Meta-analysis of incidence and outcomes of life-threatening arrhythmias in takotsubo cardiomyopathy

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Abstract

Background: Takotsubo cardiomyopathy (TC) or stress-induced cardiomyopathy is a transient heart condition that clinically resembles an acute coronary syndrome. This study aims to assess the incidence of life-threatening arrhythmias in patients with Takotsubo cardiomyopathy and evaluate the outcomes of patients with life-threatening arrhythmias (LTAs) in Takotsubo cardiomyopathy compared with those without LTAs.

Methods: We comprehensively searched the PubMed, Google Scholar, and Embase databases from inception to February 2021. The primary aim of the study was to determine the incidence of LTAs in TC patients. Other outcomes of interest were the odds of in-hospital, long-term mortality, and cardiogenic shock (CS) in TC patients with LTAs versus those without LTAs. For all statistical analyses, ReviewManager and MedCalc were used.

Results: Eighteen studies were included in this study involving 55,557 participants (2,185 with LTAs and 53,372 without LTAs). The pooled incidence of LTAs in the patients of TC was found to be 6.29% (CI: 4.70–8.08%; I² = 94.67%). There was a statistically significant increased risk of in-hospital mortality (OR = 4.74; CI: 2.24–10.04; I² = 77%, p < 0.0001) and cardiogenic shock (OR = 5.60; CI: 3.51–8.95; I² = 0%, p < 0.00001) in the LTA group versus the non-LTA group. LTAs were not associated with long-term mortality (OR = 2.23; CI: 0.94–5.28; I² = 53%, p = 0.07).

Conclusion: The pooled incidence of life-threatening arrhythmias in the patients of TC was found to be 6.29%. In the group of TC patients with LTAs, the odds of in-hospital mortality and CS, was higher than in the TC patients without LTAs.

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1. Introduction

Takotsubo cardiomyopathy (TC) is non-ischemic cardiomyopathy first described in 1990. Also named apical ballooning or stress cardiomyopathy, it is characterized by reversible left ventricular
systolic dysfunction with no evidence of obstructive epicardial coronary disease. Clinical symptoms and electrocardiographic findings resemble those of an acute myocardial infarction with approximately 2.0% of acute ST-segment elevations presentations representing TC. Post-menopausal women are more frequently affected, usually following emotional distress. Nevertheless, other triggers include subarachnoid hemorrhage, ischemic stroke, severe head injury, acute medical illness, or acute pheochromocytoma crisis.

The pathophysiology is not entirely understood but may involve catecholamine toxicity and vasospasm orchestrated by central neurogenic mechanisms, thereby explaining psychological stress as a precipitant. On biopsy, inflammatory infiltrates and contraction bands distinguish TC from coagulative necrosis seen on myocardial infarction caused by coronary artery occlusion, explaining minimal myocardial enzyme release in the setting of Takotsubo cardiomyopathy.

Whereas the prognosis is generally favorable, and improvement of left ventricular function ensues within 3–4 weeks, significant morbidity and mortality can be associated with TC. Heart-failure, left ventricular free wall rupture and fatal arrhythmias are among the possible complications. Although mild ST-segment elevation extending beyond the distribution of a single coronary artery and T-wave inversions are the most common findings on admission, explaining minimal myocardial enzyme release in the setting of Takotsubo cardiomyopathy.

