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Investigating sexual problems, psychological distress and quality of life in female patients with Takotsubo cardiomyopathy: A prospective case–control study

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Abstract

Background: Takotsubo cardiomyopathy (TSCM) has detrimental effects on both physical and psychological health of sufferers. However, little is known whether TSCM also affects sexual functioning in female patients.

Aim: The aim of this study was to investigate psychological distress (depression and anxiety), health-related quality of life, and sexual functioning in women with TSCM and compare them with women with acute myocardial infarction and with healthy controls.

Methods: A three group prospective case–control design was used. Female patients with TSCM or acute myocardial infarction, as well as healthy controls (94 in each group), were recruited across eight Iranian university hospitals. Data were collected at baseline and after six and 18 months using the Hospital Anxiety and Depression Scale, the Short Form-12, the Female Sexual Function Index and the Female Sexual Distress Scale. Multilevel logistic regression was conducted.

Results: The TSCM group showed worst sexual functioning and the highest level of anxiety and depression at baseline ($p<0.01$) compared with the two other groups. The TSCM and AMI groups showed comparable health-related quality of life at baseline, which was lower in both groups compared with the healthy controls ($p<0.01$). Overall, depression, anxiety and health-related quality of life showed a significant change over time, especially in the TSCM group, with health-related quality of life decreasing, while anxiety and depression were increasing. Compared with the acute myocardial infarction and healthy control groups, the TSCM group showed a higher prevalence of sexual problems (odds ratios = 3.10 and 2.28, respectively) across time. Moreover, sexual functioning was found to be a mediator between anxiety and health-related quality of life in the TSCM group.

Conclusion: Depression, anxiety, health-related quality of life, and sexual dysfunction tend to increase over time in female patients with TSCM; thus, healthcare providers should pay attention to these problems and provide appropriate treatment where necessary.

Keywords

Acute myocardial infarction, anxiety, depression, sexual dysfunction, Takotsubo cardiomyopathy, women

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Introduction

Takotsubo cardiomyopathy (TSCM), also known as 'stress cardiomyopathy', shows similar symptoms to acute myocardial infarction (AMI), such as shortness of breath and/or chest pain.[1] In contrast to AMI, however, TSCM symptoms are based on a temporary occlusion of the coronary arteries that may be induced primarily by catecholamine release and which usually disappears after a couple of days or weeks.[1] Different prevalence rates for TSCM have been observed ranging from 0.7% to 3.0%. Furthermore, mortality rates of up to 8% have been reported if patients do not receive appropriate and timely treatment.[2,3] In addition to physical distress, a variety of psycho-affective triggers and predispositions such as stress, anxiety, depression, phobia and anhedonia have been recognized as potential risk factors for TSCM.[4,5] Moreover, gender and age might be considered predisposing factors too, given that more than 90% of all reported cases occur in women aged between 58 and 75 years.[1] The differential diagnosis is not always straightforward and a recent study from the United States showed that up to 5% of women were misdiagnosed with AMI while actually suffering from TSCM.[6]

Sexual activity has long been recognized as an important component of people's health-related quality of life (HRQoL), which is also true for individuals suffering from cardiovascular disease (CVD).[7,8] Decreased sexual activity and functioning are common in patients with CVD[9] and are often interrelated with anxiety and depression,[10–14] but seem to express themselves differently in men and women.[15–17] According to previous studies involving patients with CVD, women suffer more frequently from impaired sexual functioning and its direct effects compared with men.[13] Furthermore, sexual satisfaction is associated with female patients' physical and psychological health, while in men sexual satisfaction seems to be associated with physical health only.[18,19] Given that psychological health is linked to a woman's sexual satisfaction and that HRQoL is related to psychological distress in CVD patients,[18–20] it is further likely that sexual functioning and sexual satisfaction might represent mediators in the association between psychological distress and HRQoL. More specifically, increased anxiety in women suffering from CVD may negatively impact on their sexual functioning and sexual satisfaction, subsequently leading to overall lower HRQoL. Emotional stressors have been shown to play an important role in TSCM disease development and maintenance/worsening, and may further indirectly and directly affect HRQoL in these patients. Therefore, investigation of these factors is crucial so that novel strategies for better disease management can be developed for female patients suffering from TSCM.

