

Psychosocial and clinical characteristics of a patient with Takotsubo syndrome and her healthy monozygotic twin: a case report

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Background

Takotsubo syndrome (TTS) is an acute heart failure syndrome characterized by transient left ventricular dysfunction, increased myocardial biomarkers, and electrocardiographic changes. Symptoms of TTS are similar to those of acute coronary syndromes, but there is often no significant coronary stenosis. Although emotional and physical stressors are often reported as having triggered TTS, the pathogenesis is largely unknown. To address this issue, we comprehensively characterized a monozygous pair of twin sisters, one of whom experienced TTS.

Case summary

The 60-year-old Caucasian monozygotic female twins with and without TTS were examined at the University Hospital Zurich in Switzerland. The twins completed questionnaires and clinical interviews assessing several sociopsychological factors. The twin sister with TTS exhibited higher levels of anxiety, vital exhaustion, social inhibition, and alexithymia, and lower levels of quality of and meaning in life. She was given the diagnoses of social phobia, adjustment disorder, specific anxiety disorder, obsessive-compulsive personality disorder, and an accentuated anxiety-avoidant personality disorder. Additionally, the twin with TTS experienced more—and also more severe—stressors involving life-threatening and dangerous situations over the life course.

Discussion

These monozygous female twins with and without TTS differed in several notable aspects of their psychological functioning, psychiatric status, personality, and lifetime stressor exposure. The results thus highlight several factors, besides genetic components, that may play an important role in the pathogenesis of TTS. Looking forward, larger studies using experimental and longitudinal designs are needed to elucidate the role that psychosocial factors play in TTS.

Keywords

Takotsubo syndrome • Stress-induced cardiomyopathy • Psychology • Monozygotic twins • Case report

ESC Curriculum

6.5 Cardiomyopathy • 8.6 Secondary prevention • 9.9 Cardiological consultations

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Learning points

- Takotsubo syndrome (TSS) is an acute heart failure syndrome, often mimicking an acute coronary syndrome.
- Emotional and physical stressors are often reported triggers of TSS.
- Psychosocial factors may play an important role in the largely unknown pathogenesis of TSS.

Primary specialties involved other than cardiology

Liaison psychiatry and psychosomatic medicine.

Introduction

The term Takotsubo syndrome (TTS) was first coined in the Japanese medical literature to describe the left ventricular appearance on ventriculography showing a rounded hypokinetic apex with a narrow hypercontracted base resembling a pot previously used in Japan to catch octopus. Clinically speaking, TTS is an acute heart failure syndrome characterized by transient left ventricular dysfunction, electrocardiographic changes, and elevated myocardial biomarkers that can mimic an acute coronary syndrome (ACS).¹

Although TTS is related to the occurrence of psychological factors and emotional triggers, the underlying mechanisms are unknown. Previously, TTS was considered to be typically preceded by an emotional trigger, with point prevalence estimates ranging from 26 to 47%. The presence of a psychological component in TTS suggests that some individuals are particularly susceptible to experiencing psychological distress.² Nevertheless, a study by Templin *et al.* (2015) with 1750 patients demonstrated that emotional precipitating life events (e.g. death of a loved one and job loss) were not as common as physical precipitating events (e.g. asthma attack and major surgery), and almost one-third of patients experienced no apparent triggering event.³

With respect to psychiatric and neurological disorders, TTS patients have higher rates of psychiatric and neurological disorders (estimated, 55.8%) as compared with those with an ACS (estimated, 25.7%). Moreover, research has shown that two-thirds of patients experiencing TTS are diagnosed with either anxiety or depression. Regarding personality traits, TTS patients have been found to exhibit greater emotionality and a higher prevalence of social inhibition than patients with an ACS. Furthermore, a dysfunctional profile in emotional competence has also been described in patients with TTS. A systematic review of traumatic life events, personality, and psychopathology found robust evidence of long-lasting psychological distress and anxiety disorders in patients with TTS.^{4,5}

These findings suggest that both psychosocial factors and psychiatric disorders may predispose or even facilitate TTS through psychophysiological mechanisms such as catecholamine-induced myocardial stunning.³ To date, one case report of identical twins who both developed TTS in response to stress shortly after menopause provided evidence of a genetic contribution to the increased risk of TTS.⁶ However, little is known about how genetic and psychosocial factors interact and might contribute to the development of TTS. To address this issue, we present the first case report of

monozygotic twin sisters of whom one was healthy and one experienced TTS. We believe the results can lead to a better understanding of the psychosocial and clinical aspects of TTS, as well as its pathogenesis.

