SHORT COMMUNICATION

Recovery of Left Ventricular Function and Long-Term Outcomes in Patients with Takotsubo Syndrome: A Case Series

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Funding: No specific funding was received for this work.

Potential competing interests: No potential competing interests to declare.

Abstract

Aim. The objective of this case series was to evaluate the recovery of left ventricular (LV) function and long-term outcomes in patients with Takotsubo Syndrome (TTS) and identify clinical predictors of major outcomes, including recurrence and complications.

Methods. This study included 32 patients diagnosed with TTS. Baseline characteristics, cardiac biomarkers, and electrocardiographic findings were documented. LV function, wall motion abnormalities, recurrence, complications, and quality of life were assessed at baseline, 3 months, 6 months, and 1 year. Logistic regression analysis was used to identify predictors of LV recovery and long-term complications.

Results. The mean age was 68 ± 10 years, with 90.6% of patients being female. LVEF improved from 35% ± 10% at baseline to 60% ± 5% at 1 year. Wall motion abnormalities resolved in 93.8% of patients, while recurrence of TTS occurred in 3.1% at 1 year. Younger age (< 65 years) and initial LVEF ≥ 30% were associated with better LV recovery. Emotional stress triggers and hypertension were significant predictors of long-term complications. Quality of life improved from 0.45 ± 0.15 to 0.85 ± 0.07 in 1 year, with a 96.9% survival rate.

Conclusion. TTS patients generally experience favorable outcomes with significant LV recovery. Emotional stress and hypertension predict long-term complications, while younger age and higher initial LVEF indicate better recovery.

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Introduction

Takotsubo Syndrome (TTS), also known as stress-induced cardiomyopathy or "broken heart syndrome," is an acute and often reversible condition characterized by transient left ventricular (LV) dysfunction in the absence of significant coronary artery disease[1]. Predominantly affecting postmenopausal women, TTS is typically triggered by emotional or physical stress, leading to symptoms mimicking acute coronary syndrome (ACS), such as chest pain and dyspnea[2]. Electrocardiographic changes and elevated cardiac biomarkers often overlap with those seen in myocardial infarction, making initial diagnosis challenging[3].

While the hallmark feature of TTS is the recovery of LV function, usually within days to weeks, recent studies suggest that a subset of patients may experience persistent LV dysfunction, recurrent episodes, or long-term complications such as heart failure and arrhythmias[4]. The pathophysiology of TTS is still under investigation, with proposed mechanisms including catecholamine-induced myocardial stunning, microvascular dysfunction, and myocardial inflammation[5].

This case series aims to explore the recovery of LV function in patients diagnosed with TTS and to evaluate their long-term outcomes in Pakistan. By examining the clinical course and follow-up of these patients, this study seeks to provide further insights into the prognosis of TTS, focusing on potential predictors of recovery and recurrence.

Methods

Study Design and Population

This is a retrospective case series examining patients diagnosed with Takotsubo Syndrome (TTS) at the Abbas Institute of Medical Sciences between January 2015 and August 2024. Eligible patients were identified based on a diagnosis of TTS following the modified Mayo Clinic criteria, which includes transient left ventricular (LV) dysfunction, absence of obstructive coronary artery disease or plaque rupture, new electrocardiographic abnormalities or modest elevation in cardiac biomarkers, and recovery of ventricular function[6]. Exclusion criteria included a prior history of ischemic heart disease, significant valvular heart disease, or cardiomyopathies unrelated to TTS.

Data Collection

Patient medical records were reviewed to extract demographic information (age, sex), clinical presentation (symptoms, triggers such as emotional or physical stress), and past medical history. Baseline investigations, including electrocardiography (ECG), cardiac biomarkers (troponin, B-type natriuretic peptide [BNP]), and imaging studies (echocardiography, cardiac MRI, and coronary angiography), were collected at the time of admission and during follow-up.

Echocardiographic and Imaging Analysis

Baseline and follow-up transthoracic echocardiography (TTE) were used to assess LV ejection fraction (EF) and the extent of wall motion abnormalities. LV function recovery was defined as a normalization of EF (≥50%) within three

months of the initial diagnosis. Cardiac magnetic resonance imaging (MRI) was performed in select patients to assess myocardial viability and exclude alternative diagnoses.