In particular, the incidence of LTAs has been reported as 1.8%–13.5% of hospitalized patients with TC. Ventricular tachycardia, ventricular fibrillation, asystole, and pulseless electrical activity are included among LTAs. There is also an increased risk of developing atrial arrhythmias due to transient left atrial dysfunction in the acute phase of the disease. Furthermore, patients with atrial fibrillation in the setting of TC may have a lower long-term prognosis. Schneider et al reported the mortality in Takotsubo cardiomyopathy patients with and without life-threatening arrhythmias, and (3) studies with patients ≥ 18 years and a sample size of ≥ 10 patients. The definition of Life-threatening arrhythmias (LTAs) was accepted as reported by the individual studies. Across all studies, LTAs included ventricular tachycardia (VT), ventricular fibrillation (VFib), ventricular flutter, second-degree atrioventricular (AV) block type II, third-degree AV block, pulseless electrical activity, asystole, Torsade de Pointes (Tdp), and high degree sinusal (SA) block. The exclusion criteria were pre-determined as follows: (1) duplicate publications, (2) studies that included information about atrial arrhythmias only, (3) studies that did not mention the outcomes of atrial and ventricular arrhythmias in TC patients separately, and (4) commentaries, reviews, and posters.

2.2. Eligibility criteria

Studies were included if they met the following inclusion criteria: (1) studies that reported the incidence of life-threatening arrhythmias, detected either on admission or during hospital stay, in the patients of Takotsubo cardiomyopathy, (2) studies that reported the mortality in Takotsubo cardiomyopathy patients with and without life-threatening arrhythmias, and (3) studies with patients ≥ 18 years and a sample size of ≥ 10 patients. The definition of Life-threatening arrhythmias (LTAs) was accepted as reported by the individual studies. Across all studies, LTAs included ventricular tachycardia (VT), ventricular fibrillation (VFib), ventricular flutter, second-degree atrioventricular (AV) block type II, third-degree AV block, pulseless electrical activity, asystole, Torsade de Pointes (Tdp), and high degree sinusal (SA) block. The exclusion criteria were pre-determined as follows: (1) duplicate publications, (2) studies that included information about atrial arrhythmias only, (3) studies that did not mention the outcomes of atrial and ventricular arrhythmias in TC patients separately, and (4) commentaries, reviews, and posters.

2.3. Data extraction and quality assessment

Two researchers independently extracted and entered the following data and into a standard Excel form: name of the first author, publication year, study design, inclusion/exclusion criteria, sample sizes, in-hospital mortality, long-term mortality, and cardiogenic shock. Any discrepancies in data were resolved by consulting a third investigator. The Newcastle–Ottawa Quality Assessment Scale was deployed to assess the quality of the selected studies and the risk of bias.

2.4. Statistical analysis

ReviewManager (Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014) and MedCalc® Statistical Software version 19.6.4 (MedCalc Software Ltd, Ostend, Belgium; https://www.medcalc.org; 2021) used for all statistical analyses. Incidence were pooled using random effect model using DerSimonian and Laird estimator of Tau2. The Mantel-Haenszel random-effects model was used to pool odds ratios (ORs) with 95% confidence intervals (CIs). The I² statistics were used to assess the heterogeneity of effect size estimates across these studies with I² (low heterogeneity: I² ≤ 25%; moderate: 25–50%; high >75%). A leave-one-out sensitivity analysis was also carried out to assess the effects of individual studies on the statistical results. Publication bias was explored using funnel plots and Egger’s regression test and Begg-Mazumdar’s rank correlation test.

3. Results

3.1. Literature search results

The initial database searches yielded 2812 potential records. After removing duplicates and screening titles and abstracts, 59 full-text articles were reviewed. Finally, 18 observational, including 55,557 participants (2,185 with LTAs and 53,372 without LTAs), were eligible for inclusion in the study. The selection process is outlined in the PRISMA flow chart.
(Supplementary Figure 1). Studies from institutions which were part of the GEIST registry we excluded from the present analysis. Only the latest national inpatient sample study was included in the present study. Measures were taken to not include studies with same patient cohort.

3.2. Study characteristics and quality assessment

Table 1 summarizes the study characteristics of the included studies. Clinical characteristics of included studies are outlined in Table 2. As shown in Supplementary Table 3, all included studies were of high quality.

