



RESEARCH ARTICLE

TAKOTSUBO CARDIOMYOPATHY OCCURRING AFTER CARDIOPULMONARY BYPASS FOR CABG OPERATION. A CASEREPORTSOF TAKOTSUBO

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ABSTRACT

The cardiomyopathy is often observed after intense stressful events such as a major surgical procedure. In a recent study, demographic and clinical course data in patients with Takotsubo cardiomyopathy were compared between the United States and Japan. Few Japanese patients with Takotsubo cardiomyopathy had a history of overt coronary disease (CAD) and family history of early-onset CAD (Kazuo Komamura *et al.*, 2014).

**Methods:** An Iranian 78 years old woman with Hypertension and IDDM, with previous CVA suddenly showed a greatly increased heart rate, and an electrocardiogram revealed elevated ST-segments. After preoperative examination she accepted for emergency CABG. We diagnosed the condition as takotsubo cardiomyopathy (acute left ventricle apical ballooning syndrome), possibly caused by catecholamine release and regional stress-induced ischemia. We reviewed the literature on takotsubo cardiomyopathy as a complication of major cardiac surgery procedures.

**Core tip:** Takotsubo cardiomyopathy (TCM) occurs more often in postmenopausal elderly women, is characterized by a transient hypokinesis of the left ventricular (LV) apex and is associated with emotional or physical stress. TCM is an important disease entity that differs from acute myocardial infarction. Wall motion abnormality of the LV apex is generally transient and resolves within a few days to several weeks. The prognosis of TCM is generally good. It has been suggested that coronary spasm, coronary microvascular dysfunction, catecholamine toxicity and myocarditis might contribute to the pathogenesis of TCM. However, its pathophysiology is not clearly understood.

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INTRODUCTION

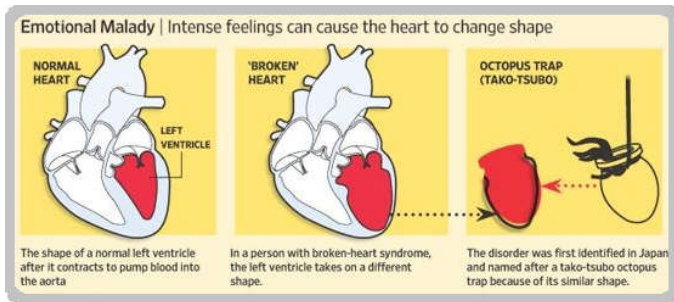
Takotsubo cardiomyopathy, also known as stress cardiomyopathy, apical ballooning, or broken heart syndrome, is a temporary heart condition (Farzaneh-Far and Farzaneh-Far, 2008). Symptoms include chest pain, difficulty breathing, and sudden loss of consciousness (Gianni *et al.*, 2006). Takotsubo cardiomyopathy most often affects women between the ages of 61-76. The condition commonly occurs immediately after experiencing extreme emotional or physical Stress.

Ballooning syndrome is a condition that has been recently described mimicking an acute coronary syndrome in its clinical, analytical, electrocardiographic and echocardiographic characteristics. Research suggests that the sudden release of stress hormones temporarily "stuns" and weakens the heart 2077. This stunning leads to inadequate circulation of blood throughout the body (Movahed and Donohue, 2007). The diagnosis is made based on coronary arteries with absence of significant obstruction, a typical left ventricular shape and complete recovery of ventricular function. Although associated complications, such as heart failure, may occur in the acute phase, its clinical course is favorable, and recurrence is exceptional (Donohue and Movahed, 2005). This condition occurs mostly in post-menopausal women under some form of physical or mental stress.

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Treatment is empirical and like that of acute myocardial infarction, with special attention in the administration of beta blockers and anticoagulation therapy. Tab.1 Fast facts on takotsubo cardiomyopathy.



