

# Evidence of Myocardial Edema in Obstructive Tako-tsubo Cardiomyopathy Complicated by Cardiogenic Shock

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## Abstract

The contemporary presence of left ventricular (LV) outflow tract obstruction, systolic anterior motion of the anterior mitral leaflet, and acute mitral regurgitation may occur in Tako-tsubo cardiomyopathy. Although myocardial edema has been reported in patients with Tako-tsubo cardiomyopathy, to the best of our knowledge it has never been described in the setting of LV outflow obstruction and the presence of cardiogenic shock. We report the case of a 65-year-old woman who developed Tako-tsubo cardiomyopathy followed by acute cardiogenic shock. The echo-Doppler assessment revealed LV apical ballooning, moderate-to-severe mitral regurgitation, and an estimated peak systolic pressure gradient at LV outflow tract of 64 mmHg. The LV outflow obstruction and mitral regurgitation resolved shortly after the intravenous administration of atenolol (1.25 mg). The cardiogenic shock was completely resolved following the infusion of low-dose dobutamine: 2  $\mu$ g/kg/min. In the following days, an echo-Doppler examination revealed a marked reduction in the thickness of the LV proximal hypertrophied septum (from 20 mm to 14 mm), while a cardiac magnetic resonance imaging study showed signs of mild edema of the mid-ventricular and apical septum.

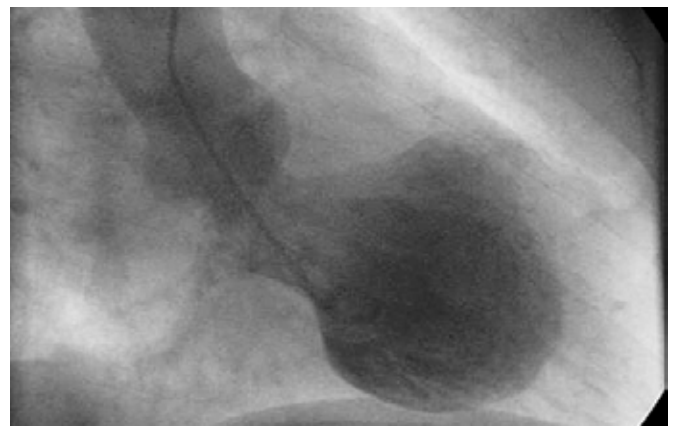
## Introduction

Tako-tsubo cardiomyopathy, also known as transient apical ballooning syndrome, is an increasingly reported syndrome of reversible acute heart failure that mimics acute coronary syndrome. It is accompanied by reversible left ventricular (LV) systolic dysfunction in the absence of angiographically significant coronary artery stenosis. The diagnosis is made by the pathognomonic wall motion abnormalities, in which the base of the left ventricle is contracting normally or is hyperkinetic while the remainder of the cavity is akinetic or dyskinetic<sup>1</sup>. The onset of stress-induced cardiomyopathy is frequently triggered by an intense emotional or physical stress. Left ventricular outflow tract (LVOT) obstruction may occur in Tako-tsubo syndrome<sup>2-4</sup>, however, the mechanisms behind its occurrence is not fully understood. Herein, we describe the clinical and angiographic characteristics of a case of obstructive Tako-tsubo cardiomyopathy complicated by acute heart failure with cardiogenic shock, that had been successfully treated with the combination of beta blocker antagonist and agonist: atenolol and dobutamine.

## Case Report

A 65-year old woman was admitted at the coronary care unit (CCU) of the Cardiac, Thoracic and Vascular Department of the University of Pisa for a prolonged chest pain and shortness of breath. She had a history of hypertension, type 2 diabetes, cigarette smoking and asthma, but no history of previous cardiovascular disease. Physical findings consisted of tachycardia and diffuse pulmonary rales. Her blood pressure was 100/70 mmHg, oxygen saturation (on pulse-oximetry) was 94%. The electrocardiogram showed sinus tachycardia (110 beats per minute), ST segment elevation up to 3 mm in the precordial leads in V3-V6. HS troponin measurements was 1133 ng/ml, serum creatine kinase MB peaked at 46.0 ng/ml and B-type natriuretic peptide levels was 527 pg/ml. The first transthoracic echo-Doppler examination showed severe LV systolic dysfunction with a LV ejection fraction of