4. Results of meta-analysis

1. Incidence of life-threatening arrhythmias in Takotsubo cardiomyopathy:

The incidence of LTAs in TC patients was reported by 16 studies. The pooled incidence of life-threatening arrhythmias in the patients of TC was found to be 6.29% (CI: 4.70–8.08%; I² = 94.67%). The data for the incidence of individual LTAs was also meta-analyzed, as shown in Table 3. Fig. 1 illustrates the forest plots for the pooled incidence of LTAs in TC.

2. In-hospital mortality:

Ten included studies reported in-hospital mortality of TC patients with LTAs compared with TC patients without LTAs. A total of 220 (20.4%) out of 1079 patients in the LTA group had an in-hospital death, while 1135 (3.1%) out of 36,116 patients in the non-LTA group died. There was a statistically significant (p < 0.0001) increased odds of mortality in the LTA group versus the non-LTA group (OR = 4.74; CI: 2.24–10.04; I² = 77%; Fig. 2(A)).

3. Long-term mortality:

We also estimated the pooled analysis of long-term mortality in the LTA and the non-LTA groups. Four studies reported long-term mortality. A total of 63 (61.2%) out of 103 patients in the LTA group died, whereas 589 (49.3%) out of 1194 patients in the non-LTA group had long-term mortality. There were similar odds of long-term mortality in the LTA group as compared with the non-LTA group (OR = 2.23; CI: 0.94–5.28; I² = 53%; p = 0.07; Fig. 2(B)).

4. Cardiogenic shock (CS):

Three studies investigated the number of TC patients who developed cardiogenic shock. A total of 34 (34.3%) out of 99 patients in the LTA group experienced CS, while only 93 (8.37%) out of 1111 patients in the non-LTA group developed it. There was statistically significant (p < 0.0001) increased odds of CS in the LTA group versus the non-LTA group (OR = 5.60; CI: 3.51–8.95; I² = 0%; Fig. 2(C))

4.1. Sensitivity analysis

The I² statistics were used to assess the heterogeneity of effect size estimates across these studies with I² (low heterogeneity: I² ≤ 25%; moderate: 25–50%; high >75%). For the in-hospital mortality, I² = 77% showed significant heterogeneity. The leave-one-out sensitivity analysis confirmed that the data by Brinjki W.