So far, no study has explored this link and while the occurrence of sexual problems in female patients suffering from CVD has been relatively well studied, to the best of our knowledge, no study has assessed sexual functioning in female patients suffering from TSCM. Given the differences in anxiety and depression between individuals with TSCM and those with acute coronary syndrome, including AMI, the effects of anxiety and depression on overall sexual health are likely to be different between TSCM and AMI patients.[21]

Aims

The objectives of the present longitudinal study were: 1) to investigate levels of psychological distress (symptoms of depression and anxiety), HRQoL and sexual functioning in women with TSCM at baseline and over an 18-month period, 2) to compare these levels with the levels of women with AMI and of a healthy control group, and 3) to determine potential associations between the psychological, sexual and HRQoL variables, as well as any significant mediation effect of sexual functioning and satisfaction.

Materials and methods

Design and study participants

This study was conducted as a multicenter longitudinal case–control study involving eight referral university hospitals (five in Tehran, one in Qazvin, one in Tabriz and one in Zahedan). Both the TSCM and AMI patients were newly diagnosed and had not received any prior treatment before being included in the study. All participants were recruited between January 2012 and February 2015. The study was approved by the ethics committee of Qazvin University of Medical Sciences. All participants provided informed consent prior to participation.

TSCM group. One hundred and sixty-three female patients with TSCM admitted to the emergency care units of the various hospitals were examined and screened for study eligibility by two trained general physicians. Patients were included in the TSCM group if they: 1) were diagnosed with TSCM according to the Mayo Clinic criteria,[22] 2) were married or had a partner, 3) were able to read and speak Persian, and 4) did not report a previous history of AMI (according to their medical records). Patients were excluded if they: 1) did not provide a written informed consent, 2) were diagnosed with severe stage of concurrent diseases such as cancer, renal failure and/or cognitive impairment, or 3) were undergoing hormone replacement therapy. Of the 163 approached female patients with TSCM, 58 were not eligible for inclusion in this study and 11 did not provide written informed consent. In the end, $n = 94$ patients with TSCM were included in the study.

AMI group. Female patients who had been admitted to the same hospitals with clinical symptoms of AMI were

screened for their eligibility by two trained general physicians. Subjects were included if they: 1) had a confirmed diagnosis of AMI by their attending physician, 2) were married or had a steady partner, 3) were able to read and speak Persian, and 4) did not report a previous history of TSCM according to their medical records. Patients were excluded if they: 1) did not provide written informed consent, 2) were diagnosed with severe stage of concurrent diseases such as cancer, renal failure and/or cognitive impairment, and 3) were undergoing hormone replacement therapy. In the end, n =94 patients with AMI were included in the study.

Healthy control group. A healthy control group of women was recruited among the TSCM and AMI patients' relatives and friends. Individuals were included as healthy controls if they: 1) were married or had a steady partner, and 2) did not have a history of TSCM, AMI and/or other CVDs (based on medical reports). Individuals were excluded if they: 1) were diagnosed with severe stage of concurrent diseases such as cancer, renal failure, and/or cognitive impairment, and 2) did not provide written informed consent. In the end, N =94 eligible age-matched healthy controls were included in the study.

Procedure

Patients were approached before their discharge from hospital and screened by two trained general physicians in terms of their eligibility to be included in the study. A trained research nurse assistant provided detailed study information to the potential participants. Interested patients were then asked to provide written informed consent and to subsequently fill in all study measures at baseline. After six and 18 months, the patients and healthy controls were contacted again via phone by two trained research assistants and asked to visit the university hospitals to recomplete the same measures for follow-up purposes.

Measures

Sociodemographic characteristics. Information on age, years of education, marriage duration, height and weight, family income, and smoking status was obtained via a semi-structure interview performed by two nurse research assistants. Clinical data on diabetes, hypertension, hyperlipidemia and menopausal status were obtained by reviewing the hospitals' medical records.

