

Our clinical experience and case series of Takotsubo cardiomyopathy

Takotsubo kardiyomiyopati üzerine klinik deneyimimiz ve vaka serimiz

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Abstract

In this study we aimed to evaluate the clinical course and prognosis of Takotsubo Cardiomyopathy cases diagnosed and treated in our clinic.

Takotsubo Cardiomyopathy was first described in 1990 by Dote et al. The reason why it is called Tako-tsubo cardiomyopathy; This is due to the appearance of the left ventricle resembling the narrow-necked, broad-bottomed container used by Japanese fishermen to catch octopuses. In addition to Takotsubo cardiomyopathy, this syndrome is also called ampulla cardiomyopathy, Human stress cardiomyopathy and Broken heart syndrome. In this study, a series of 7 cases of Takotsubo Cardiomyopathy diagnosed and treated in our clinic are presented and the clinical course and prognosis of the disease are examined.

The age range of the series, consisting of six female and one male patients, ranged from 57 to 81 years (median age 70). All of the female patients were in the postmenopausal period and physical or emotional stress was found in four of them. Moderate-to-moderate cardiac enzyme elevation was found in all of the patients. While noncritical plaques were detected in the angiography of six patients who underwent coronary angiography and ventriculography, one patient had normal coronaries. During the follow-up, in-hospital death due to non-cardiac causes (Acute Myeloblastic Leukemia) was observed in one of the patients. In the echocardiographic follow-up of six surviving patients, it was observed that the LV ejection fraction was normalized and ballooning regressed within two months.

The awareness of Takotsubo Cardiomyopathy among cardiology physicians in the world and in our country is increasing. However, information about its prevalence, clinical course and short-term prognosis in our country is insufficient. In the study, a new series was presented in addition to the first data of our country. It is thought that there may be some different physical risk factors that have not yet been identified.

Key words: Acute myocardial infarction, emotional stress, takotsubo cardiomyopathy.

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Öz

Bu çalışmada kliniğimizde teşhis ve tedavi edilen Takotsubo Kardiyomiyopati olgularının klinik seyrini ve prognozunu değerlendirmeyi amaçladık.

Takotsubo Kardiyomiyopati ilk olarak 1990 yılında Dote ve ark. Tako-tsubo kardiyomiyopati olarak adlandırılmasının nedeni; sol ventrikülün görünüşünün, Japon balıkçıların ahtapot yakalamak için kullandığı dar boyunlu, geniş tabanlı kaba benzetmesinden dolayıdır. Bu sendroma Takotsubo kardiyomiyopatisinin yanı sıra ampulla kardiyomiyopatisi, insan stres kardiyomiyopatisi ve kırık kalp sendromu da denir. Bu çalışmada kliniğimizde teşhis ve tedavi edilen 7 Takotsubo Kardiyomiyopati olgusu sunulmakta ve hastalığın klinik seyri ve prognozu incelenmektedir.

Altı kadın ve bir erkek hastadan oluşan serinin yaş aralığı 57 ile 81 yıl (ortalama yaş 70) arasında değişmekteydi. Kadın hastaların tamamı postmenopozal dönemdeydi ve dördünde fiziksel veya emosyonel stres saptandı. Tüm hastalarda orta-orta düzeyde kardiyak enzim yüksekliği saptandı. Koroner anjiyografi ve ventrikülografi yapılan altı hastanın anjiyografisinde kritik olmayan plaklar tespit edilirken, bir hastada koroner arterler normaldi. Takiplerde hastalardan birinde kalp dışı nedenlere bağlı hastane içi ölüm (Akut Miyeloblastik Lösemi) gözlemlendi. Yaşayan altı hastanın ekokardiyografik takibinde iki ay içinde LV ejeksiyon fraksiyonunun normale döndüğü ve balonlaşmanın gerilediği görüldü.