**Fig 1. Broken heart or Takotsubo syndrome (Washington University Research)**

#### Fast facts on takotsubo cardiomyopathy

- Takotsubo cardiomyopathy was first identified in 1990
- The condition is named after a Japanese trap for octopuses
- People with takotsubo cardiomyopathy often mistake it for a heart attack
- Doctors believe that the condition is caused by the sudden release of stress hormones
- Takotsubo cardiomyopathy can be set off by emotional events
- Symptoms can include nausea, irregular heartbeat and sweating
- Takotsubo cardiomyopathy is diagnosed with the same tests as a heart attack

**Tab 1. Fast facts on takotsubo cardiomyopathy (Kathleen Davis, 2016)**

#### What is it?

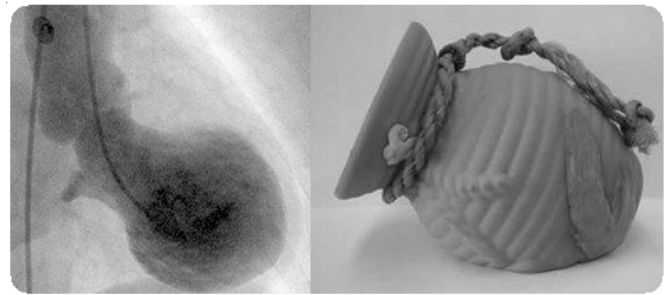
Takotsubo cardiomyopathy was first identified in Japan in 1990 and is now reported worldwide. It was named "takotsubo" cardiomyopathy because during the acute phase of the syndrome, the left ventricle bulges and takes on a balloon shape. fig-1 This shape is similar in appearance to the Japanese fisherman's "tako-tsubo" - an octopus trap. (Kathleen Davis, 2016). The condition is usually triggered by an emotionally or physically stressful event. It occurs most often in women 50 years of age and older. Most individuals with takotsubo cardiomyopathy seek emergency treatment because of concern they are experiencing a heart attack. Although it has similar symptoms to a heart attack, individuals with takotsubo cardiomyopathy show no evidence of blocked coronary arteries and recover quickly.

#### Pathophysiology

The pathophysiology of Takotsubo cardiomyopathy is not clearly understood at present. Several theories of the pathophysiology have been postulated, including multi-vessel coronary vasospasm and myocarditis Prasad, 2007. Stress is thought to be a significant risk factor for its development and currently, the leading theory is that catecholamines trigger the left ventricular abnormalities. High levels of circulating catecholamines have been measured in patients with Takotsubo cardiomyopathy (Askashi *et al.*, 2003).

#### Epidemiology

TCM symptoms were considered extremely rare until the past 20 years. The increasing number of medical reports on these symptoms has highlighted the higher incidence of TCM than that previously reported. Currently, 1000 or more studies reporting cases of TCM have been published.

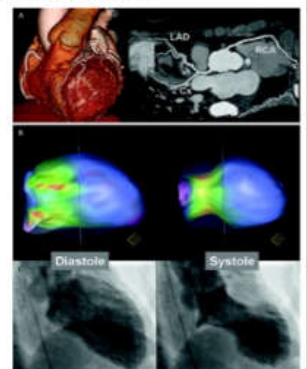


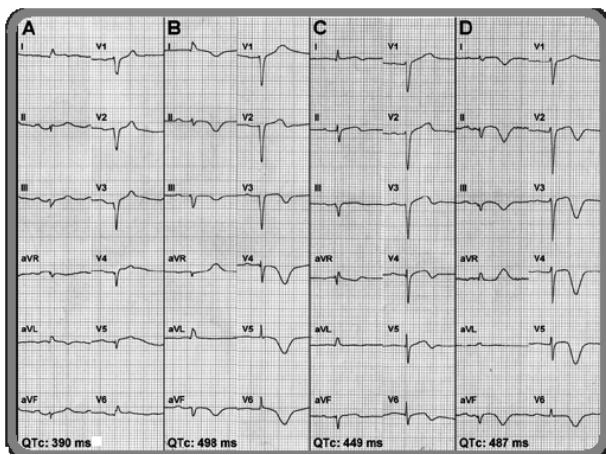
**Fig 2 . tako-tsubo" - an octopus trap**

