Journal of Geriatric Cardiology | JGC
LETTER TO THE EDITOR
J Geriatr Cardiol 2024; 21(10): 992–996

Clinical characteristics and prognosis of takotsubo syndrome patients in single center

Ye ZHU[1,2,✉], Bin-Hong TANG[1,2], Jia YOU[3], Chao XU[4]

1. Clinical Medical College of Yangzhou University, Jiangsu, China; 2. Department of Cardiology, Northern Jiangsu People's Hospital, Jiangsu, China; 3. Department of Internal Medicine, Yangzhou Maternal and Child Health Care Hospital, Jiangsu, China; 4. Department of Biostatistics and Epidemiology, University of Oklahoma Health Science Center, Oklahoma, USA

✉ Correspondence to: 307971331@qq.com
https://doi.org/10.26599/1671-5411.2024.10.007

Takotsubo syndrome (TTS) is a clinical syndrome that frequently occurs in postmenopausal women, mostly induced by stress factors. It is characterized by chest pain, ST-segment elevation, and/or T-wave changes in electrocardiogram, along with myocardial troponin elevation.[1] TTS can be easily misdiagnosed as myocardial infarction, and improper treatment may lead to serious consequences. There are few reports and research on this disease.[2] By retrospectively collecting clinical data and follow-up of patients with TTS, we aim to summarize the relevant clinical features of TTS.

The clinical and medical history data of TTS patients in Northern Jiangsu People's Hospital, Jiangsu, China from October 2013 to August 2023 were collected. Informed consent was signed by all participants in accordance with the Ethics Committee of Northern Jiangsu People's Hospital (No.2024ky009), Jiangsu, China. Patients were followed up regularly and adverse events, such as recurrence of disease or death were recorded.

Among the 20 patients of TTS had stress inducements and 5 cases had physical stress. Forty percent of the patients with TTS had a reduction in left ventricular systolic function during the acute phase. Four patients with TTS were in cardiogenic shock and intubated during the adimssion. Clinical characteristics of TTS patients were shown in Table 1.

Excluding two deceased patients and one patient who opted for transfer to a higher hospital on the third day, a comparison of the remaining 17 patients before discharge and admission revealed significant decreases ($P < 0.05$) in the patient's troponin I, alkaline phosphatase, N-terminal pro-B-type natriuretic peptide, alanine aminotransferase, aspartate aminotransferase, C-reactive protein, creatine kinase isoenzyme MB, triglyceride, total cholesterol, low-density lipoprotein cholesterol, and white blood cells. The high-density lipoprotein cholesterol, hemoglobin, and red blood cells exhibited significant increases ($P = 0.002$), as shown in Table 2.

Electrocardiographic indexes from admission to discharge was conducted for 17 patients (Figure 1). The P-wave time, QT, QTc time, and P-R interval between admission and discharge were not statistically significant ($P > 0.05$). Objective indicators of electrocardiogram are shown in Table 3. Echocardiography on admission revealed segmental wall motion abnormalities, and a left ventricular apical ventricular aneurysm was found in one case in acute stage (Figure 2). The echocardiography was repeated before discharge. Comparison of left atrium, left ventricular end-diastolic diameter, left ventricular ejection fraction, left ventricular end-systolic diameter, left ventricular fractional shortening was significantly different from those at admission ($P < 0.05$).

A total of 17 patients underwent coronary angiography, of which 12 patients had no stenosis and four patients had atherosclerotic plaque. Coronary computed tomography examination was performed in three patients, revealing no stenosis in two patients and coronary atherosclerotic plaque formation in one patient with stenosis degree < 50%. Left ventricular angiography was performed in 10 patients, of which 8 patients were typical, with decreased apical pulsation (Figure 3), and two patients were atypical, with decreased mid-ventricular contraction.

Four patients with TTS were hospitalized for cardiac

Table 1 Clinical characteristics of TTS patients.