Sexual functioning. Female sexual functioning was assessed using the Female Sexual Function Index (FSFI), a 19-item instrument consisting of six subscales: sexual desire (two items), arousal (four items), lubrication (four items), orgasm (three items), satisfaction (three items) and pain (three items). All items are scored on a five-point Likert-type scale ranging from 0 to 5 with an additional option of 'no sexual activity' for items 3 to 19. A total score can be obtained by summing up the six subscales. Higher FSFI scores indicate higher level of sexual functioning. A previous validation study has suggested a total FSFI score of $\leqslant$ 26.55 to show the best sensitivity–specificity profile in identifying women suffering from any sexual dysfunction. The translated and culturally adapted Iranian version of the FSFI has shown excellent psychometric properties.[23]

Sexual distress. Participants' concerns and distress relating to their sexual functioning were assessed using the Female Sexual Distress Scale-Revised (FSDS-R). The FSDS-R is a self-reported unidimensional measure consisting of 13 items. All items are scored on a five-point Likert-type scale ranging from 0 (never) to 4 (always), with higher scores indicating more sexual distress. A total score can be calculated by summing up the 13 item scores. The Iranian version of the FSDS-R has demonstrated acceptable validity and reliability.[24]

HRQoL. Participants' HRQoL was assessed using the Short Form-12 (SF-12), a self-administered health instrument consisting of 12 items. Two summary scores – the physical component summary (PCS) and the mental component summary (MCS) – can be computed. Higher scores in both components indicate higher HRQoL. The Iranian version of the SF-12 has been shown to be a psychometrically sound tool for assessment of HRQoL.[25]

Depressive symptoms and anxiety. Information on depressive symptoms and anxiety was collected using the Hospital Anxiety and Depression Scale (HADS), a 14-item instrument consisting of seven items related to anxiety and depressive symptoms, respectively. All items are scored on a four-point Likert-type scale ranging from 0 (not at all) to 3 (very much indeed), with higher scores indicating more psychological distress. The Iranian version of the HADS has been found to be highly valid and reliable for detecting states of depressive symptoms and anxiety.[26]

Statistical analysis. Data are presented as means with standard deviations (SD) or as frequency and percentages. The comparability of the three groups in terms of sociodemographic and clinical variables was assessed using one-way analysis of variance (one-way ANOVA) for continuous measures and chi-square statistics for categorical variables. To analyze the longitudinal data, multilevel modeling (MLM; MLwiN version 2.27) was conducted to determine the effects of the psychosocial factors on sexual functioning over time. MLM is a powerful method that allows examination of changes over time by simultaneously accounting for within-individual and between-individual effects. Several univariate multilevel analyses

Table 1. Socio-demographic characteristics by condition.

	Control (*n*=94)	AMI (*n*=94)	TSCM (*n*=94)	*p*-value
Age, years, mean ± SD	63.10 ± 6.45	62.81 ± 8.33	63.56 ± 7.48	0.92
Years of education, years, mean ± SD	5.99 ± 1.31	5.69 ± 1.26	5.80 ± 1.36	0.58
BMI, mean ± SD	22.52 ± 4.54	23.51 ± 4.13	22.98 ± 3.74	0.27
Monthly family income, *n* (%)				0.46
High, >US$1000	29 (30.85)	39 (41.49)	31(32.98)	
Intermediate, US$500–1000	32 (34.05)	28 (29.79)	37 (39.36)	
Low, < US$500	33 (35.10)	27 (28.72)	26 (27.66)	
Smoking, *n* (%)	21 (22.34)	31 (32.98)	26 (27.66)	0.06
Diabetes, *n* (%)	1 (1.06)	17 (18.08)	9 (9.57)	0.003
Hypertension, *n* (%)	11 (11.70)	53 (56.38)	51 (54.25)	<0.001
Hyperlipidemia, *n* (%)	17 (18.05)	49 (52.13)	32 (34.04)	<0.001
Menopause, *n* (%)	16 (17.02)	19 (20.21)	17 (18.05)	0.33
Female sexual dysfunction, *n* (%)	53 (56.38)	71 (75.53)	73 (77.66)	<0.001

AMI: acute myocardial infarction; TSCM: Takotsubo (stress) cardiomyopathy; BMI: body mass index.

were conducted first to identify potential confounder variables such as age, income, body mass index, comorbidities and years of education. Following these analyses, variables with a p-value < 0.15 were treated as confounders and subsequently entered into the multiple-variable models. Next, restricted iterative generalized least squares was applied to fit all MLM models to three levels: time was set at the first level, participants at the second level, and hospitals at the third level. A logistic binary multilevel regression was performed to measure the changes in prevalence of sexual problems across time and across the three study groups. To test whether the decrease in patients' HRQoL (i.e. PCS and MCS) resulting from anxiety was associated with sexual functioning and sexual distress, mediation analyses based on Krull and MacKinnon's recommendations were performed.[27] All p-values were adjusted for multiple comparisons using the Benjamini and Hochberg false discovery rate,[28] and $p \leqslant 0.05$ was considered statistically significant.

