991), pp. 203-214.

[3] Sharkey SW, Lesser JR, Zenovich AG, Maron MS, Lindberg J, Longe TF, Maron BJ, Acute and reversible cardiomyopathy provoked by stress in women from the United States, *Circulation*. 2005; 111(4):472.

[4] Gianni M, Dentali F, Grandi AM, Sumner G, Hiralal R, Lonn E. Apical ballooning syndrome or takotsubo cardiomyopathy: a systematic review. *Eur Heart J*. 2006; 27: 1523-1529.

[5] Scantlebury, Dawn & Prasad, Abhiram. (2014). Diagnosis of Takotsubo Cardiomyopathy - Mayo Clinic Criteria. Circulation journal : official journal of the Japanese Circulation Society. 78.

[6] Pelliccia F, Pasceri V, Patti G et al. A Decidedly Darker Prognosis for Takotsubo Syndrome, *J Am Coll Cardiol HF*. 2019.

[7] Paur H, Wright PT, Sikkel MB, et. al…. High levels of circulating epinephrine trigger apical cardiodepression in aβ2-adrenergic receptor/Gi-dependent manner: a new model of Takotsubo cardiomyopathy. *Circulation*. 2012 Aug; 126(6): 697-706. Epub 2012 Jun 25.

[8] Kassim TA, Clarke DD, Mai VQ, Clyde PW, Mohamed Shakir KM, Catecholamine-induced cardiomyopathy. *Endocr Pract*. 2008; 14(9): 1137.

[9] Ako J, Sudhir K, Farouque HM, Honda Y, Fitzgerald P. Transient left ventricular dysfunction under severe stress: brain-heart relationship revisited. *J Am J Med* 2006; 119(1):10.

[10] Ilan S. Wittstein, M.D.,David R. Thiemann, M.D., Joao A.C. Lima, M.D., et al….Neurohumoral Features of Myocardial Stunning Due to Sudden Emotional Stress, *N Engl J Med* 2005; 352: 539-548.

[11] Wittstein I, Thiermann D, Lima J et al. Neurohumoral Features of Myocardial Stunning Due to Sudden Emotional Stress. *N Engl J Med* 2005; 352:539-548.

[12] Wu Hm, Tzeng BH. Dynamic Left Ventricular Outflow Tract Obstruction with Cardiogenic Shock in Apical Ballooning Syndrome. *Acta Cardiol Sin*. 2013; 29(4): 370-3.

[13] O'Gara PT, Kushner FG, Ascheim DD, et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: executive summary: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Circulation. 2013; 127(4): 529. Epub 2012 Dec 17.

[14] O'Gara PT, Kushner FG, Ascheim DD et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2013; 127(4):e362. Epub 2012 Dec 17.

[15] Templin C, Ghadri JR, Diekmann J, Napp LC et al. Clinical Features and Outcomes of Takotsubo (Stress) Cardiomyopathy, *N Engl J Med*. 2015;373(10):929.

[16] Ramaraj R. Stress cardiomyopathy: aetiology and management. *Postgrad Med J*. 2007 August;83(982):543-546.

[17] Nef HM, Möllmann H, Kostin S, et al. Tako-Tsubo cardiomyopathy: intraindividual structural analysis in the acute phase and after functional recovery. Eur Heart J 2007; 28: 2456.