Timeline

	Takotsubo twin	Healthy twin
ca. July 2018	First Takotsubo event	–
December 2019	Second Takotsubo event	–
5 February 2020	Psychosocial assessments	Psychosocial assessments
1 April 2020	Clinical interviews	Clinical interviews

Case presentation

Participants

Participants were two 60-year-old Caucasian monozygotic twins, one with and one without a prior episode of TTS, recruited from the Department of Cardiology at the University Hospital Zurich, Switzerland. All psychosocial assessments were conducted on 5 February 2020, at the Hospital. The clinical interviews were conducted using Skype on 1 April 2020. Both women provided written informed consent and received no financial compensation for participating. Approval was obtained by the science ethical committee of the Hospital.

Measures

TTS diagnosis

TTS was diagnosed according to InterTAK Diagnostic Criteria based on findings in the electrocardiogram, blood samples (cardiac biomarkers), echocardiography, and coronary angiography. Wall motion abnormalities recovered after the first TTS event. The TTS patient was twice affected by TTS—first with a midventricular and second with an apical type of TTS. Further details are shown in (Figure 1).

Psychometric measures

Participants were interviewed about sociodemographic factors (i.e. age, gender, civil status, working status, highest level of education, and children), health behaviours (i.e. smoking, alcohol consumption, and physical activity), history of psychiatric symptoms and disorders, and regular medication intake. A battery of self-report questionnaires and interview-based psychiatric interviews were administered.