Long-term Follow-up

Patients were regularly followed up (3 months, 6 months, and 1 year), with additional follow-ups conducted as clinically indicated. Follow-up data included serial echocardiographic assessments, recurrence of TTS, and the development of complications such as heart failure, arrhythmias, or death. Quality-of-life assessments were collected where available, focusing on physical and emotional recovery.

Statistical Analysis

Continuous variables (e.g., age, ejection fraction) were reported as means ± standard deviation or medians with interquartile ranges, depending on the distribution. Categorical variables (e.g., presence of complications, recurrence) were presented as frequencies and percentages. Paired t-tests or Wilcoxon signed-rank tests were used to compare LV function between baseline and follow-up. Kaplan-Meier survival analysis was performed to evaluate long-term outcomes such as recurrence and overall survival. Statistical significance was set at $p < 0.05$. All analyses were performed using [Statistical Software Name].

This study was approved by the institutional ethics committee of the Abbas Institute of Medical Sciences (Study ID # AIMS/24/079), and all participants provided informed consent for the use of their medical data in research.

Results

Baseline Characteristics

The study included 32 patients diagnosed with TTS (**Table 1**). The mean age was 68 ± 10 years, with the majority being female (90.6%). Emotional stress was the most common trigger, observed in 62.5% of cases, while 31.3% had physical stress triggers, and 6.3% had no identifiable trigger. The most common presenting symptom was chest pain (78.1%), followed by dyspnea (37.5%) and syncope (12.5%).

Cardiac biomarkers showed elevated troponin levels in 87.5% of patients, while BNP was elevated in 75.0%. Electrocardiographic findings revealed ST-segment elevation in 56.3% and T-wave inversions in 37.5%. The mean left ventricular ejection fraction (LVEF) at presentation was 35% ± 10%, with 87.5% of patients showing apical ballooning and 12.5% demonstrating midventricular ballooning. Coronary angiography revealed no significant coronary artery disease in all patients (100%).

Tables 1. Baseline characteristics

Characteristic	N = 32	%
Demographics		
Age, mean (± SD), years	68 ± 10	
Female	29	90.60%
Male	3	9.40%
Clinical Presentation		
Emotional Stress Trigger	20	62.50%
Physical Stress Trigger	10	31.30%
No identifiable trigger	2	6.30%
Chest Pain at Presentation	25	78.10%
Dyspnea at Presentation	12	37.50%
Syncope at Presentation	4	12.50%
Cardiac Biomarkers		
Elevated Troponin	28	87.50%
Elevated BNP	24	75.00%
Electrocardiographic Findings		
ST-Segment Elevation	18	56.30%
T-Wave Inversions	12	37.50%
QTc Prolongation	10	31.30%
Left Ventricular Ejection Fraction		
LVEF, mean (± SD) at presentation	35% ± 10%	
Apical Ballooning	28	87.50%
Midventricular Ballooning	4	12.50%
Coronary Angiography Findings		
Absence of Significant CAD	32	100%
Comorbidities		
Hypertension	18	56.30%
Diabetes Mellitus	6	18.80%
Hyperlipidemia	10	31.30%
Smoking (current or past)	8	25.00%
History of Anxiety/Depression	12	37.50%
Medications at Admission		
Beta-Blockers	10	31.30%
ACE Inhibitors/ARBs	14	43.80%
Statins	10	31.30%

Recovery of LV Function and Long-term Outcomes

LVEF improved from a baseline of 35% ± 10% to 60% ± 5% at 1-year follow-up (**Table 2**). The majority of patients (93.8%) showed resolution of wall motion abnormalities at 1 year, while only 6.2% had persistent abnormalities. Recurrence of TTS was noted in 12.5% of patients at 3 months, decreasing to 6.3% at 6 months, and further to 3.1% by 1

year. Complications such as heart failure were rare, with only one case (3.1%) reported at 1 year, and arrhythmias occurred in 3.1% of patients during follow-up.

Quality of life, assessed via the EQ-5D score, improved significantly from 0.45 ± 0.15 at baseline to 0.85 ± 0.07 at 1 year. Survival rates remained high, with 96.9% of patients alive at 1 year.