Table 1

| First author          | Country         | Study Design  | Total Population (n) | Inclusion criteria                                                                 | Exclusion criteria                                                                 |
|-----------------------|-----------------|---------------|----------------------|------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------|
| Auzeil O et al, 2016  | France          | Retrospective case study | 90                   | > 18 years with clinical presentation of ACS                                       | No coronary angiography was performed                                            |
| Dib C et al, 2008     | United States   | Case-control study | 105                  | Patients who underwent coronary arteriography and left ventriculography and met the Mayo Clinic criteria | Patients diagnosed with cardiomyopathy, valvular disease, congenital heart disease, pheochromocytoma, cocaine abuse, paced heart rhythm, or active myocarditis |
| El-Battrawy I et al, 2020 | Germany and Italy | Prospective cohort study | 906                  | TC defined as being a transient systolic dysfunction with marked LV contraction abnormality due to akinesia or dyskinesia of the LV apical and/or midventricular or basal segments extending beyond a single coronary perfusion bed | —                                                                             |
| Jesel L et al, 2018   | France          | Retrospective study | 214                  | Patients diagnosed with TC according to Madias’criteria                           | —                                                                               |
| Madias C et al, 2011  | United States   | Cohort        | 93                   | TC was diagnosed based on characteristic patterns of left ventricular dysfunction   | —                                                                               |
| Malanchini G et al, 2020 | Italy          | Retrospective study | 10,861              | Patients with a primary diagnosis at the discharge of TC                           | —                                                                               |
| Song BG et al, 2010   | Korea           | Retrospective study | 87                   | 1) Transient coronary-artery vascular distribution                               | —                                                                               |
| Sharkey SW et al, 2010 | Cohort       |               | 136                  | 2) The absence of significant coronary artery angiograms (diameter stenosis, ≤50% by visual estimation) or angiographic evidence of acute plaque rupture | —                                                                               |
|                       |                 |               |                      | 3) New electrocardiographic changes (ST-segment changes, T-wave inversions, or Q-waves) | —                                                                               |
| First author          | Country     | Study Design                           | Total Population (n) | Inclusion criteria                                                                 | Exclusion criteria                                                                 |
|----------------------|-------------|----------------------------------------|----------------------|-------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|
| Brinjikji W et al, 2012 | United States | Retrospective study                    | 24,701               | 1) An acute cardiac event typically presenting with substernal pain                 | Patients with a diagnosis of TC                                                    |
|                      |             |                                        |                      | 2) Systolic dysfunction with marked LV contraction abnormality, extending beyond     |                                                                                    |
|                      |             |                                        |                      | the geographic territory of a single epicardial coronary artery, assessed with LV  |                                                                                    |
|                      |             |                                        |                      | angiography, CMR imaging, or 2-dimensional echocardiography                         |                                                                                    |
|                      |             |                                        |                      | 3) Absence of obstructive atherosclerotic coronary artery stenosis                   |                                                                                    |
| Regnante RR et al, 2009 | United States | Cohort study                           | 70                   | - TC was defined according to the Mayo Clinic criteria                              | Patients who died during the acute phase, before complete recovery of myocardial   |
| Bento D et al, 2019   | Portugal    | Cohort study                           | 234                  | - TC was defined according to the Mayo Clinic criteria                              | function                                                                             |
| Tsuchihashi K et al, 2001 | Japan      | Retrospective study                    | 88                   | 1. Patients with suspected ACS based on chest symptoms or ECG changes               | Patients with idiopathic cardiomyopathy, febrile disorders, pheochromocytoma or   |
|                      |             |                                        |                      | 2.Transient LV ballooning confirmed by left ventriculography or echocardiography     | prior history of myocardial infarction and those receiving                         |
|                      |             |                                        |                      | 2. No significant angiographic stenosis within excluded from this study.             | coronary revascularization therapy were                                           |
| Pant S et al, 2013    | United States | Retrospective study                    | 16,450               | - TC was defined according to the ICD-9-CM codes                                     | Patients with ACS, ischemic heart disease or any other form of cardiomyopathy     |
| Murakami T et al, 2013 | Japan      | Retrospective study                    | 107                  | 1. Transient hypokinesis, akinesis, or dyskinesis of the left ventricular midsegments with or without apical involvement; the regional wall motion abnormalities extend beyond a single epicardial vascular distribution |
|                      |             |                                        |                      | 2. Absence of obstructive coronary disease or angiographic evidence of acute plaque rupture |
| Migliore F et al, 2012 | Italy       | Prospective study                      | 61                   | - TC was defined according to the Mayo Clinic criteria                              | Patients with pheochromocytoma or myocarditis were excluded                         |
| Templin C et al, 2015 | Switzerland | Prospective and retrospective, observational study | 1750               | - TC was defined according to the Mayo Clinic criteria                              | Patients with the presence of coexisting coronary artery disease, the presence of a wall-motion abnormality that was congruent with a single coronary artery territory in a patient matching all other criteria and death during the acute phase before wall-motion recovery were excluded |
| Citro R et al, 2012   | Italy       | Partially retrospective, partially prospective observational study | 190                  | - TC was defined according to the Mayo Clinic criteria                              |                                                                                    |
| Sharkey SW et al, 2015 | United States | Prospective                           | 249                  | 1) Acute presentation typically with chest pain/ discomfort or dyspea.              |                                                                                    |
|                      |             |                                        |                      | 2) Systolic dysfunction with marked LV contraction abnormality, extending beyond     |                                                                                    |
|                      |             |                                        |                      | the geographic territory of a single coronary artery, assessed with contrast LV     |                                                                                    |
|                      |             |                                        |                      | angiography, cardiovascular magnetic resonance imaging (CMR), or 2-dimensional       |                                                                                    |
|                      |             |                                        |                      | echocardiography.                                                                  |                                                                                    |
|                      |             |                                        |                      | 3) Absence of obstructive coronary stenosis (i.e., 50% luminal narrowing of the major coronary arteries by angiography) or evidence of acute plaque rupture |
|                      |             |                                        |                      | 4) Absence of myocarditis or ischemic transmural late gadolinium enhancement on CMR |