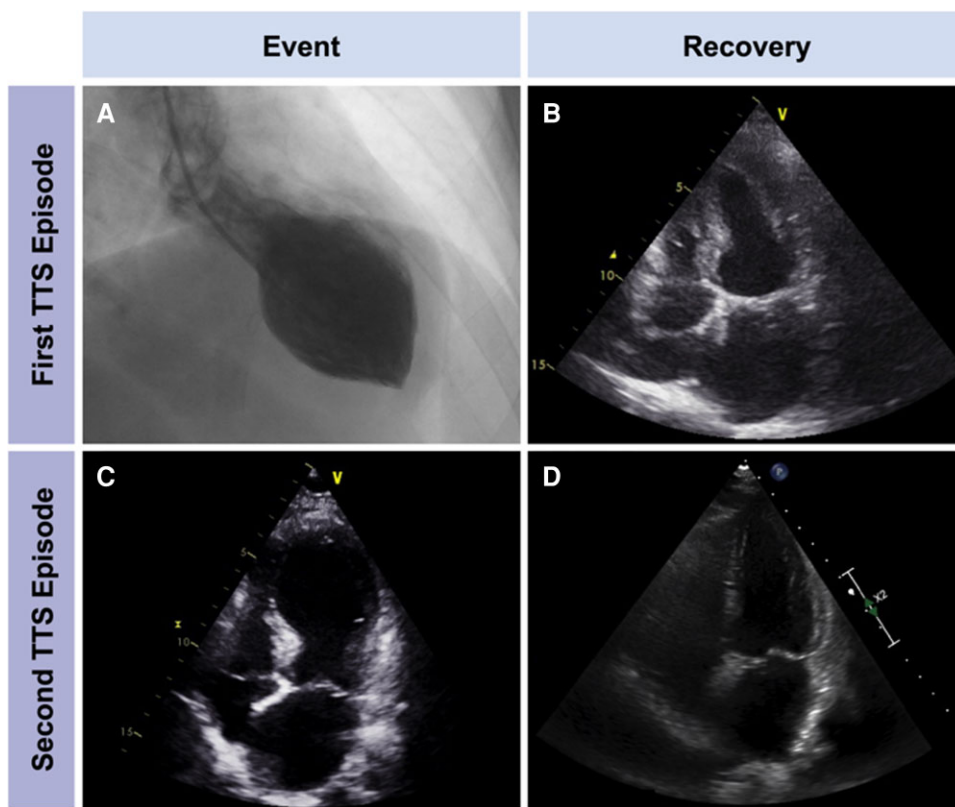


Figure 1 (A) Emergency coronary angiography with left ventriculogram during the first event was consistent with midventricular TTS type. (B) Echocardiography showing resolution of wall motion abnormalities after the first TTS event. (C) 1.5 years later, the patient had apical ballooning with basal hyperkinesis. (D) Echocardiography obtained six weeks after the second event showed complete recovery of left ventricular dysfunction. TTS, Takotsubo syndrome.

Lifetime stressor exposure

Exposure to life stressors occurring over the lifespan was assessed using the Stress and Adversity Inventory for Adults (Adult STRAIN), which is a well-validated, self-administrated online interview that assesses cumulative exposure to stressors occurring over the entire life course.⁷ The STRAIN assesses the severity, frequency, exposure timing, and duration of both acute life events (e.g. job losses and deaths of relatives) and chronic difficulties (e.g. persistent work, financial, and interpersonal stressors). Early life stressors (e.g. maltreatment and neglect) are also assessed.

Adverse childhood experiences

Adverse childhood experiences (ACEs) were assessed using the 10-item self-report ACEs questionnaire, which assesses three main types of early adversity occurring before the age of 18: childhood abuse (i.e. emotional, physical, or sexual), childhood neglect (i.e. emotional or physical), and household dysfunction (i.e. domestic violence, substance abuse, mental illness, criminal activity, or parental absence).⁸

Alexithymia

We used the German version of the 20-item Toronto Alexithymia Scale to identify difficulties in identifying and describing one's own feelings and externally oriented thinking. Each item is rated on a

5-point Likert scale, ranging from 1 (*strongly disagree*) to 5 (*strongly agree*). A total sum score of 52–60 indicates possible alexithymia.⁹

Type D (distressed) personality

Type D is defined as the joint tendency toward negative affectivity (e.g. worry, irritability, and gloom) and social inhibition (e.g. reticence and a lack of self-assurance). The Type D personality pattern was assessed with the German version of the 14-item self-report Type D scale (DS14). It includes two subscales—negative affectivity and social inhibition, containing 10 items each—which participants rated on a 5-point Likert scale from 0 (*completely disagree*) to 4 (*completely agree*). Scores ≥ 10 points on both subscales indicate Type D personality.¹⁰

Anxiety

The generalized anxiety disorder (GAD)-7 scale was used to measure participants' anxiety symptom levels. The GAD-7 is a 7-item self-report questionnaire with a 4-point Likert scale for screening and severity measuring of GAD. It can also be used as a screen for other anxiety disorders such as panic disorder and social anxiety.¹¹

Vital exhaustion

Vital exhaustion was assessed using the 9-item Shortened Maastricht Vital Exhaustion Questionnaire. Questions assess undue fatigue,

trouble falling asleep, waking up at night, general malaise, apathy, irritability, loss of energy, demoralization, and waking up exhausted.¹² Each item is rated with 0 (*no*), 1 (*don't know*), or 2 (*yes*) points.

Quality of life

We assessed health-related quality of life (QoL) using the German version of the EuroQol group five-dimension questionnaire (EQ-5D), which measures five dimensions of health-related QoL: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression.¹³

Meaning in life

The meaning in life questionnaire (MLQ) is a 10-item self-report questionnaire with a 7-point Likert scale ranging from 1 (*absolutely true*) to 7 (*absolutely untrue*). It assesses two dimensions: (1) the presence of meaning (in life) and (2) search for meaning (i.e. how much effort is given to find meaning in life).¹⁴