Results

The sociodemographic and clinical characteristics of the three groups are presented in Table 1. Women were 53 to 68 years old with a median education of four years (interquartile range: 4–7). Eighteen percent of women in the TSCM group, 20% in the AMI group and 17% of the healthy control were menopausal. Overall, cardiac risk factors (i.e. smoking, diabetes, hypertension and hyperlipidemia) were more common in the TSCM and AMI groups compared with the healthy controls (Table 1).

Table 2 shows the means and SDs for psychological distress, female sexual functioning and HRQoL for all three study groups at baseline and at six- and 18-month follow-up. The TSCM group reported higher scores at baseline for sexual distress, anxiety and depression compared with the AMI and the healthy control groups ($p<0.05$). At baseline, both the TSCM and the AMI group reported lower PCS and sexual functioning compared with the healthy controls but no significant differences in these variables could be detected between the TSCM and the AMI groups.

According to the MLM models, sexual functioning scores differed significantly between the three groups at baseline (Table 3). Overall, the TSCM group showed significantly worse sexual functioning across all six dimensions over time compared with the AMI group (coefficients = −0.57 to −0.15, $p < 0.001$ at six-month follow-up; coefficients = −0.52 to −0.11, $p < 0.001$ at 18-month follow-up) and the healthy controls (coefficients = −2.19 to −0.29, $p < 0.001$ at six-month follow-up; coefficients = −2.23 to −0.25, $p < 0.001$ at 18-month follow-up) (Table 3).

Table 4 displays the mediating effects of female sexual functioning and sexual distress in the association between anxiety and HRQoL in the TSCM group. Here, anxiety was negatively associated with both the PCS (coefficient = −1.89, $p < 0.001$ at six months; coefficient = −1.54, $p < 0.001$ at 18 months) and the MCS score (coefficient = −1.92, $p < 0.001$ at six months; coefficient = −1.71, $p < 0.001$ at 18 months). In addition, significant mediating effects of female sexual functioning (coefficient = −0.65 and −1.45 for PCS, $p < 0.001$; coefficient = −2.63 and −2.09 for MCS, $p < 0.01$) and sexual distress (coefficient = −0.39 and −2.05 for PCS, $p<0.05$; coefficient = −2.61 and −1.73 for MCS, $p < 0.01$) could be found in the relationship between anxiety and both the PCS and MCS score.

General patterns of changes in prevalence of sexual problems are shown in Figure 1. Patients with TSCM reported higher prevalence of sexual problems across time compared with the healthy controls (odds ratio

Table 2. Descriptive statistics for all outcome measures by condition and time.