**Figure 1:** Left ventriculography at end-systole showing the classic appearance of apical ballooning.



30%, akinesis of the whole ventricle except for the basal segments, estimated peak systolic pulmonary artery pressure of 45 mmHg. The patient was commenced on clopidogrel 600 mg orally and intravenous unfractionated heparin: 2500 I.U. An emergency cardiac catheterization revealed normal, patent coronary arteries. The LV angiogram showed apical dilation of the left ventricle with akinesis of the whole ventricle except for the anterior and posterior base (**Figure 1**). Based on the typical presentation of mid-apical LV ballooning, in the absence of significant coronary artery stenosis, the diagnosis of Tako-tsubo syndrome was made. At the time of cardiac catheterization, blood pressure was 75/45 mmHg. Dopamine (6  $\mu$ g/kg/min) was used for inotropic support. Owing to the lack of improvement, intra-aortic balloon pumping was instituted. In the CCU, the clinical status of the patient continued to deteriorate, blood pressure fell to 65/40 mmHg and heart rate was 95 beats per minute. The echo-Doppler revealed a persistent global and regional LV dysfunction with systolic anterior motion (SAM) of the anterior mitral leaflet, moderate-

to-severe mitral regurgitation, increased thickness of the proximal interventricular septum with a LV outflow tract (LVOT) obstruction as documented by a subvalvular pressure gradient of 64 mmHg (Figure 2). Dopamine was discontinued, but the hypotension persisted and atenolol 1.25 mg was administered. This change of medications resulted in a brief and transitory hemodynamic improvement. Finally, we attempted a combined therapy with a short acting beta-blocker (esmolol 15  $\mu$ g/kg/min) associated to a very low dose of dobutamine (2  $\mu$ g/kg/min) which achieved a slow but progressive hemodynamic improvement, with reduction of mitral regurgitation severity as well as LVOT pressure gradient. The patient was then commenced on loop diuretics with rapid clinical improvement. On a repeat echo-Doppler the day after, a marked reduction in the thickness of the LV proximal hypertrophied septum (from 20 mm to 14 mm) was apparent, while LV global and regional wall motion steadily improved until the time of discharge. The patient completely recovered and follow-up echo-Doppler examinations showed normal LV function. Ten days later, the patient had a cardiac MRI scan which showed normal LV volumes and ejection fraction, concentric hypertrophy with a septal thickness of 14 mm and mild edema of the mid-ventricular and apical septum, delayed hyperenhancement of the infero-lateral proximal wall.

## Discussion

In this report t, we described a case of obstructive Tako-tsubo cardiomyopathy complicated by cardiogenic shock that was then successfully treated medically. The unique finding of this report is the increased thickness of the proximal part of the LV septum that was evident at the onset of the acute episode and that partially reversed in the subsequent serial echocardiographic evaluations. A possible explanation of this observation is that the increased thickness of the septum might reflect the presence of myocardial edema as a result of a transient myocardial stunning secondary to an ischemia-reperfusion injury that can derive either from multiple simultaneous spasms of coronary arteries or from microvascular dysfunction.

LVOT obstruction is not an infrequent complication of Tako-tsubo syndrome, but mild, transitory patterns often remain underdiagnosed. Structural and functional factors contribute to the midsystolic development of gradients referred to as dynamic LVOT obstruction<sup>5</sup>. This report suggests that the association of increased myocardial tissue water with increased contractility of an asymmetrically hypertrophied septum may contribute to the progressive narrowing of the LVOT during systole<sup>6</sup>. Failure of the anterior mitral leaflet to coapt with the posterior leaflet in systole as a result of an abnormal SAM of the anterior leaflet may cause moderate-to-severe mitral regurgitation<sup>7</sup>. Although classically described with hypertrophic cardiomyopathy, SAM and LVOT obstruction can independently result from various clinical settings such as LV hypertrophy<sup>8</sup>, reduced LV chamber size, and hypercontractility (stress, anxiety, or inotropic agents).

In some cases of cardiogenic shock in patients with Tako-tsubo cardiomyopathy, LVOT obstruction rather than depressed LV function may become the key mechanism responsible of the low output syndrome and the use of positive inotropic agents may become harmful. In these circumstances, the negative inotropic effects of intravenous beta-blockers may be useful to reverse the LVOT obstruction<sup>9</sup>. In this case report, a successful resolution of the LVOT obstruction was obtained with the use of different beta-blockers, atenolol and esmolol, whereas the subsequent administration of a very low dose of dobutamine

contributed to stabilize the patient. In conclusion, there are reasons to believe that both the mid-apical LV ballooning and the narrowing of the LVOT during systole described in this case report were closely associated with the development of

myocardial edema. The presence of myocardial edema likely played a role in the pathogenesis of the subsequent cardiogenic shock possibly as result of a transient episode of global LV stunning together with LVOT obstruction.

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**Figure 2:** Evidence of mild edema of the mid-ventricular and apical septum at magnetic resonance imaging.