Variables	Descriptive statistics	Reference value
Age, yrs	60.35 ± 5.32	–
Female	17 (85%)	–
Body mass index, kg/m^2	21.91 ± 6.10	–
Hypertension	11 (55%)	–
Diabetes mellitus	3 (15%)	–
Current smoking	3 (15%)	–
Hypothyroidism	1 (5%)	–
Initial systolic blood pressure, mmHg	138.35 ± 38.16	–
Initial diastolic blood pressure, mmHg	84.35 ± 22.76	–
Initial heart rate, beats/min	89.05 ± 28.44	–
Onset to visit time, d	2.50 ± 2.26	–
Troponin I, ng/mL	2.82 ± 3.55	0–0.034
Myoglobin, ng/mL	39.59 ± 19.3	0–121
Creatine kinase isoenzyme MB, ng/mL	48.82 ± 49.06	0–5
D-dimer	2.03 ± 3.79	0–0.50
N-terminal pro-B-type natriuretic peptide, pg/mL	6433.88 ± 9731.09	20–300
Symptoms on admission		
Chest pain	15 (75%)	–
Dyspnoea	6 (30%)	–
Length of stay, d	9.8 ± 6.8	–
Cardiogenic shock	4 (20%)	–
Left ventricular function during acute phase		
Preserved ejection fraction	12 (60%)	–
Intermediate ejection fraction	5 (25%)	–
Reduced ejection fraction	3 (15%)	–
Normal coronary arteries	12 (60%)	–
Intubation	4 (20%)	–
Intra-aortic balloon pump insertion	4 (20%)	–
In-hospital death	2 (10%)	–

Data are presented as means ± SD or *n* (%). TTS: takotsubo syndrome.

magnetic resonance examination (Figure 4). The results showed that left ventricular apex motion was weakened and myocardial systolic function decreased. In terms of delayed reinforcement, one of them had delayed subendocardial local reinforcement in the inferior left ventricular wall, and the other three had no delayed reinforcement.

The patients were hospitalized for an average of 9.8 ± 6.8 days, with one requesting transfer to a superior hospital for treatment on the third day. Two patients experienced in-hospital deaths. The remaining patients were followed up for 3.45 ± 1.47 years, with the condition of 17 cases improved and only one case relapsed.

TTS is primarily induced by various forms of stress. But it is still not fully studied and easy to be misdiagnosed. It is crucial to inquire patients' medical history to identify psychological and physical stressor.[3] At present, it is believed that stress stimulation is the main inducement factor, with only a small number of patients lacking definite stressor.[4] Studies suggest that the pathogenesis may be through the decrease of estrogen level in postmenopausal women, which leads to hypersympathetic nerve and endothelial dysfunction.[5] In this study, creatine kinase isoenzyme MB and cardiac troponin I increased, while N-terminal pro-B-type natriuretic peptide and C-reactive protein significantly increased as well, likely related to the massive secretion of catecholamines.[6] Clini-

Table 2 Comparison of biochemical results of patients before admission and discharge.

Variables	Admitted	Discharged	Paired difference	*P*-value
Troponin I, ng/mL	2.82 ± 3.55	0.83 ± 2.03	2.00 ± 1.83	0
Creatine kinase isoenzyme MB, ng/mL	48.82 ± 49.06	12.59 ± 23.08	36.23 ± 35.89	0.017
Myoglobin, ng/mL	39.59 ± 19.1	28.54 ± 13.24	12.58 ± 14.90	0.091
N-terminal pro-B-type natriuretic peptide, pg/mL	6433.88 ± 9731.09	3614.88 ± 3934.78	2819.00 ± 6673.091	0.007
C-reactive protein, mg/L	6.18 ± 2.23	1.97 ± 1.06	4.21 ± 1.67	0.037
Aspartate aminotransferase, U/L	55.30 ± 59.53	43.20 ± 48.81	11.00 ± 23.66	0
Glutamic-pyruvic transaminase, U/L	47.00 ± 29.81	30.33 ± 16.52	16.67 ± 21.94	0.039
Lactate dehydrogenase, U/L	285.42 ± 115.72	207.71 ± 88.33	77.71 ± 88.97	0.114
Alkaline phosphatase, U/L	97.58 ± 33.24	87.75 ± 29.17	9.83 ± 24.29	0.011
Triglyceride, mmol/L	1.36 ± 0.90	1.06 ± 0.64	0.30 ± 0.38	0
Total cholesterol, mmol/L	3.67 ± 0.64	3.44 ± 0.57	0.23 ± 0.37	0.007
High-density lipoprotein cholesterol, mmol/L	1.37 ± 0.61	1.40 ± 0.65	-0.04 ± 0.33	0.002
Low-density lipoprotein cholesterol, mmol/L	1.85 ± 0.45	1.78 ± 0.47	0.07 ± 0.16	0
Red blood cells, × 10^{12}/L	4.03 ± 0.25	4.18 ± 0.72	-0.15 ± 0.55	0.030
Hemoglobin, g/L	124.50 ± 7.15	126.88 ± 19.13	-2.38 ± 14.16	0.019
White blood cells, × 10^{9}/L	8.48 ± 3.53	7.15 ± 2.17	1.33 ± 2.11	0.011
Platelets, × 10^{9}/L	183.63 ± 33.84	261.25 ± 99.81	-77.63 ± 105.11	0.984

