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Psychological disorders in adults with inherited cardiomyopathies and Takotsubo syndrome

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Abstract

We performed a narrative review about psychological disorders in adults with Takotsubo syndrome and inherited cardiomyopathies. Through the electronic database PubMed and PsycINFO we searched all relevant related manuscripts published between 2000 and 2015. We found twelve studies that explore psychological disorders in Takotsubo syndrome and eight about inherited cardiomyopathies: five enrolled patients with hypertrophic cardiomyopathy, two dilated cardiomyopathy, and one arrhythmogenic right ventricular cardiomyopathy. All papers reported the presence of psychological disorders. In Takotsubo syndrome, depression fluctuates between 20.5 and 48% and anxiety was present among 26 and 56%. A study reported that anxiety increases the probability of developing Takotsubo syndrome. In dilated cardiomyopathy, anxiety was present in 50% and depression in 22%. In arrhythmogenic right ventricular cardiomyopathy, younger age, poorer functional capacity and having experienced at least one implantable cardioverter defibrillator shock, were significant independent predictors of both device-specific and generalized anxiety. In hypertrophic cardiomyopathy, anxiety and depression were present in 45.2% and 17.9%, respectively. Thirty seven percent met diagnostic criteria for anxiety disorders and 21% for mood disorders. Nearby half hypertrophic cardiomyopathy patients report triggering of chest pain, dyspnea, and dizziness by emotional stress. Due to the small number of studies, conclusions are limited. However, we discuss some results.

Resumen

Realizamos una revisión narrativa sobre trastornos psicológicos en adultos con diagnóstico de síndrome de Takotsubo y miocardiopatías hereditarias. Utilizando las bases de datos PubMed y PsycINFO buscamos los trabajos relevantes publicados entre 2000 y 2015. Encontramos doce estudios que exploran alteraciones psicológicas en síndrome de Takotsubo y ocho estudios sobre miocardiopatías hereditarias: cinco enrolaron pacientes con miocardiopatía hipertrófica, dos miocardiopatía dilatada, uno miocardiopatía arritmogénica del ventrículo derecho. Todas las publicaciones reportaron la presencia de trastornos psicológicos. En el síndrome de Takotsubo, la depresión oscila entre el 20,5 y el 48% y la ansiedad estuvo presente entre el 26 y el 56%. Un estudio reporta que la ansiedad aumenta la probabilidad de desarrollar el síndrome de Takotsubo. En la miocardiopatía dilatada, la ansiedad estuvo presente en el 50% de los pacientes y la depresión en el 22%. En la miocardiopatía arritmogénica del ventrículo derecho, la edad más joven, peor capacidad funcional y haber experimentado al menos un shock por desfibrilador automático implantable, fueron predictores independientes significativos de ansiedad tanto específica por el dispositivo como generalizada. En la miocardiopatía hipertrófica, la ansiedad y la depresión estaban presentes en 45,2% y 17,9%, respectivamente. Treinta y siete por

ciento cumplía con los criterios de diagnóstico para los trastornos de ansiedad y 21% para los trastornos del estado de ánimo. Cerca de la mitad de los pacientes con miocardiopatía hipertrófica informan dolor en el pecho, disnea y mareos desencadenados por estrés emocional. Debido al reducido número de estudios publicados, las conclusiones son limitadas. No obstante, presentamos algunos de los resultados.

Introduction

Inherited cardiomyopathies (ICM) [1],[2],[3],[4],[5] are a clinically heterogeneous group of disorders caused by mutations in several genes, especially in those genes coding for sarcomeric protein. Patients with a genetic cardiomyopathy have a structurally and functionally abnormal heart muscle, in the absence of coronary artery disease, hypertension, valvular disease and congenital heart disease potentially responsible. They represent a major cause of morbidity and mortality in both children and adults, and are a frequent indication for cardiac transplantation. Inherited cardiomyopathy diagnosis could have negative psychological impact on patients of all ages and sometimes in relatives, compromising disease prognostic.