According to a retrospective review, patients with TCM accounted for approximately 2% of all the patients with suspected acute coronary syndrome (Parodi *et al.*, 2007 and Eshtehardi *et al.*, 2009). Further, 90% of these patients were postmenopausal women (Strunk *et al.*, 2006 and Wedekind *et al.*, 2006). Another report indicated that most men with TCM were inpatients, which suggests that physical stresses might play a role for the progress of the disease (Kurusu *et al.*, 2010). Few Japanese patients with Takotsubo cardiomyopathy had a history of overt coronary disease (CAD) and family history of early-onset CAD (Kazuo Komamura *et al.*, 2014). Takotsubo syndrome (TS) can be challenging to differentiate from acute coronary syndrome because many of its symptoms, clinical signs, echocardiographic and electrocardiographic findings are superficially like those in patients with acute coronary syndrome e.g. cardiac chest pain, ST elevation, regional wall motion abnormalities. Takotsubo syndrome is usually diagnosed by using coronary angiography depicting the absence of culprit coronary stenosis to explain the regional wall motion abnormalities which extend beyond a single coronary artery Territory (Otalvaro *et al.*, 2011). Access to urgent invasive diagnostic coronary angiography is mandatory for patients presenting with acute chest pain and ST elevation. However, if presentation is delayed (e.g. >48 hours, or pain free and stable at presentation), then CT coronary angiography may have a role as an alternative imaging investigation to exclude coronary stenosis in stable patients suspected of takotsubo syndrome (Kazuo Komamura *et al.*, 2014). Electrocardiographic (ECG) abnormalities (Fig-2&3) are usually present in patients with takotsubo syndrome, i.e. ST-segment elevation acutely, and subsequently deep and widespread T-wave inversion; these changes evolve and depend on the time from the stress and symptom onset to clinical presentation and ECG recording (Ogura *et al.*, 2003; Kurusu *et al.*, 2004; Mitsuma *et al.*, 2007; Dib *et al.*, 2009; Kosuge *et al.*, 2010; Tamura *et al.*, 2011; Takashio *et al.*, 2012; Kosuge and Kimura, 2014 and Johnson *et al.*, 2013).

#### Primary Takotsubo Syndrome Classical Clinical Presentation

- Stressful trigger
- Chest Pain, Dyspnoea
- ECG Repolarisation changes
  - ST↑, QT↑, T↓
  - Arrhythmias
- Cardiac Enzyme rise
  - >95% cases troponin +ve
- Acute Heart Failure
  - 20-40% cases
- Serum catecholamines
  - 30x normal





**Fig 3. (ECG) abnormalities in takotsubo syndrome**

The presence of ST elevation makes it challenging to distinguish from ST-elevated myocardial infarction, and access to emergency coronary angiography should not be delayed (Dib *et al.*, 2009; Kosuge *et al.*, 2010; Tamura *et al.*, 2011; Takashio *et al.*, 2012; Kosuge and Kimura, 2014 and Johnson *et al.*, 2013). Kosuge *et al.* reported the differences in the distribution of ST-segment elevation between takotsubo syndrome and STEMI (Kosuge *et al.*, 2010).

### Mortality

The prognosis of takotsubo syndrome was initially reported in a relatively favourable manner in comparison to STEMI; however, subsequent studies have demonstrated that both the acute and long-term mortality are higher than previously recognized (Elesber *et al.*, 2007; Sharkey *et al.*, 2010 and Schultz *et al.*, 2012). Pre-hospital mortality is unknown, and this should not be underestimated; the mortality during the acute phase in hospitalized patients is ~4-5%, and comparable with modern STEMI (Song *et al.*, 2010). Furthermore, despite the recovery of LV function and absence of stenotic coronary artery disease, the mortality after hospital discharge is also remarkably poor and worse than an aged-matched healthy population. Intriguingly the prognosis is greatly influenced by non-cardiac diseases (Song *et al.*, 2010), reflecting the many cases of secondary takotsubo syndrome, where the triggering medical condition may impart the poor prognosis (Patel *et al.*, 2013).

### Acute multivessel coronary spasm

In subsequent series the incidence of vasospasm has been variable, but spontaneous vasospasm is observed in ~5-10% cases. Vasospastic provocation has been studied during the acute phase, with evidence in 10-43% patients in various series (Kurisu *et al.*, 2002 and Tsuchihashi *et al.*, 2001).