Psychiatric diagnoses

The English version of the Mini International Neuropsychiatric Interview (M.I.N.I.) was used to evaluate the presence of 17 of the most common mental health disorders.¹⁵ The M.I.N.I. is a 30 min interview that has been well-validated for assessing psychiatric disorders. To assess for the presence of personality disorders, we used the English version of the Structured Clinical Interview for DSM-IV Axis II—Personality Disorder, which includes 113 items. Each item is scored on a 3-point Likert scale: 0 (*absent*), 1 (*subthreshold*), or 2 (*threshold*).¹⁶

The following measures were only administered to the twin with TTS:

Posttraumatic stress symptoms

The severity of self-reported TTS-induced posttraumatic stress was assessed with the 17-item posttraumatic diagnostic scale (PDS). The PDS measures how often a patient has experienced each of 17 DSM-IV posttraumatic stress disorder symptoms during the previous month (total score, 0–51).¹⁷

Adjustment disorder

We used the validated English version of the Adjustment Disorder—New Module 20 (ADNM-20) to assess adjustment disorder symptoms. The ADNM-20 is a self-report questionnaire consisting of 20 items. On a 4-point Likert scale, ranging from 1 (*never*) to 4 (*often*), participants indicate how often they have experienced different symptoms during the past two weeks. A cut-off value of 47.5 suggests the diagnosis of an Adjustment Disorder.¹⁸

Illness perception

Cognitive representations of the patient's heart disease were evaluated using the English version of the brief self-rated illness perception questionnaire (BIPQ-R).¹⁹

The BIPQ-R is a 9-item questionnaire that measures dimensions of illness representations (e.g. consequences, timeline, treatment control, and illness concerns). On a 10-point scale, the participant rated her beliefs and feelings about her illness.

Outcomes

Table 1 shows the patients' demographic, psychosocial, and clinical characteristics. Except for the TTS, the below described psychological problems, and a family history of hypercholesterinaemia and hypertension (father), the twins were healthy. The twins had similar demographic characteristics but different personalities, psychological functioning, and well-being scores. Specifically, the twin with TTS exhibited higher levels of anxiety, vital exhaustion, social inhibition, and alexithymia, and lower levels of QoL and meaning in life. The detailed clinical interviews revealed the diagnoses of social phobia, adjustment disorder, and specific anxiety disorder for the twin with TTS. The healthy twin also showed some signs of social phobia but did not meet the clinical criteria for diagnosis. Furthermore, the twin with TTS was diagnosed with obsessive–compulsive personality disorder and a subthreshold avoidant personality disorder. No conspicuous personality traits were evident for the healthy twin.

In addition, although the healthy twin experienced more stressors over the life course, the two sisters did not differ in terms of overall lifetime stressor severity. Both twins experienced more acute than chronic stressors. Even though the twin with TTS experienced fewer acute life events than the healthy twin, her cumulative acute stressor severity was higher. Moreover, the twin with TTS reported experiencing more—and also more severe—stressors involving life-threatening and dangerous situations over the life course than her healthy twin sister. Neither sister reported an ACE according to the ACEs questionnaire.

In terms of TTS, the TTS twin suffered two episodes of TTS. The first episode occurred at age 58 and the second at age 59. As shown in *Table 2*, both episodes were of similar clinical severity. However, the patient perceived the first TTS with much greater fear and helplessness. Further, the TTS twin reported differences in potential emotional stressors: a combination of several life stressors preceded the first episode, whereas only one highly stressful life event occurred before the second episode.

The TTS twin exhibited moderate posttraumatic stress symptoms and symptoms of an adjustment disorder after both TTS events. She also reported a high disease burden and low control over her disease (*Table 3*). At the time of the assessment, the TTS patient was treated with an ACE inhibitor and a beta-blocker.

Discussion

To our knowledge, this is the first case study of a monozygotic twin pair with and without TTS. The twin sisters assessed differed with respect to several features of their personality and psychological functioning, as well as current and lifetime stressor exposures. The self-report data revealed higher levels of anxiety, obsessive–compulsive and avoidant traits, social inhibition, and alexithymia in the TTS twin as compared to the healthy twin, which was consistent with the clinical impressions observed during the assessment. These results may suggest that psychopathology plays a potential role in increasing the risk of TTS. Contrary to a prior case report in which both twins developed TTS,⁶ our results indicate that other factors, such as psychological functioning, may play an important role in the development of TTS. However, larger studies are needed to identify precisely how psychosocial factors might lead to the development of TTS.