Takotsubo syndrome (TS) [6],[7],[8],[9],[10],[11],[12],[13],[14],[15],[16],[17],[18],[19],[20],[21] also known as transient ventricular dyskinesia, apical ballooning cardiomyopathy, stress-induced cardiomyopathy or broken heart syndrome, is a reversible cardiomyopathy characterized by transient systolic ventricular dysfunction with a clinical presentation indistinguishable from acute myocardial infarction but in the absence of significant coronary artery stenosis. The pathophysiology remains poorly understood and seems to be multifactorial. Several hypotheses have been proposed including myocardial dysfunction mediated through catecholamine-induced damage, catecholamine-induced inflammatory response, microvascular alterations, coronary artery spasm or dysfunction, and neurogenically mediated myocardial stunning. Stressful circumstances, physical or psychological, have deemed to play an important role on this condition.

We performed a narrative review about psychological disorders in adults with Takotsubo syndrome and inherited cardiomyopathies. We try to answer the following questions: Are there psychological disorders in adults with TS/ICM? Do psychological disorders increment the probability of developing Takotsubo syndrome? Do psychological disorders trigger some inherited cardiomyopathies symptoms?

Methods

Through the electronic database PubMed and PsycINFO we searched manuscripts wrote in English and published between 2000 and 2015. Case reports were excluded.

We considered psychological disorders as the presence of anxiety, depression, mood disorders, anxiety disorders and personality disorders.

We divided the broad field of inherited cardiomyopathies in five groups, for our study purposes: hypertrophic cardiomyopathy (HCM), dilated cardiomyopathy (DCM) and arrhythmogenic right ventricular cardiomyopathy (ARVC), non-compaction cardiomyopathy and restrictive cardiomyopathy.

The main data search terms were: inherited cardiomyopathies /hypertrophic cardiomyopathy /dilated cardiomyopathy /arrhythmogenic right ventricular cardiomyopathy /restrictive cardiomyopathy /noncompaction cardiomyopathy + psychology /depression /anxiety /personality /mood disorders /anxiety disorders /personality disorders /stress; Takotsubo cardiomyopathy or stress cardiomyopathy /+ psychology /depression /anxiety /personality /mood disorders /anxiety disorders /personality disorders/stress.

Results

We found twenty studies that explore psychological disorders in patients with inherited cardiomyopathies and Takotsubo syndrome: twelve about Takotsubo syndrome [22],[23],[24],[25],[26],[27],[28],[29],[30],[31],[32],[33] and eight about inherited cardiomyopathies [34],[35],[36],[37],[38],[39],[40],[41]. All papers reported the presence of psychological disorders. Main results are displayed in table 1.