### Cardiac Biomarkers

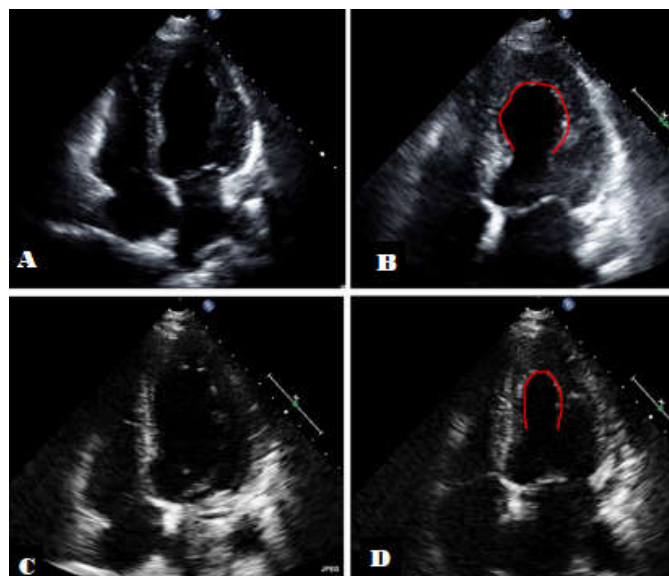
No elevation of the biomarkers has been reported in about 5% of cases of this syndrome (Movahed and Donohue, 2007). There is typically a slight increase in the creatine kinase MB and in troponins I and T, although at lower levels than occur with acute myocardial infarction (Donohue and Movahed, 2005 and Tsuchihashi *et al.*, 2001). There is no evidence of a rise in catecholamines in 30% of patients in the acute phase (Athanasiadis *et al.*, 2006). Elevation of C-reactive protein (CRP) is detected in 50% of patients and is a sign of poor prognosis and predictor of mortality in TS (Ruiz Bailén *et al.*, 2003).

### Echocardiography

The typical finding is of apical ballooning of the left ventricle (Fig-4). This is due to akinesia, hypokinesia, or dyskinesia of the apical and middle segments of the LV and hyperkinesia of the basal segments (Kawai *et al.*, 2007 and Pavin *et al.*, 1997). The LVEF is low or very low from the initial phase, with values below 30% in some cases and up to 75% (Pavin *et al.*, 1997 and Cocco and Chu, 2007).

### Causes

Although the exact cause of the syndrome is not known, research suggests that the sudden release of stress hormones (norepinephrine, epinephrine, and dopamine) "stuns" the heart. Stunning the heart triggers changes in heart muscle cells and coronary blood vessels (Cheng, 2007). Events that could trigger takotsubo cardiomyopathy. This hormone effect weakens the left ventricle, preventing it from pumping much needed oxygen-rich blood throughout the body. 28.5% of individuals have no clear triggers, takotsubo myopathy is typically triggered by an unexpected emotionally or physically stressful event.



**Fig. 4 Echocardiography changes in takotsubo cardiomyopathy with apical ballooning of the left ventricle**



**Events that could trigger takotsubo cardiomyopathy include:**

- The sudden death of a loved one
- Domestic abuse
- Natural disasters
- Motor vehicle accident
- Fierce argument
- Relationship conflicts
- Severe financial or gambling losses
- Being diagnosed with a medical condition
- Exhausting physical effort
- Surgery
- Acute medical illness
- Head trauma
- Public speaking
- Extreme fright

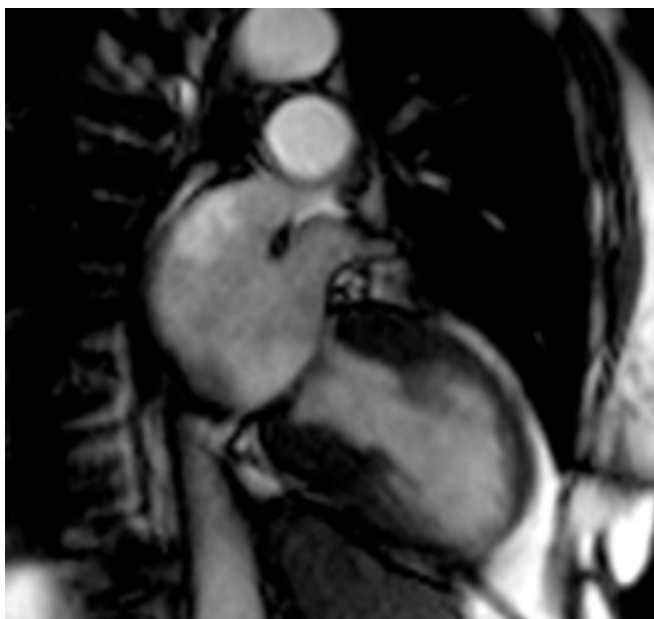
**Tab 2. Events that could trigger takotsubo cardiomyopathy (Kathleen Davis, 2016)**

**Diagnosis**

The tests and procedures for takotsubo cardiomyopathy are like those used to diagnose a MI. These tests include various blood tests, electrocardiogram (EKG), and echocardiography (Kathleen Davis, 2016). A diagnosis is confirmed with cardiac angiography, an X-ray of the blood (fig-5) vessels done with contrast dye in a hospital's cardiac catheterization laboratory.