Dünyada ve ülkemizde kardiyoloji hekimleri arasında Takotsubo Kardiyomiyopati farkındalığı giderek artmaktadır. Ancak ülkemizde prevalansı, klinik seyri ve kısa dönem prognozu ile ilgili bilgiler yetersizdir. Çalışmada ülkemizin ilk verilerine ek olarak yeni bir seri sunulmuştur. Henüz tanımlanmamış bazı farklı fiziksel risk faktörlerinin olabileceği düşünülmektedir.

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Anahtar kelimeler: Akut miyokard enfarktüsü, duygusal stres, takotsubo kardiyomyopati.

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Introduction

Takotsubo Cardiomyopathy (TC) was first described in 1990 by Dote et al. [1]. The reason why it is called tako-tsubo cardiomyopathy; This is because the appearance of the left ventricle is similar to the narrow-necked, broad-based vessel used by Japanese fishermen to catch octopuses. Apart from Takotsubo cardiomyopathy, this syndrome is also called Ampulla cardiomyopathy, Human stress cardiomyopathy and Broken heart syndrome. TC is one of the most common causes of MINOCA (Myocardial infarction non-obstructive coronary arteries) [2].

Ventriculography and echocardiography are important in the diagnosis of Takotsubo cardiomyopathy. According to the differences in wall movements, Shimizu et al [3]. They made the TC classification.

Shimizu TC classification: 1. Takotsubo type: Apical akinesia and basal hyperkinesia 2. Reverse Takotsubo: Basal akinesia and apical hyperkinesia 3. Mid-ventricular type: Mid-ventricular ballooning accompanied by basal and apical hyperkinesia 4. Localized type: Takotsubo- ballooning in any part of the left ventricle accompanied by clinical findings of similar left ventricular dysfunction [3].

There are often stressful physical and emotional events in the history of the cases before the onset of symptoms. Most patients present with chest pain similar to angina at rest. Dyspnea may also be an accompanying initial symptom. Patients who usually present with acute coronary syndrome and ST segment changes [4, 5] may sometimes progress asymptotically [6]. Syncope, cardiac arrest, heart failure, supraventricular and ventricular arrhythmias are less common forms of presentation. Cardiogenic shock, respiratory failure, and pulmonary edema can be seen in the acute phase. Left ventricular rupture resulting in death has been observed [7]. Sometimes, cerebral or peripheral embolism may develop due to thrombi formed in the left ventricular aneurysmatic or dyskinetic segments [8].

Its clinical presentation is acute reversible heart failure without occlusive coronary artery disease and myocardial stunning [9]. Although there is no definitively agreed clinical criteria for Takotsubo cardiomyopathy, the Mayo clinical criteria are still used in the diagnosis.

1) Transient midventricular akinesia / dyskinesia in an area larger than the area fed by a single vessel (may accompany apical involvement), often (not necessarily) triggering stress factor is present.

2) ECG changes such as newly developing ST segment elevation or T wave negativity or moderate troponin elevation.

3) No significant stenosis ($\geq 50\%$) or acute plaque rupture on coronary angiography.

4) The absence of myocarditis and pheochromocytoma.

Cases

In our clinic, seven patients were diagnosed with TC in the last four years. The age range of the series consisting of six female and one male patients ranged from 57 to 81 years (median age 70). All of the female patients were in the postmenopausal period and physical or emotional stress was detected in four of them. Five patients had ST-T changes in the anterior leads (Figure 1), one patient had pacemaker rhythm and one patient had non-specific ST segment elevation. Moderate cardiac enzyme elevation was found in all cases. Color Doppler Echocardiography was performed in all cases on arrival and at the controls and the data were recorded (Figure 2). Non-critical plaques were detected in the angiography of six patients who underwent coronary angiography and ventriculography, while one patient had normal coronary arteries (Figure 3). In-hospital death due to non-cardiac causes (Acute Myeloblastic Leukemia) was observed in one of the patients during follow-up. In the echocardiographic follow-up of six survivors, it was observed that the LV ejection fraction normalized and ballooning regressed within two months. No

recurrent cardiovascular events were observed in the mean 2-year follow-up of our patients (Table 1-3).

