Biventricular Takotsubo Cardiomyopathy: Case Study and Review of Literature

Biventricular takotsubo cardiomyopathy is associated with more hemodynamic instability than is isolated left ventricular takotsubo cardiomyopathy; medical management is more invasive and the course of hospitalization is longer.

In March 2011, a 62-year-old woman presented at our emergency department with abdominal pain, nausea, and vomiting. On hospital day 2, she experienced chest pain. An electrocardiogram and cardiac enzyme levels suggested an acute myocardial infarction. She underwent cardiac angiography and was found to have severe left ventricular systolic dysfunction involving the mid and apical segments, which resulted in a left ventricular ejection fraction of 0.10 to 0.15 in the absence of obstructive coronary artery disease. Her hospital course was complicated by cardiogenic shock that required hemodynamic support with an intra-aortic balloon pump and dobutamine. A transthoracic echocardiogram revealed akinesis of the mid-to-distal segments of the left ventricle and mid-to-apical dyskinesis of the right ventricular free wall characteristic of biventricular takotsubo cardiomyopathy. After several days of medical management, the patient was discharged from the hospital in stable condition.

To the best of our knowledge, this is the first review of the literature on biventricular takotsubo cardiomyopathy that compares its hemodynamic instability and medical management requirements with those of isolated left ventricular takotsubo cardiomyopathy. Herein, we discuss the case of our patient, review the pertinent medical literature, and convey the prevalence and importance of right ventricular involvement in patients with takotsubo cardiomyopathy. (Tex Heart Inst J 2013;40(3):305-11)

Transient left ventricular apical ballooning syndrome (TLVABS) is an acute cardiac syndrome that typically is characterized by transient left ventricular (LV) wall-motion abnormalities, electrocardiographic (ECG) findings of ST-T segment changes, and minimal release of cardiac enzymes in the absence of significant stenosis of the coronary arteries (<50% luminal stenosis).1-8 This syndrome was first described in Japan in 1991 and named takotsubo-like LV dysfunction in reference to the asynergy, which consists of hypokinesis or akinesis of the mid-to-apical LV and hyperkinesis of the basal LV extending over more than one coronary artery region.8,11 Since then, this asynergy has been called takotsubo cardiomyopathy (TC), stress cardiomyopathy, ampulla syndrome, broken-heart syndrome, and neurogenic stunned myocardium.12-14 Takotsubo cardiomyopathy presents clinically with chest pain and dyspnea associated with ECG changes, thereby mimicking ST-segment elevation myocardial infarction that is often preceded by emotional or physical stress.1-7,8,10 Indeed ST-segment elevation is the most common ECG abnormality, reported in approximately 82% of patients with TC, followed by T-wave inversion in 64%.8,15 This peculiar cardiac syndrome results in severe impairment of systolic function.

There are several variants of TC. Isolated LV involvement is the most common variant, but right ventricular (RV) involvement is gaining increased recognition. Although there is only one documented case of isolated RV stress cardiomyopathy,16 the recognition of biventricular TC is increasing. It has been reported that RV involvement affects approximately 25% to 42% of patients diagnosed with TC.11-13,17,18 In addition to isolated LV, isolated RV, and biventricular involvement, a variety of ballooning patterns has been observed. The typical apical-ballooning shape, with akinesis of the apical and mid-ventricular LV segments, is the most common; however, a mid-ventricular variant with apical sparing and a variant with isolated basal ballooning have been recognized.18

Left ventricular systolic dysfunction and heart failure—with simultaneous RV dysfunction—identifies a patient population with an extremely poor prognosis.19 Therefore, it is not surprising that TC with RV involvement appears to be associated with
more severe LV dysfunction that results in significantly longer hospitalization and hemodynamic instability that is associated with a worse prognosis. Clinicians need to be aware of the prevalence and complications of RV involvement and dysfunction, because it can affect patient management, morbidity, and, ultimately, mortality rates in substantial ways.

The data concerning RV involvement in TC are sparse, because they are derived from several case reports and case series studies. This review of the literature documents the prevalence, pathophysiology, diagnostic imaging characteristics, clinical findings, management, and prognosis of patients with biventricular TC. Throughout this article, TC with RV involvement will be referred to as biventricular TC, whereas classic left ventricular TC (with apical ballooning) will be referred to as TLVABS. All of the documented cases of biventricular TC have been evaluated and analyzed in regard to how the patient presented, how the TC was diagnosed and managed, and how we can improve in managing the even more hemodynamically unstable biventricular TC, in comparison with TLVABS.