ABS: Apical ballooning syndrome, ACS: acute coronary syndrome, CAG: coronary angiogram, CMR: cardiovascular magnetic resonance, ECG: electrocardiogram, LTAs: life-threatening arrhythmias, LV: left ventricle, SC: stress cardiomyopathy, SCM: stress cardiomyopathy, SD: standard deviation, TLVBS: transient left ventricular ballooning syndrome, TC: takotsubo cardiomyopathy, VA: ventricular arrhythmias, VF: ventricular fibrillation, VT: ventricular tachycardia.
Table 2
Baseline Clinical characteristics of the included studies.

| Author                  | Total Population (n) | Participant description and Mean age (SD) | Type and prevalence of LTAs | In-hospital mortality | Long-term mortality | Follow-up for long-term mortality |
|-------------------------|----------------------|------------------------------------------|------------------------------|----------------------|---------------------|-----------------------------------|
| Auzel O et al, 2016     | 90                   | Patients with a clinical presentation of ACS who underwent coronary arteriography at the coronary care unit: - Female: 97% - 72 years (13) - 46% Hypertension - 29% Dyslipidemia | Ventricular arrhythmias: non-sustained and sustained VT and VF. n = 5 (10%) | LTA group - 0/9 | - Non-LTA group - 2/81 | - |
| Dib C et al, 2008       | 105                  | Patients with a diagnosis of TC who underwent coronary arteriography and left ventriculography in the Mayo Clinic Cardiac Catheterization database - Female: 100% - 69 years (8.9) | Significant arrhythmia: VF and asystole. n = 6 (5.7%) | LTA group - 1/6 | - Non-LTA group - 0/99 | - |
| El-Battrawy I et al, 2020 | 906                | Patients with a diagnosis of TC who were enrolled in the GErman Italian STress cardiomyopathy (GEIST) registry - Female: 89.4% - 70 ± 11 years - 70.1% Diabetes - 70.1% Hypertension | LTAs were defined as VT, VF, or sudden cardiac arrest. Malignant ventricular arrhythmias: VF and torsade de points (TdP), and asystole or complete atrioventricular block. n = 67 (7.4%) | LTA group - 7/67 | - No LTA group - 32/839 | - |
| Jesel L et al, 2018     | 214                  | Patients with a diagnosis of TC in the Cardiac Catheterization Laboratory database of Strasbourg University Hospital - Female: 81.3% - 69 years (12.6) - Hypertension (56.5%) - Dyslipidemia (39.8%) | - No LTA group - 17/191 | LTA group - 50/67 | - No LTA group - 530/839 | - |
| Madias C et al, 2011   | 93                   | Patients with the diagnosis of TC in the database of 2 institutions in Massachusetts - Female: 86% - 67 years - Hypertension 53% - Hypercholesterolemia 33% | - No LTA group - 77% | LTA group - 85% | 2 years |
| Malanchini G et al, 2020 | 10,861             | Patients with a diagnosis of TC in the database of the Italian National Healthcare System Database - Female: 91.7% - 70.7 years (11.9) - Hypertension 23.2% - Hypercholesterolemia 12% | - No LTA group - 4/85 | LTA group - 85% | 2 years |
| Song BG et al, 2010     | 87                   | Patients with a diagnosis of TLVBS at a tertiary-care center in Korea. - Female: 74% - Nonsurvivors: 72 years - Survivors: 61 years - Hypertension (45%) - Hypercholesterolemia (25%) | Third-degree atrioventricular block, VF, VT, and cardiac arrest. Survivors n = 4 (6%) | 8/87 (9%) | 20/87 (23%) | 42 months |
| Sharkey SW et al, 2010  | 136                  | Patients who presented with SC to the emergency – and hospital facilities of the Minneapolis Heart Institute and Abbott Northwestern Hospital (Minneapolis, Minnesota) - Female: 96% - 68 years (13) | LTA group - 1/33 | LTA group - 1/3 | - No LTA group - 2/67 | - |
| Brnjikji W et al, 2012  | 24,701               | Patients with a diagnosis of TC in the National Inpatient Database Samples. - Female: 89% - 66.8 years (30.7) - Hypertension (58.4%) - Hyperlipidemia (37.5%) | Sustained ventricular arrhythmias: VF or VT n = 3 (4%) | LTA group - 1/3 | - No LTA group - 0/67 | - |
| Regnante RR et al, 2009 | 70                  | Patients who presented with emergent cardiac catheterizations with findings consistent with TC at 2 major hospitals in Rhode Island - Female: 95% - 67 years (11) - Hypertension (66%) - Hyperlipidemia (45%) | LTA group - 1/3 | LTA group - 1/3 | - No LTA group - 2/67 | - |
| Bento D et al, 2019     | 234                  | Patients with a diagnosis of TC in 12 Portuguese hospitals - Female: 89.7% - 68 years (12) - Hypertension (67.9%) - Hyperlipidemia (54.3%) | LTA group - 2/3 | LTA group - 4/4.4 | 33 ± 33 months | - |
| Tsujihishi K et al, 2001 | 88                  | Patients with transient LV apical wall motion abnormalities without stenosis on CAG enrolled | LTA group - 1% | LTA group - 2% | 13 ± 14 months | - |
et al were the main source of heterogeneity in the analysis of the in-hospital mortality. The I² value dropped to 20% after omitting the data from this study, as shown in Fig. 2(D).