Patient Confirmation: Information about the diagnosis and the procedure to be performed was provided to the patient or relatives of the patients, and a confirmation document was signed.

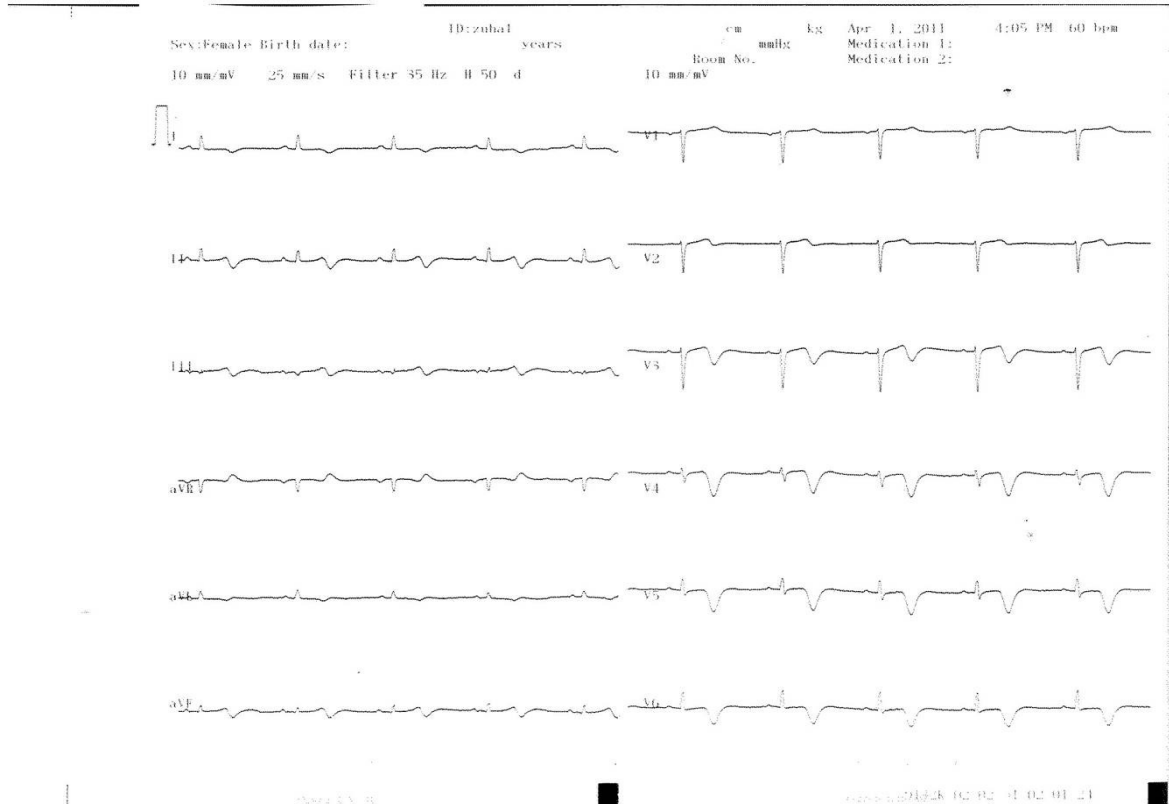


Figure 1. Electrocardiography

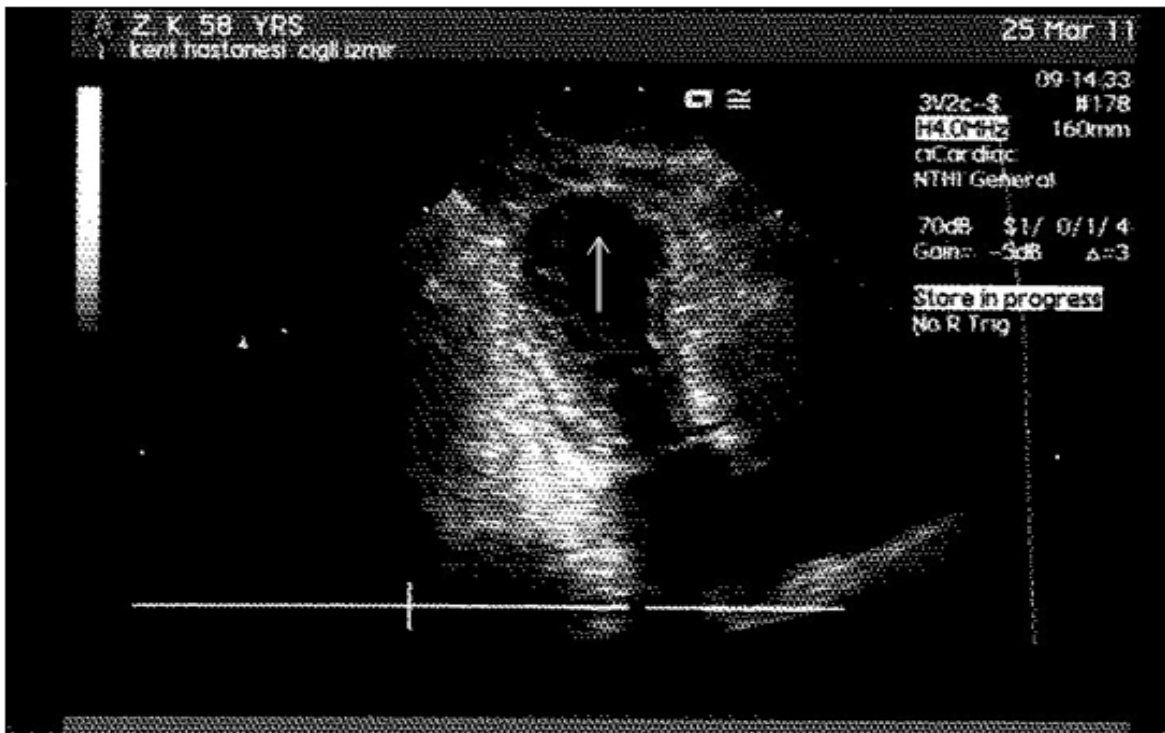


Figure 2. Echocardiography

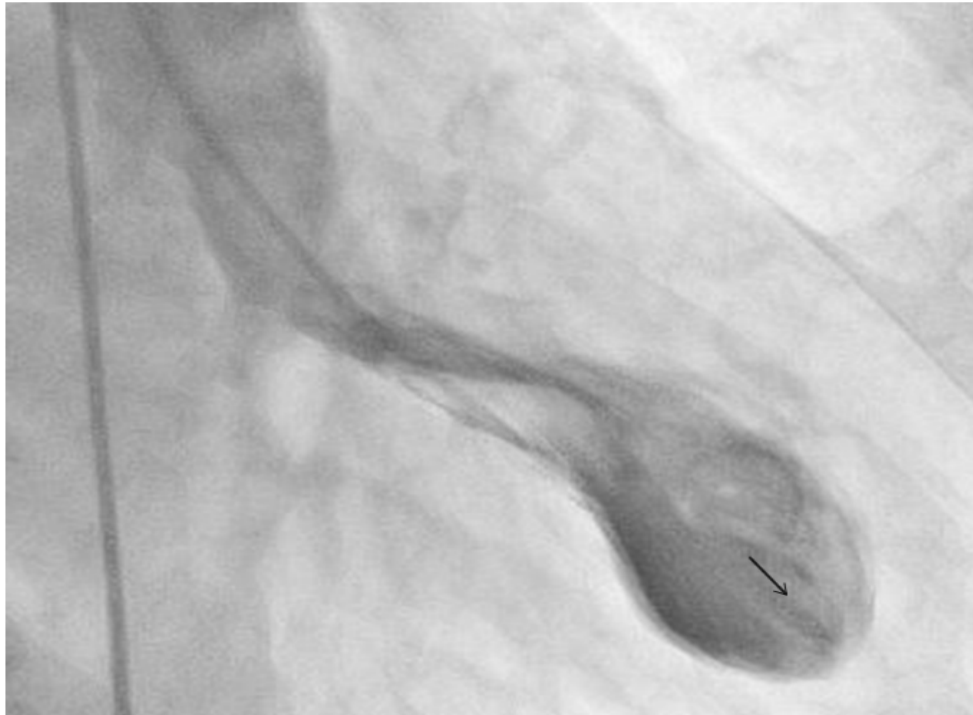


Figure 3. Ventriculography

Table 1. Clinical and demographic characteristics of patients

Age	Gender	Cardiovascular Risk Factors	ECG	Echocardiography
71	Female	HT, HPL		Apex hypokinetic
66	Female	HT, DM	V1-4 ST elevation	Apex dyskinetic, anterior apical akinetic
81	Female	OSAS	V1-4 ST elevation	Apex mild aneurysm, Inferior apical aneurysmatic
57	Male	-	V1-4 ST elevation	1/3 apical of all hypokinetic
77	Female	HT, HPL	Pace rhythm	Progressive hypokinesia to be more apex
58	Female	HT	V1-4 ST elevation	Apex dyskinetic
63	Female	-	V2-4 ST elevation	Anteroapical aneurysmatic

HT: Hypertension, HPL: Hyperlipidemia, DM: Diabetes Mellitus Type 2, OSAS: Obstructive sleep apnea syndrome

Table 2. Troponin level and coronary angiography of patients

