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RESEARCH ARTICLE
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OUTCOMES IN TAKOTSUBO SYNDROME FOLLOWING LEFT VENTRICULAR EJECTION FRACTION IMPROVEMENT

Payal Bai[1*], Raj Kumar[2], Hina[3], Arzoo Pir Mohammad[4], Maham Fatima[5], Pehlaj Rai[6], Robish Kishore[7], Simran Kaur[8], Karan Kumar[9], Muhammad Shoaib Khan[10]

[1*]Liaquat University Hospital Jamshoro, Sindh, pk.payalkumar@gmail.com
[2]Medical Officer, Horbachevsky Ternopil National Medical University drrajkumar98@outlook.com
[3]FNU, Medical Officer, Liaquat National College and Hospital Karachi.hinarajput3031@gmail.com
[4] Kabul University of Medical Sciences Faculty of Medicine arzoo.pmd@gmail.com
[5]CMH Multan, Research Fellow at Weill Cornell Mdmahamfatima@gmail.com
[6]Medical Officer, Ghulam Muhammad Mahar Medical College Sukkur raipehlaj333@gmail.com
[7]Medical Officer, Ghulam Muhammad Mahar Medical College Sukkurrobishkishore12@gmail.com
[8]Resident Medical Officer, Ghulam Muhammad Mahar Medical College Sukkur simrankaur.kataria28@gmail.com
[9]Medical Officer, Ghulam Muhammad Mahar Medical College Sukkur Karankumarmakhija987@gmail.com
[10]Latin American School of Medicine Cuba/ House Physician Wyckoff Heights Medical Center Brooklyn New York balochcuba@gmail.com

***Corresponding Author:** Payal Bai
*Liaquat University Hospital Jamshoro, Sindh, pk.payalkumar@gmail.com

Abstract

Background: Takotsubo Syndrome (TTS), a transient form of stress-induced cardiomyopathy, often presents with acute left ventricular systolic dysfunction.

Objectives: To evaluate long-term clinical outcomes in patients with Takotsubo Syndrome who demonstrated improvement in left ventricular ejection fraction (LVEF), and to identify predictors of adverse events during follow-up.

Methods: This retrospective observational study was conducted at NICVD and tabba hospital Karachi during Feb 2024 to July 2024. A total of 78 patients were added to the study. Data were extracted from electronic health records using a standardized questionnaire. Baseline variables included patient demographics such as age, sex, and ethnicity; clinical presentation including type of stressor (emotional or physical), chest pain, electrocardiogram findings, and troponin levels; and imaging findings with particular attention to LVEF at admission, nadir, and follow-up.

Results: The mean age was 67.4 ± 11.2 years, and 78.2% of the cohort were female. Despite LVEF recovery, 26.9% of patients experienced MACE during follow-up. Heart failure hospitalizations (11.5%), new-onset arrhythmias (9.0%), and recurrent TTS (6.4%) were the most common adverse events. Independent predictors of MACE included diabetes mellitus (HR 2.34; 95% CI 1.01–5.42; p=0.047), baseline LVEF <35% (HR 2.89; 95% CI 1.15–7.23; p=0.024), and in-hospital arrhythmias (HR 3.12; 95% CI 1.19–8.14; p=0.019).

Conclusions: It is concluded that patients with Takotsubo Syndrome remain at significant risk for cardiovascular complications even after LVEF improvement. Risk factors such as diabetes, low initial LVEF, and arrhythmias during hospitalization should inform post-discharge care strategies.

Keywords: Takotsubo syndrome, left ventricular ejection fraction, cardiac recovery, outcomes, prognosis.

Introduction

TTS serves as a distinctive clinical condition leading to temporary left ventricular systolic dysfunction through stress-related triggers [1]. Japanese physicians identified this reversible regional wall motion abnormality in the late 1990s and its characteristic presents above a single coronary artery distribution area but angiographic tests show no obstructive coronary artery disease [2]. The medical condition happens mainly in postmenopausal women and doctors worldwide detect more cases because they have improved their cardiac imaging methods along with increasing their awareness of the diagnosis [3]. TTS demonstrates a common characteristic of complete LVEF recovery which becomes observable during a brief period of up to weeks following diagnosis [4]. A quick rise in left ventricular ejection fraction has long been used to deduce that TTS manifests as a harmless condition with outstanding outcomes. Most healthcare approaches to management prioritize crisis stabilization instead of following patients after their heart function appears healed [5].