Data are presented as means ± SD.

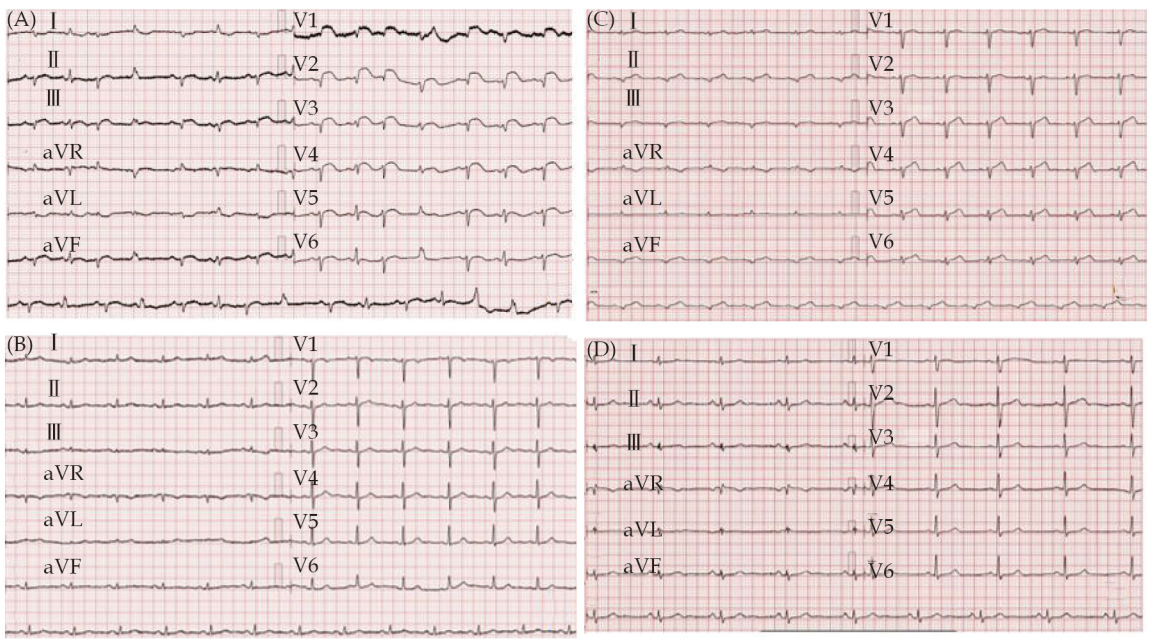

Figure 1 The representative ECG of the patient. (A): Early onset ECG of the same patient: sinus rhythm with atrial and ventricular premature beats; and images of extensive anterior myocardial infarction in acute stage; (B): the same patient convalescent ECG: normal ECG; (C): ECG in the acute stage in the same patient: sinus rhythm, ST-T changes, inferior and anterior myocardial infarction; and (D): ECG in the convalescent stage of the same patient: sinus bradycardia. ECG: electrocardiogram.

cal manifestations of TTS often mimic acute coronary syndrome.[7] Patients with TTS also showed related electrocardiographic changes, and after follow-up, electrocardiogram of them returned to normal, which was consistent with previous research.