Variable	Condition	Baseline	Month 6	Month 18
		Mean ± SD	Mean ± SD	Mean ± SD
Anxiety	Control	5.39 ± 1.63	5.41 ± 1.57	5.38 ± 1.51
	AMI	8.75 ± 2.88	8.79 ± 2.13	8.77 ± 2.47
	TSCM	9.68 ± 2.63	9.81 ± 2.31	9.83 ± 2.59
Depression	Control	5.26 ± 1.49	5.22 ± 1.31	5.25 ± 1.40
	AMI	7.22 ± 3.53	6.68 ± 2.78	6.64 ± 2.41
	TSCM	7.37 ± 4.44	7.73 ± 4.06	7.71 ± 4.12
Desire	Control	3.27 ± 1.20	3.26 ± 1.46	3.30 ± 1.27
	AMI	2.30 ± 1.01	2.27 ± 1.12	2.28 ± 1.11
	TSCM	2.25 ± 0.78	2.03 ± 0.71	1.95 ± 0.58
Arousal	Control	3.08 ± 1.58	3.05 ± 1.37	3.10 ± 1.41
	AMI	2.24 ± 0.91	2.19 ± 0.91	2.12 ± 0.88
	TSCM	2.22 ± 0.59	1.80 ± 0.50	1.72 ± 0.51
Lubrication	Control	3.66 ± 1.18	3.69 ± 1.10	3.65 ± 1.15
	AMI	2.63 ± 0.88	2.51 ± 0.83	2.50 ± 0.80
	TSCM	2.59 ± 0.64	2.34 ± 0.55	2.29 ± 0.51
Orgasm	Control	4.21 ± 1.72	4.23 ± 1.77	4.22 ± 1.69
	AMI	2.56 ± 0.91	2.50 ± 0.84	2.47 ± 0.85
	TSCM	2.54 ± 0.78	2.20 ± 0.77	2.14 ± 0.70
Satisfaction	Control	3.78 ± 1.76	3.80 ± 1.81	3.81 ± 1.80
	AMI	2.81 ± 0.88	2.70 ± 0.81	2.68 ± 0.80
	TSCM	2.80 ± 0.93	2.46 ± 0.71	2.41 ± 0.65
Pain	Control	3.99 ± 1.14	3.98 ± 1.10	4.00 ± 1.20
	AMI	3.91 ± 0.86	3.07 ± 0.80	3.00 ± 0.78
	TSCM	3.92 ± 0.85	2.95 ± 0.73	2.89 ± 0.77
Total FSFI	Control	22.35 ± 3.58	22.38 ± 3.49	22.54 ± 3.62
	AMI	16.45 ± 3.01	15.26 ± 3.08	15.09 ± 2.98
	TSCM	16.33 ± 3.30	13.81 ± 3.24	12.48 ± 3.19
FSDS-R	Control	5.90 ± 2.71	5.94 ± 2.77	5.93 ± 2.69
	AMI	13.97 ± 5.34	14.08 ± 5.38	14.13 ± 5.41
	TSCM	16.78 ± 5.72	17.16 ± 5.82	17.23 ± 5.64
PCS	Control	74.31 ± 10.82	73.92 ± 10.28	74.33 ± 10.61
	AMI	44.81 ± 7.34	34.51 ± 6.25	31.22 ± 6.11
	TSCM	44.16 ± 6.11	40.68 ± 6.01	38.12 ± 5.88
MCS	Control	62.31 ± 9.58	61.42 ± 9. 61	61.34 ± 9.52
	AMI	45.49 ± 7.46	43.71 ± 7.10	42.32 ± 7.17
	TSCM	41.66 ± 7.38	35.14 ± 6.87	31.23 ± 6.67

AMI: acute myocardial infarction; TSCM: Takotsubo (stress) cardiomyopathy; FSFI: Female Sexual Function Index; FSDS-R: Female Sexual Distress Scale-Revised; PCS: physical component summary; MCS: mental component summary.

(OR)= 3.10, p= 0.001) and the AMI group (OR= 2.28, p= 0.001).

Discussion

In this multi-center longitudinal study we found that the symptoms of anxiety and depression were more frequent, while HRQoL and sexual function were significantly lower in female patients with TSCM compared with healthy controls. Women with TSCM further showed less favorable outcomes across all study variables except for HRQoL (physical functioning) compared with the AMI group. Sexual functioning showed a stronger decline over time in the TSCM group compared with the AMI group and turned out to be a mediator in the relationship between anxiety and HRQoL. Finally, while anxiety and depression increased over time, HRQoL and sexual function tended to decrease in both groups but especially in the TSCM group, potentially indicating a reversed association between these variables.

Findings from a number of studies have shown that female patients reporting AMI or TSCM also report higher levels of mental, physical and overall health impairment compared with the general population.[5,29,30] A study by Christensen et al., for example, found that neuroticism, depression and anxiety were considerably higher in patients with TSCM compared with the healthy general population.[31] When comparing TSCM and AMI patients, the authors further observed higher levels of anxiety in the

Table 3. Three-level multiple linear regression models predicting desire, arousal, lubrication, orgasm, satisfaction, pain and total score of the FSFI.