Scientific evidence has started to counter the prevailing concept. Research has revealed that TTS patients who demonstrate recovery of LVEF still face numerous adverse outcomes [6]. Patients with TTS have elevated risks of heart failure and arrhythmias especially ventricular arrhythmias and atrial fibrillation and face threats of thromboembolic events and stroke as well as TTS recurrence and possibly death [7]. The mortality rate for patients with TTS over long periods turns out equal to those with acute myocardial infarction when considering patients who experience in-hospital complications [8]. Research indicates that LVEF recovery alone does not lead to complete cardiac or systemic recovery following TTS events because discharged TTS patients remain in a high-risk classification [9]. Clinical research needs to clarify why LVEF normalization exhibits insufficient correlation with patient outcomes. The use of LVEF readings serves adequately for detecting myocardial recovery in TTS cases. What mechanisms underlie the persistence of risk despite apparent functional improvement? Which specific demographic or health conditions combined with biomarkers and imaging results increase the risk factor for patients not to show recovery after LVEF normalization? The necessary next step involves answering these fundamental questions so we can redefine the standard methods to assess both recovery and prognosis in TTS patients. The psychological and neurological features of the syndrome must receive adequate attention. The diagnostic association between TTS occurs with psychiatric illnesses together with neurological diseases such as subarachnoid hemorrhage and epilepsy [10]. External triggers together with psychological factors play a role in both starting the initial cardiovascular event and determining both long-term healing and treatment compliance and risk of another event.

Objective

To evaluate long-term clinical outcomes in patients with Takotsubo Syndrome who demonstrated improvement in left ventricular ejection fraction (LVEF), and to identify predictors of adverse events during follow-up.

Methodology

This retrospective observational study was conducted at NICVD and Tabba Hospital Karachi during Feb 2024 to July 2024. A total of 78 patients were added to the study.

Inclusion criteria

- Adult patients aged ≥18 years
- Confirmed diagnosis of Takotsubo Syndrome
- Documented improvement in LVEF (defined as an increase ≥10% from baseline or normalization to ≥50%) within 8 weeks post-presentation
- At least 6 months of clinical follow-up data available

Exclusion criteria

- Incomplete echocardiographic data
- Presence of significant coronary artery disease (>50% stenosis)
- Recurrent TTS events during the initial hospitalization
- Concurrent diagnosis of myocarditis, pheochromocytoma, or peripartum cardiomyopathy

Data Collection

Data were extracted from electronic health records using a standardized questionnare. Baseline variables included patient demographics such as age, sex, and ethnicity; clinical presentation including type of stressor (emotional or physical), chest pain, electrocardiogram findings, and troponin levels; and imaging findings with particular attention to LVEF at admission, and follow-up. Echocardiographic assessments were performed using the biplane Simpson's method by standard imaging protocols.

Clinical details such as the use of pharmacotherapy, requirement for intensive care, and in-hospital complications including arrhythmias, thrombus formation, and cardiogenic shock were recorded. Post-discharge follow-up included documentation of recurrent TTS events, new cardiovascular conditions such as heart failure or arrhythmias, thromboembolic complications, and all-cause mortality.

Statistical Analysis

Data were analyzed using SPSS v21. Continuous variables were presented as means with standard deviations or medians with interquartile ranges, depending on data distribution, and were compared using independent t-tests. Categorical variables were expressed as frequencies and percentages, with comparisons made using chi-square tests. A p-value of less than 0.05 was considered statistically significant.