Disease	Authors	Methods and materials	Main results
Takotsubo syndrome	Kastaun, et al. 2014	Case-control, 19 TS, 20 STEMI, 20 healthy control. Freiburger Personality Inventory-Revised (FPI-R), Symptom Checklist-Revised (SCL-90-R)	Higher percentage of anxiety and greater emotional lability in TS. Severe arguments: 39% TS vs 5% STEMI.
	Deshmukh et al. 2012	Cross-sectional, 6.837 TS. International Classification of Diseases, Ninth Revision, Clinical Modification. ICD-9-CM codes.	Anxiety was significantly associated with higher odds of developing TS.
	Summers, et al. 2010	Case-control, 25 TS, 25 STEMI, 50 healthy control. Medical and psychiatric records.	Anxiety: 56% TS vs 12% STEMI. Depression: 48% TS vs 28% STEMI. Anxiety or depression: 68% TS vs 36% STEMI vs 30% health control. Statistical differences between groups were founded for anxiety.
	Dias, et al. 2013	Retrospective, 78 TS. Medical and psychiatric records.	Depression: 20.5%. Anxiety: 30.8%. Trigger by stressful emotional event: 57%.
	Waldenborg, et al. 2011	Prospective, 13 TS. Posttraumatic Stress Syndrome 10-Questions Inventory (PTSS-10) and Montgomery-Åsberg depression rating scale (MADRS).	No statistical differences in scores between 3 months were found.
	Compare et al. 2013	Case-control, 37 TS experienced emotional triggering, 37 AMI experienced emotional triggering, 37 TS without emotional triggers. Type D Scale (DS14).	Type D: 76% TS emotional trigger vs 43% ST without emotional trigger vs 32% AMI.
	Del Pace, et al. 2011	Case-control, 50 TS, 50 STEMI. Spielberger Trait Anxiety Inventory.	High-anxiety trait: 60% TS vs 52% STEMI.
	Lacey et al. 2014	Case-control, 31 sporadic TS, 27 earthquake-related TS. Eysenck Personality Questionnaire Brief Version.	Statistical differences were found in neuroticism between control and TS groups.
	Delmas, et al. 2013	Case-control, 45 TS, 50 ACS. Mini International Neuropsychiatric Interview.	Major depressive disorder: 73% TS vs 26% ACS. Generalized anxiety disorders: 26% TS vs 6% ACS. Emotional stressor triggers 56% TS vs 16% ACS. Friendship or romance disappointment: TS 13% vs 4% ACS.
	El-Sayed et al., 2012	Case-control, 24.701 TS, 25.069 AMI, 24.601 orthopedic patients. International Classification of Diseases, Ninth Revision, Clinical Modification. ICD-9-CM codes.	TS: anxiety disorder 8.9%, mood disorder 15%. AMI: anxiety disorder 3.4%, mood disorder 7.2%.
	Sharkey, et al. 2014	Prospective, 130 TS, stressful events recorded.	Intense emotional event: 49%.
	Compare et al., 2014	Prospective, 37 TS, 37 AMI, Psychological distress was assessed using the Psychological General Well-Being Index (PGWBI).	TS patients had significant increases in levels of psychological distress compared to AMI patients and tends to become more negative over time compared with AMI patients.
Hypertrophic cardiomyopathy	Ingles, et al., 2008	Transversal, n=109 patients and at risk-relatives, HADS.	Anxiety and depression in the HCM group was 45.2% and 17.9% respectively, and in the at-risk group was 32.0% and 4.0%, respectively. No significant differences between at-risk relatives and HCM patients in levels of anxiety and depression.
	Serber et al., 2007	Prospective, 22 obstructive hypertrophic cardiomyopathy, Center for Epidemiologic Studies Depression Scale (CES-D).	Clinically relevant levels of depression 57%, symptoms of anxiety 57%.
	Lampert, et al., 2010	Transversal, n=1297.	Close to half of the patients reported triggering of chest pain, dyspnea, and dizziness by emotional stress.
	Morgan, et al., 2008	Transversal, n=148, Structured Clinical Interview for DSM Disorders.	37% patients fulfilled criteria for anxiety disorder and 21% for mood disorder.
	Igoumenou et al., 2012	Prospective, n=121, CES-D, Beck Depression Inventory (BDI).	Patients with HCM are more depressed than the general population. Depressive symptoms and risk factors for sudden death were not related.
Dilated cardiomyopathy	Griez, et al., 2000	Transversal, 50 dilated cardiomyopathy, 43 other cardiac diseases. Mini International Neuropsychiatric Interview.	50% met the criteria for a disorder. Panic disorder was no more prevalent in the cardiomyopathy group compared to patients with other cardiac diseases.
	Steptoe, et al., 2000	Transversal, n=60, SF-36, Hospital Anxiety and Depression Scale (HADS).	50% anxiety. 22% depression.
Arrhythmogenic right ventricular cardiomyopathy	James, et al., 2012	Transversal, n=86, HADS.	31% anxiety. 9% depression.

TS: Takotsubo syndrome
STEMI: ST-segment elevation myocardial infarction
ACS: acute coronary syndrome
AMI: acute myocardial infarction
HCM: hypertrophic cardiomyopathy

Table 1. Main findings scheme

Most of the papers that study Takotsubo syndrome include female patients over 55 years. Patients with Takotsubo syndrome had higher percentages of psychological disorders than those with acute coronary syndromes (ACS) [22],[25],[28],[29],[30],[31],[32],[33]. Percentages of psychological factors vary between studies. The presence of depression fluctuates between 20.5 and 48% [25],[26]. Anxiety was present among 26 and 56% [22],[23],[25],[26]. Five studies describe higher percentage of anxiety in Takotsubo syndrome patients [22],[23],[25],[29],[30]. One study reported statistical differences between Takotsubo syndrome and acute coronary syndromes groups for anxiety [25]. Another study reported that anxiety increases the probability of developing Takotsubo syndrome [23].