Variable	Month	Desire		Arousal		Lubrication		Orgasm		Satisfaction		Pain		FSFI	
		β (SE)	*p*-value	β (SE)	*p*-value	β (SE)	*p*-value	β (SE)	*p*-value	β (SE)	*p*-value	β (SE)	*p*-value	β (SE)	*p*-value
AMI		−0.28 (0.06)	<0.001	−0.12 (0.04)	0.002	−0.20 (0.06)	<0.001	−0.22 (0.07)	0.002	−0.16 (0.09)	0.07	−0.02 (0.10)	0.84	−0.74 (0.45)	0.10
TSCM		−0.37 (0.06)	<0.001	−0.18 (0.03)	<0.001	−0.38 (0.08)	<0.001	−0.27 (0.05)	<0.001	−0.24 (0.07)	<0.001	−0.14 (0.07)	0.045	−0.28 (0.16)	0.08
Month	6	−0.59 (0.07)	<0.001	−0.17 (0.04)	<0.001	−0.41 (0.06)	<0.001	−0.42 (0.11)	<0.001	−0.20 (0.06)	<0.001	−0.12 (0.05)	0.016	−1.74 (0.41)	<0.001
AMI *vs.* control	6	−0.27 (0.10)	0.007	−0.12 (0.05)	0.016	−0.26 (0.05)	<0.001	−0.19 (0.03)	<0.001	−0.22 (0.08)	0.006	−0.21 (0.10)	0.03	−1.62 (0.61)	0.007
TSCM *vs.* control	6	−0.56 (0.11)	<0.001	−0.29 (0.06)	<0.001	−0.32 (0.06)	<0.001	−0.29 (0.04)	<0.001	−0.30 (0.03)	<0.001	−0.59 (0.14)	<0.001	−2.19 (0.66)	<0.001
TSCM *vs.* AMI	6	−0.24 (0.10)	0.016	−0.16 (0.07)	0.02	−0.41 (0.11)	<0.001	−0.15 (0.07)	0.03	−0.24 (0.09)	0.008	−0.38 (0.16)	0.017	−0.57 (0.18)	0.001
Month	18	−0.57 (0.07)	<0.001	−0.14 (0.05)	0.004	−0.52 (0.09)	<0.001	−0.12 (0.05)	0.02	−0.04 (0.09)	0.66	−0.16 (0.09)	0.07	−0.46 (0.06)	<0.001
AMI *vs.* control	18	−0.38 (0.10)	<0.001	−0.13 (0.05)	0.009	−0.37 (0.14)	0.008	−0.18 (0.06)	0.003	−0.16 (0.07)	0.02	−0.28 (0.11)	0.01	−1.97 (0.66)	0.002
TSCM *vs.* control	18	−0.51 (0.09)	<0.001	−0.25 (0.06)	<0.001	−0.46 (0.10)	<0.001	−0.42 (0.11)	<0.001	−0.34 (0.04)	<0.001	−0.54 (0.12)	<0.001	−2.23 (0.64)	<0.001
TSCM *vs.* AMI	18	−0.61 (0.11)	<0.001	−0.19 (0.07)	0.007	−0.26 (0.08)	0.001	−0.29 (0.07)	<0.001	−0.11 (0.05)	0.03	−0.32 (0.13)	0.01	−0.52 (0.24)	0.03
Anxiety		−0.39 (0.02)	<0.001	−0.12 (0.03)	<0.001	−0.23 (0.09)	0.01	−0.18 (0.09)	0.045	−0.10 (0.04)	0.01	−0.21 (0.06)	<0.001	−0.74 (0.13)	<0.001
Depression		−0.21 (0.04)	<0.001	−0.02 (0.01)	0.045	−0.11 (0.04)	0.006	−0.29 (0.08)	<0.001	−0.14 (0.08)	0.08	−0.09 (0.05)	0.07	−0.18 (0.07)	0.10
Sexual distress		−0.24 (0.07)	<0.001	−0.47 (0.12)	<0.001	−0.32 (0.14)	0.022	−0.25 (0.04)	<0.001	−0.23 (0.04)	<0.001	−0.14 (0.05)	0.005	−0.26 (0.08)	0.001
PCS		0.14 (0.02)	<0.001	0.06 (0.02)	0.003	0.28 (0.18)	0.12	0.09 (0.05)	0.07	0.10 (0.05)	0.045	0.03 (0.02)	0.13	0.17 (0.05)	<0.001
MCS		0.43 (0.09)	<0.001	0.30 (0.08)	<0.001	(0.42 (0.11)	<0.001	0.31 (0.06)	<0.001	0.18 (0.06)	0.003	−0.18 (0.03)	<0.001	0.16 (0.06)	0.007
Diabetes		−0.13 (0.06)	0.031	−0.03 (0.04)	0.45	−0.11 (0.09)	0.22	−0.16 (0.11)	0.15	−0.08 (0.05)	0.11	0.04 (0.06)	0.50	−0.86 (0.76)	0.26
Smoking		−0.02 (0.04)	0.61	−0.08 (0.05)	0.11	−0.04 (0.03)	0.18	−0.19 (0.09)	0.03	0.04 (0.05)	0.42	−0. 14 (0.11)	0.20	−0.10 (0.26)	0.70
Hypertension		−0.06 (0.04)	0.13	−0.58 (0.36)	0.11	−0.06 (0.02)	0.003	−0.05 (0.07)	0.47	−0.07 (0.06)	0.24	−0.10 (0.06)	0.09	−0.75 (0.30)	0.12
Hyperlipidemia		0.04 (0.05)	0.42	−0.47 (0.24)	0.049	0.12 (0.08)	0.13	−0.04 (0.02)	0.045	−0.09 (0.08)	0.25	0.08 (0.07)	0.25	−0.37 (0.27)	0.17
Intercept		0.79 (0.02)	<0.001	0.98 (0.09)	<0.001	0.73 (0.04)	<0.001	0.32 (0.02)	<0.001	0.48 (0.01	<0.001	0.60 (0.04)	<0.001	34.60 (0.92)	<0.001