**Treatment**

A person with takotsubo cardiomyopathy needs supportive care in a hospital setting until left ventricular function is restored to the heart (Kathleen Davis, 2016). Monitoring takes place in the intensive care unit for at least 24 hours. People with takotsubo cardiomyopathy often need a total hospital stay of 3-7 days.



**Fig 5. CT angiography with apical ballooning**

The echocardiographic, ventriculographic, and even electrocardiographic changes usually indicate severe cardiac disturbances, but these are not reflected in the enzyme levels, which are closer to values found in conditions such as myopericarditis or the non-ischemic cardiomyopathies (Prasad et al., 2008).

**Atypical forma of Takotsubo**

Reuss et al. described apical akinesia with normal midventricular movement and apical hypercontractility. Haghi et al. (2006 described transient midventricular ballooning or hawk’s beak with movement of the apex and basal segments and akinesia of the middle region (Table 3) (Haghi et al., 2006; Hurst et al., 2006 and Padayachee L. Levosimendan, 2007). Kim et al. described basal akinesia, normal midventricular movement, and basal hypokinesia (Bybee and Prasad, 2008 and Ueyama et al., 2003). Midventricular disorders are detected in 7–40% of cases, with 5% in the inverse syndrome and 7% in the other forms (Hansen, 2007 and Kurowski et al., 2007).

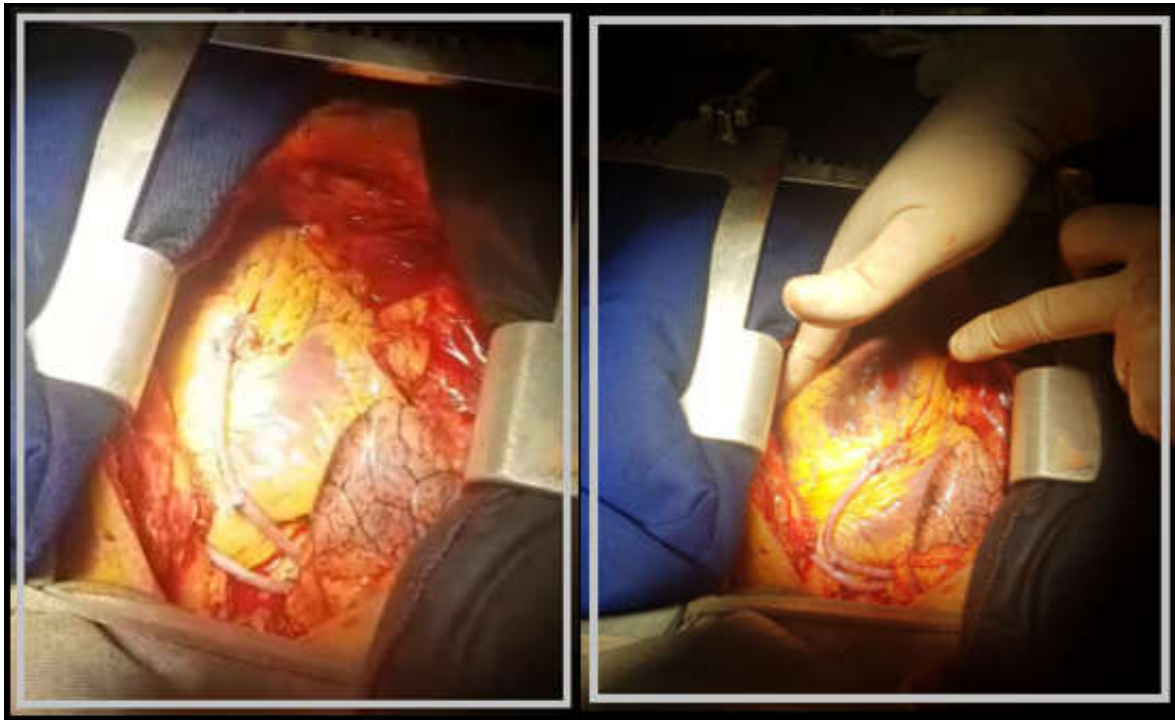
**Atypical forms of Takotsubo.**

<b>Type I.</b>	Takotsubo cardiomyopathy with apical ballooning.
<b>Type II.</b>	Midventricular ballooning
<b>Type III.</b>	Cardiomyopathy with apical hypercontractility
<b>Type IV.</b>	Basal ballooning
<b>Type V.</b>	Involvement of other segments.