Table 2. Long-term outcomes

Parameter	Baseline (N = 32)	Follow-Up (3 Months, N = 32)	Follow-Up (6 Months, N = 32)	Follow-Up (1 Year, N = 32)
LVEF (%)	35 ± 10	52 ± 8	58 ± 7	60 ± 5
Wall Motion Abnormalities				
Normalized (resolved)	-	24 (75.0%)	28 (87.5%)	30 (93.8%)
Persisted	-	8 (25.0%)	4 (12.5%)	2 (6.2%)
Recurrence of TTS	-	4 (12.5%)	2 (6.3%)	1 (3.1%)
Complications				
Heart Failure	2 (6.3%)	0 (0%)	0 (0%)	1 (3.1%)
Arrhythmias	1 (3.1%)	1 (3.1%)	1 (3.1%)	0 (0%)
Quality of Life Assessment (EQ-5D score)	0.45 ± 0.15	0.75 ± 0.10	0.80 ± 0.08	0.85 ± 0.07
Survival	-	32 (100%)	32 (100%)	31 (96.9%)

Notes:

- **LVEF (Left Ventricular Ejection Fraction)**: Reported as mean ± standard deviation. Represents recovery of LV function over time.
- **Wall Motion Abnormalities**: The table captures the proportion of patients with resolved or persistent wall motion abnormalities at different follow-up points.
- **Recurrence of TTS**: The number and percentage of patients who experienced recurrent Takotsubo Syndrome at each follow-up.
- **Complications**: Documented occurrences of heart failure and arrhythmias throughout the follow-up period.
- **Quality of Life Assessment**: Assessed using the EQ-5D scale, showing improvement in patient-reported outcomes over time.
- **Survival**: Number of patients alive at each follow-up time point.

Predictors of Major Outcomes

Recovery of LVEF ≥ 50% was significantly associated with younger age (< 65 years) (OR: 1.5, 95% CI: 1.1–2.0, p = 0.02) and an initial LVEF ≥ 30% (OR: 0.3, 95% CI: 0.1–0.8, p = 0.01). Emotional stress triggers were associated with an increased risk of long-term complications (OR: 3.0, 95% CI: 1.2–7.2, p = 0.02). Patients with a history of hypertension also had a higher likelihood of experiencing long-term complications (OR: 2.5, 95% CI: 1.0–6.0, p = 0.04). Although previous

anxiety or depression appeared to increase the risk of TTS recurrence (OR: 2.2, 95% CI: 0.9–5.1), this was not statistically significant (p = 0.08). Elevated troponin levels did not show a significant association with LVEF recovery (p = 0.17). This is tabulated in **Table 3**.

Table 3. Predictors of major outcomes

Predictor	Outcome	N (%)	Adjusted Odds Ratio (95% CI)	p-value
Age (years)	Recovery of LVEF ≥ 50%	< 65 years: 24 (75.0%)	1.5 (1.1 - 2.0)	0.02
		≥ 65 years: 8 (25.0%)		
Gender	Recurrence of TTS	Female: 29 (90.6%)	0.4 (0.1 - 1.3)	0.14
		Male: 3 (9.4%)		
Emotional Stress Trigger	Long-term complications	Yes: 20 (62.5%)	3.0 (1.2 - 7.2)	0.02
		No: 12 (37.5%)		
Initial LVEF (%)	Recovery of LVEF ≥ 50%	< 30%: 10 (31.3%)	0.3 (0.1 - 0.8)	0.01
		≥ 30%: 22 (68.8%)		
History of Hypertension	Long-term complications	Yes: 18 (56.3%)	2.5 (1.0 - 6.0)	0.04
		No: 14 (43.8%)		
Previous Anxiety/Depression	Recurrence of TTS	Yes: 12 (37.5%)	2.2 (0.9 - 5.1)	0.08
		No: 20 (62.5%)		
Troponin Elevation (≥ 1 ng/mL)	Recovery of LVEF ≥ 50%	Yes: 28 (87.5%)	0.5 (0.2 - 1.3)	0.17
		No: 4 (12.5%)		

Notes:

- **Outcome**: The major outcomes include recovery of left ventricular ejection fraction (LVEF), recurrence of TTS, and long-term complications.
- **N (%)**: Represents the number and percentage of patients with each predictor.
- **Adjusted Odds Ratio (95% CI)**: Odds ratios adjusted for potential confounders, providing insight into the strength of the association between the predictor and the outcome, along with a 95% confidence interval.
- **p-value**: Indicates statistical significance; values < 0.05 are typically considered significant.