As for papers that study inherited cardiomyopathies, five enrolled patients with hypertrophic cardiomyopathy [34],[35],[36],[37],[38], two dilated cardiomyopathy [39],[40], and one arrhythmogenic right ventricular cardiomyopathy [41]. We could not find studies dealing with noncompaction cardiomyopathy or restrictive cardiomyopathy.

About arrhythmogenic right ventricular cardiomyopathy, a study that assessed depression and anxiety using HADS reported anxiety 31% and depression 9% [41].

In relation to dilated cardiomyopathy, one study assessed anxiety and depression using HADS [40] and one study assess the presence of psychological disorders according to DSM criteria [39]. Anxiety was present in 50% and depression in 22% [40]. According to DSM criteria, 50% had psychological disorders [39].

Regarding to hypertrophic cardiomyopathy three studies assessed depression [34],[35],[38], one study assessed anxiety [34], one paper assessed the presence of psychological disorders following DSM criteria[37], and one study explored the relationship between symptoms and emotional stress [36]. Anxiety and depression were present in 45.2% and 17.9%, respectively [34]. Diagnostic criteria for anxiety disorders were met in 37% and for mood disorders in 21% [37]. Nearby half hypertrophic cardiomyopathy patients report triggering of chest pain, dyspnoea, and dizziness by emotional stress [36].

Discussion

Due to the small number of studies, conclusions are limited. However, we discuss some results.

The study of psychological disorders in adults with Takotsubo syndrome and inherited cardiomyopathies have received less attention than another disease, which also describe psychological disorders, such as heart failure and acute myocardial infarct. This could be due to the fact that heart failure and acute myocardial infarct are more common diseases than Takotsubo syndrome and inherited cardiomyopathies. The fact that all studies revised report psychological disorders does not necessarily mean that psychological disorders are associated with pathologies revised. In our review, in one study, anxiety was found to be significantly associated with higher odds of developing Takotsubo syndrome, and in other study, higher anxiety scores were associated with poorer functional capacity in arrhythmogenic right ventricular cardiomyopathy patients.

The study of psychological disorders in cardiovascular diseases is worth considering because the presence of psychological disorders usually accompanied by an impairment in patient´s quality of life and could have negative influence in medical compliance. On one hand, psychological disorders might adversely affect prognosis. In our review, one study reported that Takotsubo syndrome patients had significant increases in levels of psychological distress compared to acute myocardial infarction patients tending to become more negative over time compared with acute myocardial infarction patients. As for inherited cardiomyopathies, a study reports emotion-triggered symptoms in hypertrophic cardiomyopathy patients, particularly in women. On the other hand, functional medical status might increase the probability of anxiety. In one study, in arrhythmogenic right ventricular cardiomyopathy, poorer functional capacity and having experienced at least one implantable cardioverter defibrillator shock, were significant independent predictors of anxiety.

As we mentioned above, in Takotsubo syndrome and inherited cardiomyopathies, percentages of anxiety were higher than percentage of depression. Patients with anxiety usually have higher catecholamine response to stressful situations. High levels of catecholamine might exacerbate functional medical conditions, Takotsubo syndrome and inherited cardiomyopathies.

As for Takotsubo syndrome, anxiety was significantly associated with higher odds of developing Takotsubo syndrome. High levels of catecholamine could induced endocardial endothelial dysfunction, affecting areas of the left ventricle (LV) where surface-to-volume ratios are highest, contributing to a transient impairment of the left ventricle. The relatively reduced left ventricle size in females might also predispose to more frequently Takotsubo syndrome development in women. Some authors suggest that some physiological changes associated with post-menopause could make them more vulnerable to Takotsubo syndrome development: sympathetic dominance replaces parasympathetic dominance as the main regulator of cardiovascular system, baroreflex sensitivity decrease significantly, cardiovascular beta adrenoreceptor responsiveness decreases and alfa 1 adrenoreceptor responsiveness increases. These results suggest that psychological screening, specially anxiety, and then psychological treatment, could contribute to prevent Takotsubo syndrome development in postmenopausal women.