Trigger Factor	TnT <u>ng/mlt</u>	Coronary Angiography	Conclusion
Emotional Stress	0.028	Normal Coronary arteries	Healing
Emotional Stress	0.089	Noncritical stenosis	Healing
COPD, Pneumonia	3.020	Noncritical stenosis	Healing
AML, Pulmonary Aspergillous	2.600	Plaque	<u>Exitus (non-cardiac reason)</u>
---	0.182	Plaque	Healing
Emotional Stress, Stomach Ca	0.244	Plaque	Healing
----	0.458	Plaque	Healing

TnT: Troponin T, COPD: Chronic Obstructive Pulmonary Disease
AML: Acute Myeloblastic Leukemia

Table 3. Echocardiography of patients

Before Treatment			After Treatment		
LVD (mm)	LVS (mm)	EF%	LVD (mm)	LVS (mm)	EF%
49	29	45	46	24	60
45	30	30	43	25	60
41	25	45	42	23	60
48	35	30	-EX	-EX	-EX
52	37	35	46	37	50
47	29	45	40	25	60
50	32	30	44	28	60

LVD: Left Ventricul Diastolic, LVS: Left Ventricul Systolic

Discussion

Approximately 90% of Takotsubo cardiomyopathy cases are postmenopausal women [10]. All six female cases were in the postmenopausal period and one case had a history of early menopause. All of the patients met the criteria for Takotsubo cardiomyopathy with clinical, ECG, echocardiographic and angiographic findings. In addition to ST segment elevation, T wave reversal or QT prolongation can also be seen on ECG [11]. Six of the seven patients in our series had ST-T changes in the precordial leads, while one case had a pacemaker rhythm.

Cardiac enzymes are often moderately elevated. For these reasons, it is often misdiagnosed as ST-elevation myocardial infarction (STEMI). The correct diagnosis can be made after further investigations by echocardiography or ventriculography with typical hypokinetic and ballooning visualization of the apex of the left ventricle, performing coronary angiography to show normal flow in the coronary arteries, and detecting the absence of late gadolinium involvement in cardiac magnetic resonance imaging, although it is not found in most clinics [12]. Moderate enzyme elevation was observed in all our cases. Coronary angiography revealed normal coronary arteries or plaques with noncritical stenosis. While apical bubbling was demonstrated by ventriculography in six cases, ventriculography was not performed in one case due to renal dysfunction. In this case, apical dysfunction was confirmed by echocardiography.