**Case Report**

In March 2011, a 62-year-old woman presented at our emergency department with one week’s duration of abdominal pain, nausea, vomiting, and diarrhea. Three weeks before, she had undergone a kidney biopsy, which showed thin basement membrane disease. The patient’s vital signs were stable upon presentation.

During hospital day 2, she experienced chest pain, T-wave inversion in leads V2 through V6, and elevated levels of troponin I (3.84 ng/mL) and creatine kinase–MB (11.3 ng/mL). The patient underwent cardiac catheterization for a suspected acute myocardial infarction. During angiography, the coronary arteries were seen to be absent of significant luminal stenosis. A left ventriculogram showed akinesis of the mid-to-apical LV segments, hyperkinesis of the basal segments, and an LV ejection fraction (LVEF) of 0.10 to 0.15 (Fig. 1). The patient went into cardiogenic shock that necessitated hemodynamic support with dobutamine and an intra-aortic balloon pump (IABP).

A transthoracic echocardiogram showed severe LV systolic dysfunction (LVEF, 0.15), with akinesis of the mid-to-distal segments of the LV, along with mid-to-apical dyskinesis of the RV free wall suggestive of biventricular TC (Fig. 2). Grade 3 mitral valve insufficiency was also noted.

The patient was medically managed (standard therapy) for heart failure with severe LV systolic dysfunction. After 9 days, she was discharged from the hospital in stable condition. Her cardiac medications at discharge included simvastatin, aspirin, furosemide, lisinopril, and metoprolol.

A follow-up transthoracic echocardiogram at 5 weeks showed complete resolution of the LV systolic dysfunction and the RV wall-motion abnormalities. The LVEF was 0.50 to 0.55 upon follow-up (Fig. 3). Once LV sys-
tolic dysfunction resolved, heart-failure medications were discontinued. Aspirin and simvastatin were continued to treat nonobstructive coronary artery disease.

**Literature Review**

**Methods**

We performed a careful electronic search of the English-language literature, cross-referencing published studies and identifying 10 that pertained to biventricular TC. Two of the articles, by Haghi and colleagues and Elesber and associates, compared multiple patients with TLVABS to those with biventricular TC who had presented to their institutions over a period of time. There has been one documented case of isolated right ventricular stress cardiomyopathy.

All case studies were retrospective. Each study reported results on 1 to 9 patients. This review of biventricular TC encompasses 25 documented cases of patients with biventricular TC, our report of 1 additional case of biventricular TC, and 1 report of an isolated RV case.

**Results**

The main characteristics of the 26 cases of biventricular TC and the 1 case of isolated RV stress cardiomyopathy included in this review are summarized in Table 1. Several studies have reported that TC accounts for approximately 2% of all ST-segment-elevation acute coronary syndromes. Furthermore, several reports have concluded that the RV is involved in roughly 25% to 42% of all TC presentations.

In evaluating transient RV involvement and associated dysfunction by means of conventional echocardiography, Elesber and associates showed that 8 of 25 patients (32%) had biventricular involvement. These clinicians evaluated the hemodynamic impact of RV involvement by comparing patients with biventricular TC to those with TLVABS. There was no statistical difference between the 2 groups regarding age, coronary artery risk factors, discharge cardiac medications, presentation, ECG findings, cardiac catheterization findings, and maximal troponin release. However, patients with biventricular TC had significant reduction in LVEF (0.29 vs 0.42), were hospitalized 4 days longer (11 vs 7 d) on average, presented with notably increased tricuspid regurgitation velocity, and had an increased complication rate in comparison with TLVABS patients (but not at follow-up). Seven patients (88%) with RV involvement had severe congestive heart disease or required IABP placement, intubation, or cardiopulmonary resuscitation (CPR), compared with 2 patients (12%) with no RV involvement. Furthermore, the study showed that only when the RV is involved is there an association with IABP use, intubation, and CPR, all of which suggests greater hemodynamic instability. Similarly, there were 2 deaths (25%) associated with RV involvement, compared with only 1 death (5.8%) associated with TLVABS.