AMI: acute myocardial infarction; TSCM: Takotsubo (stress) cardiomyopathy; PCS: physical component summary; MCS: mental component summary; FSFI: Female Sexual Function Index.

Table 4. Female sexual dysfunction and quality of life, mediators and mediation effect in patients with Takotsubo (stress) cardiomyopathy.

Outcome	Time, month	Mediator	Anxiety effect on outcome *C* (SE)	Anxiety effect on mediator *A* (SE)	Mediator effect on outcome *B* (SE)	Mediated effect *A*B* (SE)
PCS	6		−1.89 (0.12)***			
		FSFI		−1.23 (0.07)***	0.53 (0.12)***	−0.65 (0.15)***
		FSDS-R		1.16 (0.06)***	−0.34 (0.16)*	−0.39 (0.18)*
	18		−1.54 (0.18)***			
		FSFI		−1.42 (0.11)***	1.02 (0.13)***	−1.45 (0.22)***
		FSDS-R		1.25 (0.09)***	−1.64 (0.19)***	−2.05 (0.28)***
MCS	6		−1.92 (0.26)***			
		FSFI		−1.83 (0.10)***	1.44 (0.24)***	−2.63 (0.46)***
		FSDS-R		1.28 (0.26)***	−2.04 (0.43)***	−2.61 (0.76)***
	18		−1.71 (0.35)***			
		FSFI		−1.63 (0.49)***	1.28 (0.19)***	−2.09 (0.70)**
		FSDS-R		1.21 (0.32)***	−1.43 (0.28)***	−1.73 (0.57)**

*$p<0.05$.
**$p<0.01$.
***$p<0.001$.
PCS: physical component summary; MCS: mental component summary; FSFI: Female Sexual Function Index; FSDS-R: Female Sexual Distress Scale-Revised.