In arrhythmogenic right ventricular cardiomyopathy patients, higher anxiety scores were associated with younger age (aged 18 to 79 years, mean age 46 years), poorer functional capacity and having experienced an implantable cardioverter defibrillators (ICD) shock.

Moreover, younger age, poorer functional capacity, having experienced at least one implantable cardioverter defibrillator shock, were significant independent predictors of both device-specific and generalized anxiety. Having an inherited cardiomyopathy is usually accompanied by unique anxieties and worries over patients' health risks and death, and over family members' health risks. Studies that explore anxiety in adults with implantable cardioverter defibrillator report that anxiety is associated with an increased risk of ventricular arrhythmias and mortality. Mechanisms underlying this association is not yet well understood. However low heart rate variability is shown to be associated with both, arrhythmias and anxiety [42],[43],[44]. Implantable cardioverter defibrillators are frequently used in arrhythmogenic right ventricular cardiomyopathies for treatment of ventricular arrhythmias and prevention of sudden cardiac death, to maximize implantable cardioverter defibrillators adjustment it is important to identify these patients at risk for anxiety and provide them psychological care.

It worth considering that near half of hypertrophic cardiomyopathy patients (N=1297) report triggering of chest pain, dyspnoea, and dizziness by emotional stress and that women were more likely to report emotion-triggered symptoms. According to a previous study, women with hypertrophic cardiomyopathy were more likely to report symptoms. Authors suggest that gender differences in central processing of sensory information and socialization to the acceptability of reporting symptoms contribute to greater symptom reporting in women. Explanations about emotion-triggered symptoms include the autonomic and hemodynamic changes associated with emotional stress, such as increased contractility and decreased ejection time. In addition, authors propose that hypertrophic cardiomyopathy patients may be particularly sensitive to endogenous catecholamine's that increases induced by emotional stress. Studies report that exogenously catecholamine administration lead to exaggerate the abnormalities of cardiovascular function in hypertrophic cardiomyopathy patients and also describe catecholamine reuptake decreased at sympathetic nerve terminals [45],[46]. Results suggest that hypertrophic cardiomyopathy patients may benefit with interventions aimed at emotional stress reduction or management.

Conclusions

Although the number of studies published are little, owing to all papers reported the presence of psychological disorders, psychological care by mental health professionals seems appropriate in each diseases revised. However, further research about psychological disorders in Takotsubo syndrome and inherited cardiomyopathies is needed. For example, future research might assess mediating variables among anxiety and functional capacity in arrhythmogenic right ventricular cardiomyopathy and explore pathways linking hypertrophic cardiomyopathy symptoms and emotional stress. Moreover, studies might evaluate whether treating anxiety would improve arrhythmogenic right ventricular cardiomyopathy functional capacity and if treating anxiety might reduce the risk of developing Takotsubo syndrome. Although bio-psycho-education could help inherited cardiomyopathies patients understanding about inherited cardiomyopathies and promote patient´s psychological adjustment, studies about psychological evidence-based interventions for inherited cardiomyopathies are lacking. Associations between genetic, clinical presentation and psychological variables in inherited cardiomyopathies are not yet studied. Perhaps, might be a psychological profile that is common between patients and relatives with the same disease but it is not present in relatives without disease diagnoses.

Notes

From the editor

The authors originally submitted this article in Spanish and English. The *Journal* has not copyedited the English version.

Conflicts of interest

The authors completed the ICMJE conflict of interest declaration form, translated into Spanish by *Medwave*, and declare not having received funding for the preparation of this report, not having any financial relationships with organizations that could have interests in the published article in the last three years, and not having other relations or activities that might influence the article´s content. Forms can be requested to the responsible author or the editorial direction of the Journal.

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