Using cardiac magnetic resonance (CMR) to detect RV involvement, Haghi and colleagues showed that 9 of 34 cases of TC (26%) had biventricular apical ballooning. They also found that 6 patients (67%) with RV involvement had pleural effusions, compared with 2 patients (8%) without RV involvement. However, bilateral (44%) or noteworthy (22%) pleural effusions did not occur unless both ventricles showed abnormal wall movements. It is postulated that as LV function declines, pulmonary venous pressure increases, which can result in leakage of fluid from the visceral pleural surface. In addition, patients with RV dysfunction also experience an increase in systemic venous pressure, which increases the filtration of fluid from parietal capillaries and simultaneously decreases lymphatic flow from the pleural cavity, resulting in an even more pronounced accumulation of fluid in the pleural cavity.

Eitel and co-authors also stated that significant bilateral pleural effusion was evident only when the RV was involved, which suggests that pleural effusion in TC is a reliable indicator of RV involvement, as we have mentioned.

Polak and coworkers conducted a series of studies to determine how RV dysfunction affects LV systolic function. They found that depressed RV function was linked to more severely compromised LV function, as confirmed by a greater reduction in LVEF and by an increase of LV dyskinesia. Moreover, these patients had a greater prevalence of chronic obstructive pulmonary disease, increased pulmonary capillary wedge pressure, and significant increases in both indices of RV overload (pulmonary artery pressure and pulmonary vascular resistance). In conclusion, depressed RV ejection fraction is an indicator of increased morbidity and mortality rates among patients who have chronic congestive heart failure secondary to atherosclerotic heart disease.

**Hemodynamics**

Takotsubo cardiomyopathy with RV involvement is associated with more severe systolic dysfunction, congestive heart failure, the need for IABP and CPR, more in-hospital complications, and pleural effusions. Therefore, it is of great importance to note the treatment requirements and regimens that have been documented in patients with biventricular TC; unfortunately, very few case studies provide such documentation. Elesber and associates stated that 6 of 8 patients (75%) with RV involvement had severe congestive heart failure, 5 required intubation (63%), 3 required IABP (38%), and 1 required CPR (13%).

Mrđović and colleagues documented the first and only reported case of isolated right ventricular TC, but
### TABLE I. Published Cases Identifying the Characteristics in Patients with Biventricular Takotsubo Cardiomyopathy, and Their Management

<table>
<thead>
<tr>
<th>Report</th>
<th>No. Pts.</th>
<th>Age, yr</th>
<th>Sex</th>
<th>Chief Presenting Symptoms</th>
<th>Triggering Factor</th>
<th>ECG Abnormalities</th>
<th>Cardiac Markers</th>
<th>BNP, pg/mL</th>
<th>WBC count/nL (normal range, 4–10 nL)</th>
<th>Imaging Method</th>
<th>Initial LVEF</th>
<th>Follow-up Method Used (time after resolution)</th>
<th>Hemodynamic Support</th>
</tr>
</thead>
<tbody>
<tr>
<td>Korlakunta H, et al.1* (2011)</td>
<td>1</td>
<td>89 F</td>
<td></td>
<td>CP and SOB, Bronchitis</td>
<td>—</td>
<td>Positive</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>CMR</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Eitel I, et al.3 (2011)</td>
<td>1</td>
<td>79 F</td>
<td></td>
<td>CP and SOB, Dog died</td>
<td>Positive</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>CMR</td>
<td>—</td>
<td>CMR (3 mo)</td>
<td>—</td>
</tr>
<tr>
<td>Novak G, et al.4 (2007)</td>
<td>1</td>
<td>65 F</td>
<td></td>
<td>CP and SOB, Tragic news about youngest son</td>
<td>Positive</td>
<td>Positive</td>
<td>4,430</td>
<td>20.8</td>
<td>Ventriculography and TTE</td>
<td>0.18 TTE (3 mo)</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Kuriso S, et al.6 (2005)</td>
<td>1</td>
<td>78 F</td>
<td></td>
<td>CP and SOB, Grandchild’s sudden death</td>
<td>Positive</td>
<td>Positive</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>Ventriculography (16 d)</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Citro R, et al.7* (2011)</td>
<td>1</td>
<td>81 F</td>
<td></td>
<td>CP and SOB, Unexpected death of family member</td>
<td>Positive</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>Ventriculography and TTE</td>
<td>0.35 TTE (18 d)</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Haghi D, et al.8 (2006)</td>
<td>9</td>
<td>70 ± 8 F, 1 M</td>
<td>CP, SOB, and nausea</td>
<td>—</td>
<td>Positive</td>
<td>Positive</td>
<td>—</td>
<td>CMR</td>
<td>0.40 ± 0.06</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Elesber AA, et al.9 (2006)</td>
<td>8</td>
<td>70 ± 13 F</td>
<td></td>
<td>—</td>
<td>—</td>
<td>Positive</td>
<td>—</td>
<td>—</td>
<td>TTE</td>
<td>0.29 ± 0.09</td>
<td>TTE (—)</td>
<td>3 of 8 (38%) required IABP</td>
<td>—</td>
</tr>
<tr>
<td>Nishikawa S, et al.11 (2004)</td>
<td>1</td>
<td>84 F</td>
<td></td>
<td>CP</td>
<td>Positive</td>
<td>Positive</td>
<td>1,010</td>
<td>15.7</td>
<td>Ventriculography (14 d)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Current case</td>
<td>1</td>
<td>62 F</td>
<td></td>
<td>Nausea, Recent medical diagnosis</td>
<td>Positive</td>
<td>Positive</td>
<td>742</td>
<td>22.8</td>
<td>TTE</td>
<td>0.10 TTE (4 wk)</td>
<td>IABP</td>
<td>—</td>
<td>IABP</td>
</tr>
</tbody>
</table>