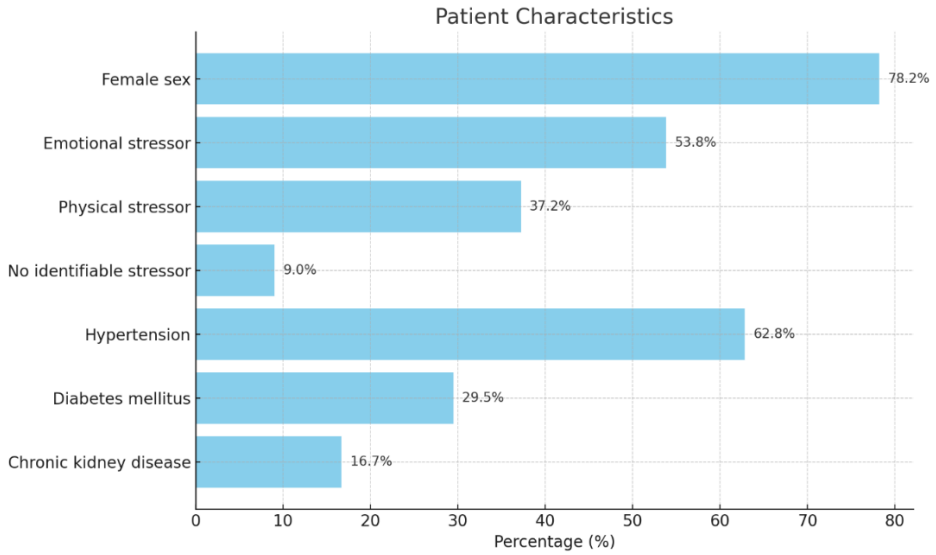
Results

A total of 78 patients were included in the study, with a mean age of 59.4 ± 11.2 years, and a predominance of females (78.2%). Emotional stressors were the most common trigger (53.8%), followed by physical stressors (37.2%), while no identifiable trigger was found in 9.0% of cases. At presentation, the mean baseline left ventricular ejection fraction (LVEF) was 38.5 ± 6.7%, which improved to 56.1 ± 5.4% after recovery. Common comorbidities included hypertension in 62.8% of patients, diabetes mellitus in 29.5%, and chronic kidney disease in 16.7%.

Table 1: Baseline Characteristics of the Study Cohort

Characteristic	Value
Number of patients	78
Age, mean ± SD (years)	59.4 ± 11.2
Female sex, n (%)	61 (78.2%)
Emotional stressor, n (%)	42 (53.8%)
Physical stressor, n (%)	29 (37.2%)
No identifiable stressor, n (%)	7 (9.0%)
Baseline LVEF, mean ± SD (%)	38.5 ± 6.7
Recovered LVEF, mean ± SD (%)	56.1 ± 5.4
Hypertension, n (%)	49 (62.8%)
Diabetes mellitus, n (%)	23 (29.5%)
Chronic kidney disease, n (%)	13 (16.7%)