### 4.2. Publication bias

Supplementary Figure 2 illustrates the funnel plots for the outcomes of in-hospital mortality, long-term mortality, and cardiogenic shock. Assessment of publication bias, using Egger’s regression test and Begg-Mazumdar’s rank correlation test revealed no significant publication bias for overall incidence of life-threatening arrhythmias in Takotsubo cardiomyopathy (Egger’s regression test; \( p = 0.3982 \), Begg-Mazumdar’s rank correlation test; \( p = 0.4713 \)).

### 5. Discussion

Our study aimed to report the incidence of LTAs patients with Takotsubo cardiomyopathy and their outcomes. We found a pooled incidence of 6.29% LTAs in our study, with ventricular tachycardia as the most common arrhythmia (3.43%). Further our study reported an increased odds of in-hospital mortality and cardiogenic shock among TC patients with LTAs compared with those without LTAs. However, there was no difference in the odds of long-term mortality.

Life-threatening arrhythmias in TC have been reported with a varying incidence in literature. While a study from Italy reported an incidence of 8.2% for LTAs during hospitalization for TC,¹ results from Stiermaier et al indicate a higher-than-expected incidence at 13.5%.¹² A recent study demonstrated that LT ventricular
Arrhythmias (VAs) were more common in patients that developed sub-acute VAs during hospitalization, occurring in 6% of the total population. These LTAs seemed to have a strong clinical impact on patient outcomes and survival, since mortality was higher in the VAs group than in the non-VAs group ($P = 0.03$). Additional studies have supporting evidence, such as reported by Jesel et al, in-hospital (39.1%; $p < 0.001$) and 1-year mortality (47.8%; $p < 0.001$) was significantly increased in the LTA group as compared with non-LTA TC patients. Thus we urge for awareness about this
potential complication, since it can be critical for further patient management.