Table 1 Sociodemographic, lifestyle, psychosocial, and clinical characteristics of a patient with Takotsubo syndrome and her healthy twin

	Takotsubo twin	Healthy twin	Difference in %
Age (years)	60	60	–
Gender	Female	Female	–
Civil status	Married	Married (2nd time)	–
Living status	With someone	With someone	–
Working status	Unemployed	Unemployed	–
Highest level of education	University (MSc in economics)	High school (nurse)	–
Children	2 (age: 25, 29)	2 (age: 28, 34)	–
Current smoking	No (since age of 26)	No (since age of 40)	–
Alcohol consumption	1–2x/month	2x/month	–
Physical activity	No (active before TTS)	No	–
History of social phobia	Yes	Unclear	–
History of other anxiety disorders	Yes	Yes	–
History of psychotherapy	Yes	No	–
Medication	Propranolol (due to anxiety disorder)	Propranolol (if required due to anxiety disorder)	–
	Estrogen	Estrogen	
	Progesterone	Progesterone	
	Since TTS:		
	Angiotensin-converting enzyme inhibitor		
	Carvedilol		
Psychiatric diagnosis (M.I.N.I.)			
Social phobia	Yes	Unclear	–
Adjustment disorder	Yes	No	
Other anxiety disorder	Yes	No	
Personality disorders (SCID-II)			
APD	Accentuation	No	–
OCPD	Yes	No	
Anxiety (GAD-7)/21	9	4	5 (23.8%)
Vital exhaustion (VE)/18	6	1	5 (27.8%)
Type D personality (DS14)			
Negative affectivity scale/28	3	2	1 (3.6%)
Social inhibition scale/28	17	0	17 (60%)
Alexithymia (TAS-20)/100	53	31	22 (22%)
Quality of life (EuroQoL5D VAS)/100	30	75	–45 (45%)
Meaning in life (MLQ)			
Total/70	16	32	–16 (22.9%)
Presence subscale	11	23	–12 (47.8%)
Search subscale	5	9	–4 (55.6%)
ACEs	0	0	–
Stress and Adversity Inventory for Adults (Adult STRAIN)			
Total lifetime stressors			
Count	15	25	
Severity	63	64	
Acute lifetime stressors			
Count	12	18	
Severity	48	31	
Chronic lifetime stressors			
Count	3	7	

Continued

Table 1 Continued

	Takotsubo twin	Healthy twin	Difference in %
Severity	15	33	
Life-threatening stressors			
Count	4	2	
Severity	20	6	
Physical danger stressors			
Count	8	5	
Severity	35	17	

APD, avoidant personality disorder; GAD-7, generalized anxiety disorder-7; M.I.N.I., Mini-International Neuropsychiatric Interview; MLQ, meaning in life questionnaire; OCPD, obsessive-compulsive personality disorder; SCID-II, Structured Clinical Interview for DSM-IV; TAS, Toronto alexithymia scale; TTS, Takotsubo syndrome; VAS, visual analogue scale

Table 2 Characteristics of the two TTS episodes

	1st TTS Episode	2nd TTS Episode
Time	1.5 Years before assessment (58 years old)	6 Weeks before assessment (59 years old)
Severity	No loss of consciousness No resuscitation needed	No loss of consciousness No resuscitation needed
Emotions		
Emotions the day before TTS	Happy, active, relaxed	Insecure, sad
Emotions 2 h before TTS	Powerless, sad, weak, tired	Powerless, insecure, sad
Emotions during TTS (0–10)	Fear of dying: 9–10 Helplessness: 9–10 Pain: 6	Fear of dying: 1 Helplessness: 0 Pain: 6
Possible preceding stressors	Several chronic stressors End of the vacation Emotionally stressful conversation with a friend about his sorrows	Cousin's death and funeral
Type of Takotsubo	Midventricular	apical

TTS, Takotsubo syndrome.