Figure: 1

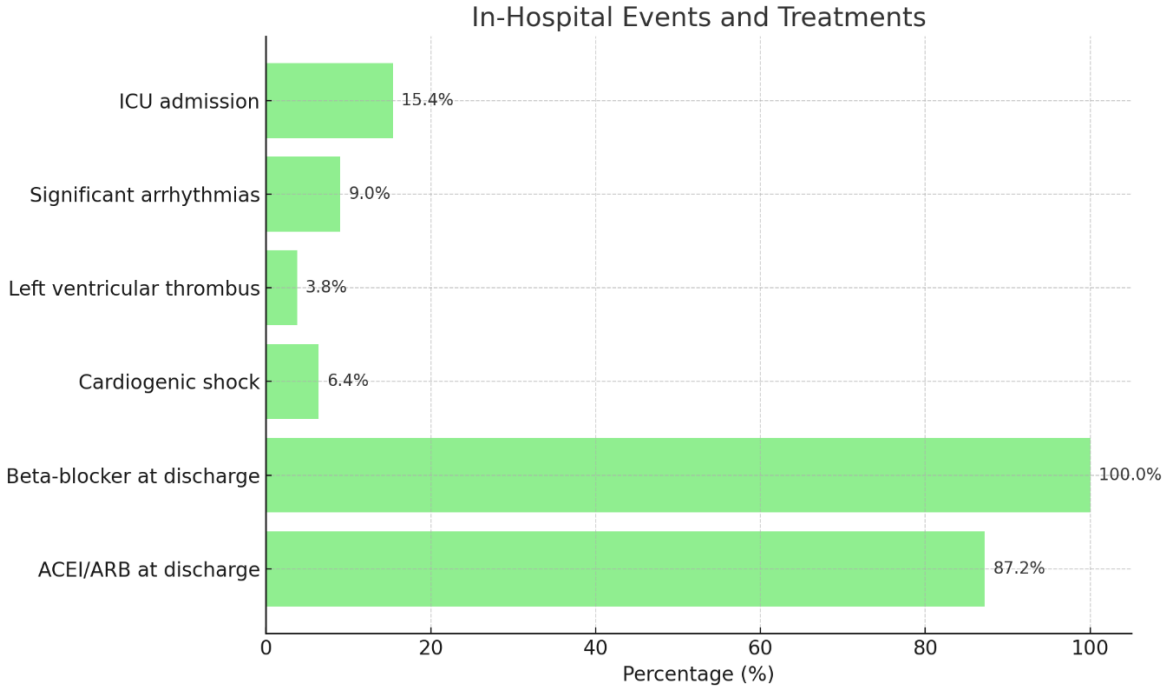


During the index hospitalization, 15.4% of patients required ICU admission, and 9.0% experienced significant arrhythmias. Left ventricular thrombus was identified in 3.8% of cases, while 6.4% developed cardiogenic shock. At discharge, all patients (100%) were prescribed beta-blockers, and the majority (87.2%) received either ACE inhibitors or ARBs, reflecting standard post-TTS management practices.

Table 2: In-Hospital Events and Discharge Treatments

In-Hospital Event or Treatment	Patients
ICU admission, n (%)	12 (15.4%)
Significant arrhythmias, n (%)	7 (9.0%)
Left ventricular thrombus, n (%)	3 (3.8%)
Cardiogenic shock, n (%)	5 (6.4%)
Beta-blocker at discharge, n (%)	78 (100%)
ACEI/ARB at discharge, n (%)	68 (87.2%)

Figure: 2

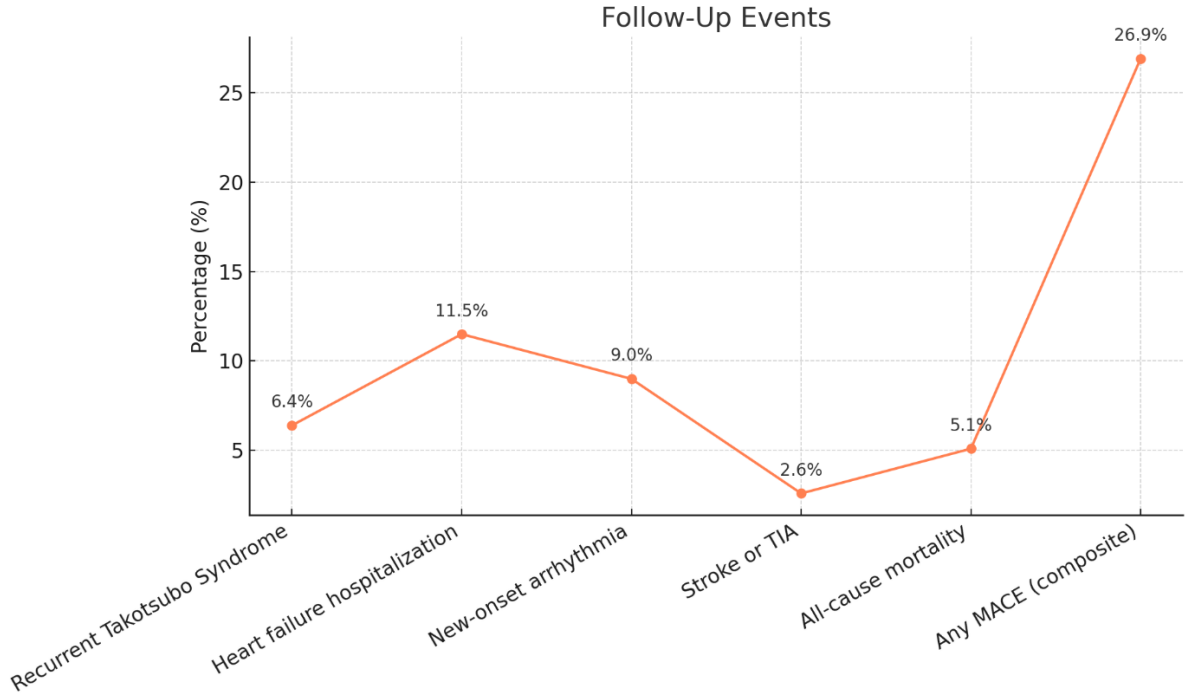


During a median follow-up period, 26.9% of patients experienced at least one major adverse cardiovascular event (MACE). Heart failure hospitalizations were the most frequent (11.5%), followed by new-onset arrhythmias (9.0%) and recurrent Takotsubo Syndrome episodes (6.4%). Stroke or transient ischemic attack occurred in 2.6% of patients, and the all-cause mortality rate was 5.1%, underscoring the long-term risks even after LVEF recovery.