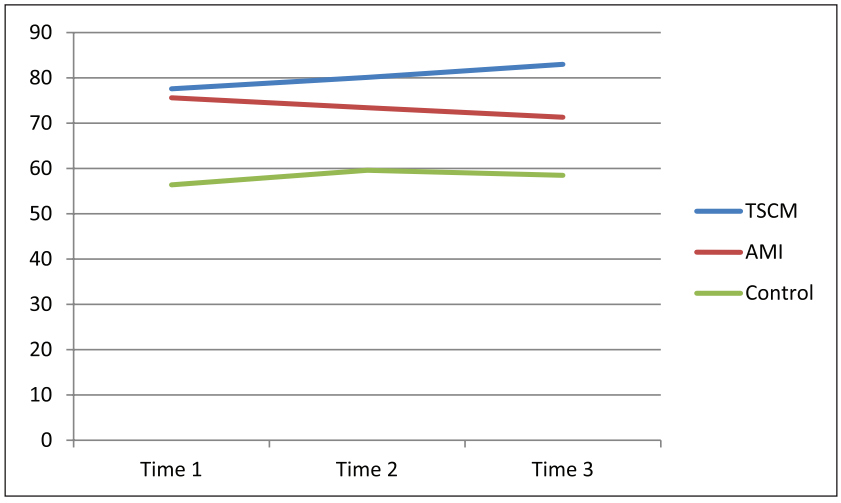

Figure 1. General patterns of change in prevalence of sexual dysfunction among study groups including patients with Takotsubo (stress) cardiomyopathy (TSCM), patients with acute myocardial infarction (AMI) and control group.

TSCM group compared with the AMI group. In another, similar, study, Goh et al. found a higher level of anxiety, but not depression, in the TSCM group compared with women with AMI.[21] Somewhat in accordance with these previous findings we were also able to observe differences in anxiety, depression and overall psychological health between female patients with TSCM, those with AMI and healthy controls.

In terms of sexual health, women with TSCM reported more sexual problems and also showed a stronger decline over time in functioning compared with the AMI group and the healthy controls. We further detected a mediating effect of sexual functioning in the association between anxiety and HRQoL in the TSCM group. In other words, with increasing anxiety and decreasing HRQoL, sexual functioning also decreased over time. The importance of anxiety in sexual functioning has been investigated in other studies and study populations, such as patients with AMI. A study by Oskay et al.,[12] for example, found that nearly 75% of women with AMI suffered from some sort of sexual dysfunction and scored lower in all domains of the FSFI compared with healthy controls. In line with previous findings in patients with AMI, we also found higher levels of sexual problems in women with TSCM and even observed a steeper decline in sexual functioning over time compared with AMI or healthy controls. This may be explained by the increase of anxiety over time. Indeed, evidence suggests that anxiety can negatively impact on sexual functioning, and without appropriate intervention lead

to worsening and further deterioration of sexual functioning in a progressive pattern.

Limitations

Certain limitations need to be considered. First, although a longitudinal study design with low attrition was used, data were collected by self-report, which may have led to recall or information biases. Second, despite our attempts to match the three study groups for sociodemographic characteristics, some differences, for example in terms of clinical conditions such as diabetes and hypertension, may have led to confounding and limited the comparability of the samples. Finally, other factors such as social support and differences in coping strategies that have previously been shown to influence sexual functioning were not explored in the current study due to the unavailability of the data.

Conclusion

In conclusion, our study findings indicate that depressive symptoms, anxiety, HRQoL and sexual functioning are impaired in women with TSCM. Women with AMI also showed higher levels of impairment compared with healthy controls but were less affected compared with women with TSCM. Sexual functioning further turned out to be a mediator that could negatively influence HRQoL over time. Future studies are needed to increase our understanding of such mediation mechanisms. Based on our findings we conclude that there is an urgent need to design health interventions for preventing exacerbation of mental conditions and sexual problems in female patients with TSCM.

Implications for practice

- Clinicians need to assess psychological distress and health-related quality of life among women with Takotsubo cardiomyopathy since both were shown to be even poorer than among female patients with acute myocardial infarction.
- Clinicians need to increase their awareness of how Takotsubo cardiomyopathy impairs sexual functioning in female patients.
- Sexual ability mediates the effects of anxiety on health-related quality of life and sexual functioning. Sexual distress should therefore be included in screening measures to identify women with Takotsubo cardiomyopathy in need of interventions to improve health-related quality of life.
- Clinicians should collaborate with researchers and patients with Takotsubo cardiomyopathy to develop a measure and intervention program for sexual counseling adapted to the female patients' situation, including both physical and psychosocial aspects.

Declaration of conflicting interests

The authors declare that there is no conflict of interest.

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