Early echocardiography showed transient abnormal movement of left ventricular wall motion, which often returned to normal within a few weeks.[8] Most of the indica-

Table 3 Comparison of electrocardiography and echocardiography of 17 patients before and after admission.

Variables	Admitted	Discharged	Difference	*P*-value
Internal diameter of left atrium, mm	32.58 ± 4.96	32.92 ± 5.62	−0.33 ± 4.33	0.017
Left ventricular end-diastolic diameter, mm	46.25 ± 6.41	45.42 ± 6.41	0.83 ± 3.51	0.001
Left ventricular ejection fraction, %	55.00 ± 10.11	57.17 ± 7.95	2.17 ± 5.47	0.001
Left ventricular end-systolic diameter, mm	32.18 ± 6.59	31.73 ± 5.46	0.45 ± 3.01	0
Thickness of interventricular septum, mm	9.59 ± 1.16	9.91 ± 1.14	−0.32 ± 1.35	0.352
Left ventricular fractional shortening, %	30.45 ± 5.96	31.4 ± 0.73	−0.55 ± 3.96	0.008
P, ms	97.65 ± 8.78	97.67 ± 9.99	−0.01 ± 8.93	1.000
QT, ms	322.65 ± 39.78	392.78 ± 37.78	70.02 ± 38.14	0.123
QTc, ms	451.67 ± 32.35	498.33 ± 60.35	46.67 ± 48.17	0.298
QRS, ms	96.33 ± 6.35	74.67 ± 4.16	−21.33 ± 3.31	0.004
P-R, ms	155.33 ± 39.11	124.66 ± 29.64	−30.67 ± 32.75	0.390

Data are presented as means ± SD.

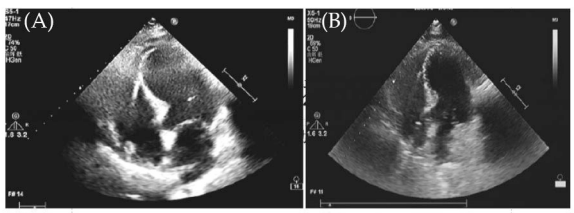

Figure 2 The representative echocardiography of this patient. (A): The same patient developed apical ventricular aneurysm in the early stage; and (B): apical ventricular aneurysm of the same patient disappeared and heart function recovered.

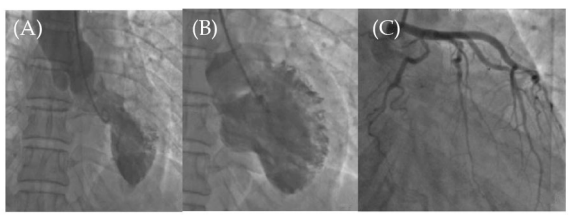

Figure 3 The representative left ventricular angiography of the patient. (A): One patient of reduced apical pulsation during systolic period by left ventricular angiography at the early stage of onset; (B): left ventricular angiography diastolic image of the same patient at the early stage of the disease; and (C): coronary angiography in the same patient showed no stenosis.

tors were significantly improved compared to admission, indicating that most of the TTS patients returned to normal within day to weeks. In this study, coronary angiography did not show significant stenosis or occlusion. The patient with the most severe stenosis had proximal 40%–50% segmental lesions in the left anterior descending artery. According to left ventriculography, the disease is classified into 4 types, typically with decreased systolic function and spherical expansion in the heart apex and nearby area. The other 3 types were atypical wall motion abnormalities.[9] A total of 10 left ventricular angiography was

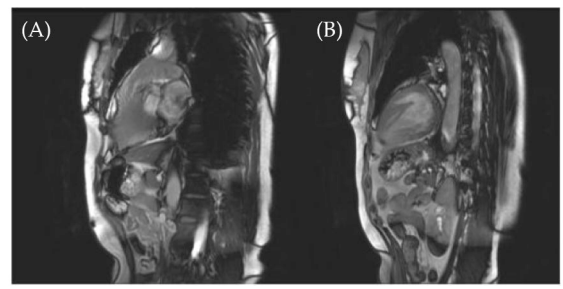

Figure 4 The representative cardiac magnetic resonance examination of this patient. (A): Local myocardial injury in the lower wall of the left ventricle; and (B): the local delay phase of the lower wall of the left ventricle could be seen as a flake signal increase.

performed in this study, with 8 cases being typical and 2 cases atypical, characterized by weakened midventricular contraction.