Table 3: Long-Term Follow-Up Events

Follow-Up Event	Number of Patients	Percentage (%)
Recurrent Takotsubo Syndrome	5	6.4%
Heart failure hospitalization	9	11.5%
New-onset arrhythmia	7	9.0%
Stroke or TIA	2	2.6%
All-cause mortality	4	5.1%
Any MACE (composite)	21	26.9%

Figure: 3



Cox regression analysis revealed that diabetes mellitus (HR 2.34; 95% CI: 1.01–5.42; p = 0.047), baseline LVEF < 35% (HR 2.89; 95% CI: 1.15–7.23; p = 0.024), and in-hospital arrhythmias (HR 3.12; 95% CI: 1.19–8.14; p = 0.019) were significant independent predictors of major adverse cardiovascular events.

Table 4: Predictors of MACE (Cox Regression Analysis)

Variable	Hazard Ratio (HR)	95% Confidence Interval	p-value
Diabetes mellitus	2.34	1.01–5.42	0.047
Baseline LVEF < 35%	2.89	1.15–7.23	0.024
In-hospital arrhythmias	3.12	1.19–8.14	0.019
Age > 70 years	1.45	0.65–3.23	0.39
Female sex	1.12	0.54–2.35	0.77

Discussion

A total of 78 TTS patients who showed improvement in left ventricular ejection fraction (LVEF) suffered major adverse cardiovascular events (MACE) according to retrospective cohort findings at a rate of 26.9%. The medical community now faces new questions about TTS because LVEF improvement does not necessarily indicate a benign and self-limiting disease status. Standard

echocardiographic measurements showed recovery in patients but they nonetheless faced an elevated threat of heart failure together with arrhythmias along with new TTS occurrences and death risks. The results support current research demonstrating that LVEF improvement fails to guarantee complete myocardial recovery and it cannot protect against future adverse outcomes [11]. Healing events mostly led to heart failure admission (11.5%) and arrhythmias (9.0%) among patients. Previous research has shown that diastolic dysfunction and myocardial fibrosis usually evades standard imaging machines but continues to exist after systolic improvement occurs [12]. Patient recurrence of TTS materialized in 6.4% of cases according to the study findings and this recurrence frequency matched previously documented results that show TTS recurrent rates between 2% and 10% in other patient groups [13]. The continuing risk factor requires monitoring through long-term surveillance after patients demonstrate functional recovery.

The research study demonstrated multiple critical factors which affected MACE occurrence. Patients with diabetes mellitus along with LVEF less than 35% or any cases of in-hospital arrhythmias experienced poorer outcomes during the study period. The relationships reflect how cardiovascular vulnerability alongside the level of myocardial damage at the beginning present together. Diabetes both hurts endothelial functioning and triggers autonomic dysfunction that act as core mechanisms of TTS pathophysiology. The identified clinical factors enable healthcare providers to recognize patients at high risk thereby directing them to receive enhanced medical supervision with personalized care plans. The analysis from our multivariate model showed that age and female gender do not affect long-term outcomes on their own. The data shows that sex itself does not predict disease outcome after Complete Left Ventricular Ejection Fraction recovery among TTS patients. Multiple studies agree with our results that the long-term outcomes between inciting stressors categorized as either emotional or physical stresses do not differ significantly [14][15]. The main strengths of this research are its well-identified patient population combined with comprehensive echocardiographic measurements and long-term tracking of patient status. The study has several restrictions that researchers should acknowledge. The retrospective evaluation method generates possible data collection errors alongside event measurement errors. Second, the sample size, although reasonable for a single-center study, limits the generalizability of the findings. Our study lacks data on global longitudinal strain and cardiac MRI parameters because these measurements would extend understanding regarding myocardial recovery as well as residual dysfunction.

Conclusion

It is concluded that patients with Takotsubo Syndrome, even after improvement in left ventricular ejection fraction, remain at substantial risk for major adverse cardiovascular events during long-term follow-up. Despite the apparent normalization of systolic function, a significant proportion of patients in this study experienced complications such as heart failure, arrhythmias, recurrent TTS episodes, and mortality. These findings underscore the importance of recognizing that LVEF recovery does not equate to full myocardial healing or prognostic reassurance.

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