BNP = pro-brain natriuretic peptide; CMR = cardiac magnetic resonance; CP = chest pain; ECG = electrocardiography; F = female; IABP = intra-aortic balloon pump; LVEF = left ventricular ejection fraction; M = male; Pts = patients; SOB = shortness of breath; TTE = transthoracic echocardiography; WBC = white blood cell

*Isolated right ventricular stress cardiomyopathy

Patient’s age is presented as number or as mean ± SD.
no hemodynamic requirements or treatment regimens were discussed within the case report.

Gianni and colleagues described the different presenting clinical findings, complications, treatments, and outcomes of 14 different case-review articles (covering 286 cases) on TC. They noted that only 8 of these articles specified the treatment in the acute phase and that very few reported the ongoing medical regimen. However, they did document that in the 14 articles, cardiogenic shock was a serious clinical presentation in 4.2% of cases, and that 23 of the 212 patients (10.8%) were treated with intra-aortic balloon counterpulsation. Unfortunately, within the 14 case-review articles analyzed, we do not know which cases, if any, involved the RV. However, on the basis of our knowledge of the current literature, we believe it probable that those requiring IABP and other more serious interventions had RV involvement complicating medical management.

Similarly, when members of the Angina Pectoris-Myocardial Infarction (AP-MI) investigations in Japan retrospectively registered and analyzed patients with TLVABS, they concluded that out of 88 patients with characteristics of TLVABS, 13 (15%) experienced cardiogenic shock, 7 (8%) required IABP, and 17 (19%) required dopamine or dobutamine; there was 1 sudden death. However, because we do not know which, if any, cases involved the RV, we cannot compare TLVABS with biventricular TC in regard to hemodynamic differences.

Although they are excellent sources of information regarding TC, Gianni and colleagues and the AP-MI investigations in Japan further illustrate the under-recognition of RV involvement in patients diagnosed with TC and the need to document that involvement more thoroughly. It is of interest that these 2 studies, in common with most previous studies of TC, depended upon either echocardiography or left ventriculography to identify patients with TC, thereby under-recognizing RV involvement. As CMR is used more widely throughout the world, RV involvement in patients with TC is gaining recognition.

Eitel and co-authors performed a prospective study at 7 tertiary care centers in Europe and North America, using CMR to define the exact prevalence and clinical spectrum of TC in a large population. Their findings are consistent with previously mentioned studies insofar as RV involvement occurs in 34% of patients with TC. They concluded that biventricular TC resulted in a significantly lower LVEF (0.43) than that in patients without RV involvement (0.48); and patients with biventricular TC tended to be older (73.4 vs 66.5 yr), to have significantly more stressful events preceding presentation (86% vs 65%), and to experience longer hospitalizations (7 vs 5 d). In addition, pleural effusions were more common in patients with biventricular TC (62% vs 19%).