Table 3 TTS-related characteristics

	Sum score	Maximum score
Posttraumatic stress symptoms (PDS)	16 (Moderate symptom severity)	51
Adjustment disorder symptoms (ADNM-20)	60 (Cut-off: 47.5)	100
Illness perception (BIPQ)		
Consequences	9	10
Timeline	9	10
Personal control	3	10
Treatment control	0	10
Identity	3	10
Illness concern	10	10
Coherence	10	10
Emotional representation	10	10

ADNM9-20, Adjustment Disorder—New Module 20; BIPQ, brief illness perception questionnaire; PDS, posttraumatic diagnostic scale.

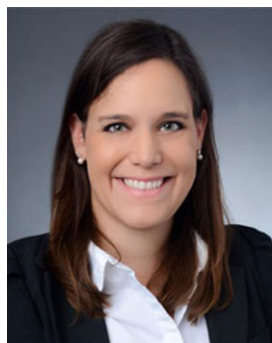
Furthermore, we found that the twin with TTS had higher levels of anxiety, vital exhaustion, and lower levels of QoL. These findings could represent the psychosocial consequences of TTS and are consistent with the reported TTS-related symptoms of posttraumatic stress and adjustment problems evident in the twin with TTS. Indeed, TTS appears to be a high psychosocial burden for the affected patient. However, whether these symptoms of anxiety, exhaustion, and impaired QoL emerged before or after TTS remains unclear. Therefore, no conclusions can be drawn about directionality or causality.

Finally, our data demonstrate that the twin sister with TTS differed in both her exposure to and appraisal of stressors occurring over the life course. Although the healthy twin experienced more total lifetime stressors, the two sisters did not differ in terms of their total lifetime stressor severity. At the same time, however, the twin with TTS experienced more—and also more severe—stressors involving life-threatening and dangerous situations over the life course. What psychological or perceptual processes might lead to these differences in the experienced severity of these lifetime stressors needs to be addressed in future research.

Together, these data highlight two possibilities for how life stressors may contribute to TTS. One possibility is that patients at risk of TTS may have a lower threshold for mounting biological responses to stress that leads to TTS. According to the catecholamine hypothesis, TTS is induced through an excessive release of catecholamines followed by myocardial stunning.¹ Affected patients may also have less favourable stress management strategies available, as has been previously hypothesized. A second possibility is that TTS patients may be more likely to experience specific types of stressors that promote biological changes that increase the risk of TTS. According to the Social Safety Theory, for example, increases in sympathetic arousal and inflammatory activity are most strongly triggered by stressors involving physical threats.²⁰ Therefore, the present data are consistent with a stressor characteristics perspective on TTS, whereby experiencing social and physical threats, in particular, are most likely to increase the risk of the condition.

In conclusion, this case report shows that there are psychosocial processes associated with TTS that should be considered in addition to other factors such as genetics, age, and sex. Given the limitations of case report data, precisely how psychosocial factors are involved in the pathogenesis of TTS needs to be further elucidated. Larger studies and experimental methods examining, for example, autonomic, neuroendocrine, and immunological responses to acute stressors in patients with TTS and healthy controls, would provide further insights.

Lead author biography



Dr Rebecca E. Langraf-Meister is a psychotherapist working in the fields of cardiopsychology, burnout, and chronic depression at University Hospital Zurich and Clenia Schlössli AG. After graduating in 2012 in psychology at the University of Zurich, she did her doctoral thesis on a project examining a short intervention in patients with acute myocardial infarction to reduce posttraumatic stress at the University

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Supplementary material

Supplementary material is available at *European Heart Journal – Case Reports* online.

Slide sets: A fully edited slide set detailing these cases and suitable for local presentation is available online as [Supplementary data](#).

Consent: The authors confirm that written consent for submission of the case report including images and associated text has been obtained from the TTS patient and her healthy twin in line with COPE guidance.

Conflict of interest: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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