**Tab 3. Atypical forma of Takotsubo**

## Biventricular involvement

Nyui *et al.* were the first to describe TS with right ventricular dysfunction (Nyui *et al.*, 2000). There are no clinical differences in TS with right ventricular dysfunction but there is more systolic dysfunction and heart failure greater dilatation of the right ventricle (RV), greater involvement of the lateral and inferior segments more marked pleural effusion a greater need for hemodynamic support and cardiopulmonary resuscitation and a longer hospital stay (Elesber *et al.*, 2006; López-Candales *et al.*, 2006 and Haghi, 2006). Severe right apical dysfunction due to hypokinesia occurs in 14.29% of cases. Biventricular involvement is present in 26–40% of cases (Haghi and Suselbeck, 2007; Song and Ma, 2007; Haghi *et al.*, 2005 and Haghi, 2006).



**Fig-6 Post CABG and apical ballooning**

## Treatment

A correct diagnosis will avoid treatment of ischemic heart disease (Ana María Castillo Rivera *et al.*, 2004). Now, treatment of TS is symptomatic and, as with other cardiomyopathies, is determined by the complications occurring during the acute phase (Ana María Castillo Rivera *et al.*, 2004). The use of intra-aortic balloon pump (IABP) support has been required and even cardiopulmonary support techniques and renal replacement therapy such as continuous veno-venous hemodiafiltration (Ana María Castillo Rivera *et al.*, 2004 and Patel *et al.*, 2007). The use of inotropes is controversial due to the increase in circulating catecholamines (Ana María Castillo Rivera *et al.*, 2004). Levosimendan may be beneficial for its inotropic and vasodilator effects (Lyon *et al.*, 2008). IABP is required by 8–46% of patients, less than in the ACS (Ana María Castillo Rivera *et al.*, 2004). Up to 36.36% of patients require vasoactive drugs and inotropes are used in 20–43.75% (Ana María Castillo Rivera *et al.*, 2004). Short-term anticoagulation may be considered, at least until recovery of ventricular function. The implantation of defibrillators is controversial; they are implanted in 2.5–8.3% of cases (Ana María Castillo Rivera *et al.*, 2004).

## CASE REPORTS

An Iranian 78 years old woman with Hypertension and IDDM, with previous CVA, suddenly showed a greatly increased heart rate, and an electrocardiogram revealed elevated ST-segments. Coronary angiography showed 3 vascular disease. After preoperative examination by cardiologist she accepted for emergency CABG by cardiac surgeon. After revascularization, and weaning from cardiopulmonary bypass (ECC) (LIMA to LAD and vein graft (VSM) to CX, OM1 and PDA), we mentioned abnormal wall motion in the inferior region and apical ballooning of the left ventricle. We diagnosed the condition as takotsubo cardiomyopathy (acute left ventricle apical ballooning syndrome), with trance esophageal – Echocardiography.

A total ECC was 41 min and aortic X-clamping 28 min. Patient did not get any type of catecholamine, before or during initiation of ECC (Fig -6). Patient transferred to Cardiac Intensive Care Unit, with anti-arrhythmic, anti-coagulation medications. Echocardiography 32 hours post-operative showed some dyskinesia of left ventricle but, no evidence of apical ballooning of the left ventricle. She had sufficient Cardiac out-put vid EF 56%. Her arterial blood gas was normal with saturation 98%. She discharges 4 days post-operatively to cardiac rehabilitation ward. Possibly this condition caused by catecholamine release and regional stress-induced ischemia. She was very afraid of hospital atmosphere and when she realized she must be operated on, she showed the symptoms of emotional shock.

## Conclusion

Surgery can be a major stressor and trigger massive catecholamine release itself. After cardiac surgery takotsubo cardiomyopathy should be suspected if clinical and instrumental criteria are met, and promptly differentiated from the more frequent acute myocardial infarction. Myocardial stunning secondary to the cardiopulmonary bypass was

hypothesized as the causative event. Prognosis may be favourable if appropriate conservative medical treatment is promptly started. The medical staff initiated the standard short-term treatment for takotsubo cardiomyopathy: combined beta-blocker, aspirin, and diuretic therapy.

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