Cardiac magnetic resonance examination, with advantages incomparable to other examinations, is mainly used for auxiliary examination of myocardial activity in coronary heart disease. Four patients with TTS hospitalized who underwent cardiac magnetic resonance examination were found to have reduced left ventricular apex and adjacent ventricular wall motion, along with significantly reduced systolic function. About 52% of patients with TTS may develop severe acute complications leading to sudden cardiac death.[10] Elderly TTS patients combined with cardiogenic shock have a high mortality rate during hospitalization.[11] The limitation of this study is its single-center nature, which may omit emergency critically ill patients, warranting prospectively studies with multicenter and large-sample designs in the future.

In conclusion, abnormal segmental wall motion is common in early-stage TTS, accompanied by abnormal hea-

rt function. After treatment, abnormal wall motion can disappear, and heart function can be restored. Careful attention should be emphasized on improving the diagnostic efficiency of TTS to reduce the symptoms and recurrence.

ACKNOWLEDGMENTS

This study was supported by the National Natural Science Foundation of China (No.81800250), the China Postdoctoral Science Foundation (No.2022M711417), the Jiangsu Province Traditional Chinese Medicine Project (MS-2023137), and the Yangzhou Science and Technology Plan Social Development Project (YZ2023096). All authors had no conflicts of interest to disclose.

REFERENCES

[1] Amin HZ, Amin LZ, Pradipta A. Takotsubo cardiomyopathy: a brief review. *J Med Life* 2020; 13: 3–7.
[2] Bayón J, Reyes MÁ, Santás-Álvarez M, *et al*. The role of invasive coronary physiology in takotsubo syndrome. *Rev Cardiovasc Med* 2021; 22: 1357–1360.
[3] Wittstein IS. Why sex matters in takotsubo syndrome. *J Am Coll Cardiol* 2022; 79: 2094–2096.
[4] Looi JL, Chan C, Bridgman P, *et al*. Takotsubo syndrome in New Zealand: current knowledge and future challenges. *Intern Med J* 2022; 52: 1863–1876.
[5] Del Buono MG, Potere N, Chiabrando JG, *et al*. Takotsubo syndrome: diagnostic work-up and clues into differential diagnosis. *Curr Opin Cardiol* 2019; 34: 673–686.
[6] Lüscher TF, Akhtar MM. Looking deeper into takotsubo's heart. *Cardiovasc Res* 2022; 118: 1851–1853.
[7] Horowitz JD, Nguyen TH. Takotsubo syndrome: severe early coronary vasculitis predicts slow recovery. *JACC Cardiovasc Imaging* 2022; 15: 1796–1798.
[8] Ko T, Morita H. Takotsubo cardiomyopathy and peripartum cardiomyopathy. *Int Heart J* 2022; 63: 651–653.
[9] Salamanca J, Alfonso F. Novel hemodynamic insights in takotsubo syndrome. *J Am Coll Cardiol* 2023; 81: 1992–1995.
[10] Nuñez-Gil IJ. Takotsubo syndrome in China: serious but not so different. *Int J Cardiol* 2023; 390: 131177.
[11] Nagata T, Mohri M. The clinical features and outcomes of patients with takotsubo syndrome: the experience at an emergency general hospital. *Intern Med* 2018; 57: 641–645.

Please cite this article as: ZHU Y, TANG BH, YOU J, XU C. Clinical characteristics and prognosis of takotsubo syndrome patients in single center. *J Geriatr Cardiol* 2024; 21(10): 992–996. DOI: 10.26599/1671-5411.2024.10.007