### Cardiac Magnetic Resonance

Cardiac magnetic resonance has emerged as a noninvasive imaging method to accurately quantify LV and RV function, visualize regional wall-motion abnormalities, and help differentiate TC from similar causes of acute cardiac disease by evaluating markers for reversible (inflammation, ischemic edema) and irreversible (necrosis/fibrosis) injury. Previous studies that used CMR to evaluate TC considered the absence of late gadolinium enhancement (LGE) as an important finding, because it differentiates TC from acute myocardial infarction and myocarditis. The lack of delayed gadolinium enhancement suggests that the area of ballooning does not undergo irreversible damage, which might explain the complete recovery of LV and RV function in patients with TC.

Nakamori and associates monitored 23 patients who met certain criteria for the diagnosis of TC. Patients underwent CMR to evaluate LGE signal characteristics among patients who presented acutely with TC. Upon presentation, all patients manifested wall-motion abnormalities from the mid-ventricular to apical regions of the LV. Myocardial edema on T2-weighted magnetic resonance imaging was observed in 22 of 23 patients (96%). Late gadolinium enhancement was observed in 5 of 23 patients (22%). All instances of LGE were observed in an area that exhibited both wall-motion abnormalities and edema in a transmural distribution. In patients with TC, the contrast-to-noise ratio of these segments was significantly lower than the contrast-to-noise ratio of infarcted segments in patients with acute myocardial infarction.

At the 3-month follow-up, CMR revealed no edema on the T2-weighted magnetic resonance imaging in any of the patients of Nakamori and associates. All patients who had no segments showing LGE had complete recovery of wall motion. Among the 5 patients who manifested LGE in the acute phase, 2 patients showed no evidence of LGE at the 3-month follow-up. However, residual wall-motion abnormalities were observed in the remaining 3 patients; at 12-month follow-up CMR, both LGE and wall-motion abnormalities in these patients were completely resolved.

Cardiac magnetic resonance performed by Eitel and co-authors found that 117 of 139 patients (84%) who presented with TC had myocardial edema with a transmural distribution. Focal or patchy LGE was seen in 21 of 139 patients (15%).

Cardiac magnetic resonance findings in TC are summarized in Table II.

Nakamori and Eitel and their respective colleagues have been pivotal in determining the imaging diagnostic criteria and the pathophysiology for TC. Cardiac magnetic resonance that exhibits a gray myocardial signal on LGE has been found in approximately 20% of patients who present with TC. Furthermore, the pres-
We can conclude from this review of the literature that biventricular involvement has a substantial impact on hospitalization length and hemodynamic instability, thereby affecting the patient’s prognosis, morbidity, and outcome. Recognition of RV involvement in patients diagnosed with TC will better prepare physicians to treat the increased hemodynamic instability that is associated with RV involvement, potentially leading to decreased morbidity and mortality rates.

In the absence of studies that specifically document medical regimens for the treatment of biventricular TC, that treatment continues to be entirely case dependent and should be individualized in accordance with the patient’s characteristics and hemodynamic requirements at the time of presentation and throughout hospitalization. The fact is that standard heart-failure therapy (aspirin, β-blockers, angiotensin-converting enzyme inhibitors/angiotensin II receptor blockers, vasodilators, and diuretics) has proved beneficial in the management of patients with stress cardiomyopathy.8,11,18,24

**Limitations.** Our case study and literature review has certain limitations. First, all our data are derived from retrospective research; therefore, not all information (such as laboratory values) was documented, and not all cardiac procedures were performed in a manner that would support or weaken our conclusions. Second, the lack of data on biventricular TC is probably attributable to the diagnosis of most TC cases by means of left ventriculography during cardiac catheterization; right ventriculography is seldom performed, because it increases risk and yields no particular benefit. However, CMR is becoming more common in diagnosing TC, and it has the added benefit of noninvasively visualizing the RV and providing LGE markers to determine the extent of edema and inflammation, which might help to predict recovery time. Third, we probably have not accounted for all cases of documented biventricular TC, despite our careful electronic searches and cross-referencing of published articles for RV involvement; consequently, our review draws from a small number of cases and reports. However, this present analysis is the most complete review of the available data on biventricular TC to date.

**Acknowledgment**

We express sincere appreciation to Darlene Frankhouser, RDCS, Technical Director of the Echocardiography Laboratory at Memorial Hospital, for her assistance in organizing and preparing the cardiac images.

**References**