Our pooled analysis showed a significantly higher odds of in-hospital mortality in TC patients with LTAs. The majority of the patients had ventricular arrhythmia, for example, ventricular fibrillation (Vfib). Ventricular arrhythmias are thought to be the most common LTA to occur in TC patients and can cause a worse long-term prognosis of the disease. Although the exact theory is uncertain, there are some proposed mechanisms such as coronary vasospasm, re-entry, and triggered activity. Catecholamine-induced myocardial stunning can cause abnormal automaticity and depolarization anomalies such as a prolonged QT interval, a known predisposing risk factor for Vfib. Conduction defects such as Atrioventricular (AV) Heart Block, although rare, are another recurring LTA in TC patients described across multiple reports. AV blocks can persist long term after TC presentation, and may require interventions such as a pacemaker; Baranchuk et al reported a patient in whom high-degree AV block was persistent after 1 year of the TC event, eventually resolving after 2 years of follow-up. While another case of TC had a high AV block 20 months after the inciting event. Hence, it is important to recognize and manage the patient timely, to ensure their safety.
Additionally, our study demonstrates similar odds of long-term mortality for TC patients with LTAs as compared with those who do not. Although cardiovascular abnormalities have been shown in some reports to affect the mortality of Takotsubo Cardiomyopathy patients, multiple studies have shown that non-cardiac comorbidities and complications seem to play a strong prognostic role in predicting long-term outcomes for these patients. A systematic review conducted by Pelliccia et al found that 78% of TC patient deaths were due to non-cardiac causes, while only 22% of deaths were cardiac. As collated in a study on 1109 patients, the most common comorbidities in TC patients included psychiatric and psychological illnesses, pulmonary disease, and malignancies, followed by neurocological, chronic kidney, and thyroid diseases. These extra-cardiac conditions can also predispose to TC since they can increase catecholamine synthesis as part of the disease process. Furthermore, long-term mortality rates of TC exceed those of patients with STEMI as concluded by Stiermaier et al (24.7% vs 15.1%, p = 0.02); hence, there is a need to raise awareness regarding the optimal treatment of comorbidities and risk factors, with management aimed at prevention of stressful events.

Our results revealed a significantly higher odds of CS in TC patients with LTAs than in those without an LTA. Although there is a paucity of data available regarding long-term complications of CS in TC patients, it is a severe complication of the acute phase of the disease and requires urgent treatment with otherwise imminent short-term mortality. A registry-based study concluded that short-term mortality of CS in TC patients was 29% while another prospective single-center found their acute fatality rate to be very similar, at 28.6%. However, the short-term mortality of CS due to myocardial infarction is still much greater than that of CS-TC. A national representative study found that myocardial infarction-CS had higher in-hospital mortality rates, hospital costs, and lower home discharges often compared with TC-CS admissions. This most likely is due to the reversibility of the LV dysfunction in TC patients. Further studies are needed for insight into the long-term effects of CS in TC patients, which will allow for the development of better longitudinal care and lower adverse outcomes.

Our study has several limitations, one of which is the inherent limitations of an observational nature of the studies selected, such as the accuracy of medical documentation and missing information. We were unable to comment on the co-morbidities of all patients involved; hence, a potential confounder may be present affecting the mortality of TC patients with LTAs. This is a study level meta-analysis and study level pooled estimates are limited in their ability explain heterogeneity of pooled estimates. Further, treatment modalities, medications used in this TC patients were not reported consistently among included studies.

6. Conclusion

The pooled incidence of LTAs in the patients of TC was found to be 6.29%, with ventricular tachycardia being the most common arrhythmia (3.43%). In the group of TC patients with LTAs, the odds of in-hospital mortality and cardiogenic shock were significantly higher than in the TC patients without LTAs. However, there was no significant difference in long-term mortality between the two groups.

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Declaration of competing interest

The authors declare they have no conflict of interest.
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