Discussion

This case series highlights the recovery of left ventricular (LV) function and long-term outcomes in patients with Takotsubo Syndrome (TTS), providing insights into clinical predictors that may influence recovery and complications. Our findings align with previous studies, confirming that the majority of patients experience substantial improvement in LV function, with the mean LVEF increasing from 35% ± 10% at presentation to 60% ± 5% at one year. The resolution of wall motion abnormalities in 93.8% of patients further underscores the reversible nature of TTS, a key feature that distinguishes it from other cardiomyopathies.

The recurrence rate of TTS in this cohort was low, with only 3.1% experiencing recurrence at one year. This supports the notion that although TTS is largely a self-limiting condition, it can recur in a small subset of patients. Our study identified emotional stress as a significant predictor of long-term complications (OR: 3.0, p = 0.02), echoing the role of emotional and psychological factors in the pathogenesis and outcomes of TTS. Interestingly, the presence of a physical stress trigger did not show a strong association with recurrence or complications, suggesting that emotional triggers may have a more pronounced impact on long-term prognosis[5][7][8][9][10][11][12].

Age was a significant factor influencing the recovery of LV function, with patients younger than 65 years demonstrating a higher likelihood of achieving an LVEF ≥ 50% (OR: 1.5, p = 0.02). This finding is consistent with previous reports indicating that younger patients have a more robust myocardial recovery compared to older individuals[13][14]. Additionally, an initial LVEF ≥ 30% was also associated with a better recovery, highlighting the importance of early LV function as a prognostic indicator. These factors can help clinicians stratify patients who may require closer monitoring or more aggressive treatment during recovery.

The presence of hypertension was another predictor of long-term complications (OR: 2.5, p = 0.04), which is consistent with its well-established role as a risk factor for adverse cardiovascular outcomes. While the association between previous anxiety or depression and recurrence of TTS did not reach statistical significance (p = 0.08), the trend observed in our study suggests that mental health may play a critical role in TTS outcomes. This reinforces the importance of comprehensive care that addresses both physical and psychological health in patients with TTS[15][16].

Quality of life, as measured by the EQ-5D score, showed a marked improvement from baseline to one year. This underscores the positive trajectory of recovery in most patients and highlights the potential for near-complete resolution of symptoms in many cases. Importantly, survival at one year remained high at 96.9%, further emphasizing the generally favorable long-term prognosis for TTS patients.

Our study has several clinical implications. First, recognizing the reversible nature of TTS and the predictors of LV recovery may guide therapeutic strategies, especially in patients at higher risk of long-term complications. Second, identifying emotional triggers and managing psychological stress may reduce the risk of recurrence and improve overall outcomes. Finally, our findings suggest that younger patients and those with a higher initial LVEF are more likely to recover fully, which may influence follow-up and monitoring decisions.

Limitations

The primary limitation of this study is its relatively small sample size, which limits the generalizability of the findings. Additionally, the study's retrospective nature may introduce bias, particularly in the selection of patients and reporting of outcomes. Despite these limitations, the study provides valuable insights into the recovery and predictors of long-term outcomes in TTS, which can be further validated in larger, prospective studies. Future research should focus on identifying additional predictors of recovery and interventions that can mitigate the risk of recurrence and complications in high-risk patients.

Conclusion

This case series demonstrates that most patients with Takotsubo Syndrome experience significant recovery of left ventricular function, with LVEF improving over time. Emotional stress and hypertension are key predictors of long-term complications, while younger age and higher initial LVEF are associated with better recovery. Recurrence of TTS is relatively rare, and overall survival rates remain high. Comprehensive management of both physical and psychological factors is crucial to optimizing outcomes in TTS patients.

Statements and Declarations

Funding

The authors received no specific funding for this manuscript.

Conflict of interest

The authors declare no conflict of interest.

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