Takotsubo cardiomyopathy is known as a stress-induced disease. Emotional stress has

been described in 30-40% of patients [13]. Maekawa et al. [14] found a psychological or physical stress in more than 50% of the patients in their study. Emotional or physical stress was detected in five (71%) of our patients. While emotional stress was present in three cases, no stress factor was found in two cases. COPD is also considered in the etiology of TC. A history of COPD or bronchial asthma was reported in half of 32 patients who met the criteria and were diagnosed with TC, out of 17 thousand patients with normal coronary angiography [15]. In our series, one case had a history of COPD and it was observed that the case became complicated with pneumonia. OSAS was present in one of our cases. There is not yet a study investigating the frequency or relationship of TC in OSAS cases. In another study, a high rate of arterial hypertension was reported in 76% of patients with acute TC [16]. Hypertension was present in 57% of our cases. MVP was found in one of our patients. There is no literature data on a causal relationship between MVP and TC. It has been reported that severe transient mitral regurgitation and related acute pulmonary edema developed in a TC case [17]. In our series, an increase in the degree of mitral regurgitation was observed with the decrease in EF in a female TC patient who was also diagnosed with MVP. In our case, there was no wall motion defect other than apical ballooning. We observed that mitral regurgitation regressed in parallel with the increase in EF following medical treatment. Therefore, we think that MVP may be a facilitating factor with a different mechanism in the etiology of TC, even if it is a single case. In our female case, a milder TC clinic with another emotional stress attack occurred 6 months later, following complete

clinical recovery. Our patient was relieved by increasing the dose of beta blocker. This one case observation suggests the hypothesis that the beta blocker dose should be maintained at the optimal dose to prevent recurrences.

Initial medical treatment of the patients was arranged as the treatment of acute coronary syndrome. Drug preferences and doses (beta blocker, ACEI and diuretic, etc.) were adjusted according to the presence of additional problems.

The short, medium and long-term prognosis of these patients is close to perfect, except for those presenting with cardiogenic shock [18, 19]. Complications of Takotsubo cardiomyopathy include apical thrombus formation, cardiac rupture, embolic events and conduction disorders [20]. No conduction disorder or malignant arrhythmia was observed in any of our patients. Aphasia was observed in one of our patients during his hospitalization. In this case, thrombus was not detected with TTE and it was observed that completely regressed in the follow-up after the addition of anticoagulant treatment. No serious shock requiring IABP was observed in any of the patients.

Although left ventricular functions may be severely reduced at first admission and they recover within a few days. They return to their normal function within a few months [21]. In a study conducted by the French, death in hospital was reported in 1 out of 10 patients [22] and in 1 case in Desmet's 13 disease series [23]. In the American study, death was not observed in any of the 19 patients [24]. One of our TC cases (14%) was lost. This patient was receiving chemotherapy due to hematological malignancy (AML) and died due to non-cardiac causes. Except for this patient who died, recovery was observed in all patients who applied to our clinic. In the RETEKO (National Registry on TAKOsubo syndrome) Registry, malignancy was reported in 129 (11.8%) of 1097 TC cases followed in 38 centers between 2002 and 2019 [25]. There was malignancy in 2 cases (28.5%) in our series. In one case, recurrent clinic appeared after 6 months and with milder symptoms but treatment was performed without the need for hospitalization.

In conclusion, the awareness of TC among cardiologists in the world and in our country is increasing. However, information about

its frequency, clinical course and short-term prognosis in our country is insufficient. In the study, a new series was presented in addition to the first data of our country. It is thought that there may be some other physical risk factors that have not yet been determined.

Conflict of interest: No conflict of interest was declared by the authors.

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Informed consent: Information about the diagnosis and the procedure to be performed was provided to the patient or relatives of the patients, and a confirmation document was signed.

Authors' contributions to the article

A.S. and M.Z., have constructed the main idea and hypothesis of the study. A.S., M.Z., M.M.T. and S.H.M. developed the theory and arranged/edited the material and method section. A.S. and M.Z., have done the evaluation of the data in the results section. Discussion section of the article written by A.S., M.Z., M.M.T. and S.H.M. reviewed, corrected and approved. In addition, all authors discussed the entire study and approved the final version.