Journal of Affective Disorders 194 (2016) 38–49

Contents lists available at ScienceDirect

Journal of Affective Disorders

journal homepage: www.elsevier.com/locate/jad

Review article

Is there cardiac risk in panic disorder? An updated systematic review

Daniela Caldirola [a,*], Koen R Schruers [b,d], Antonio E Nardi [e], Domenico De Berardis [f], Michele Fornaro [g], Giampaolo Perna [a,b,c]

[a] Department of Clinical Neurosciences, Hermanas Hospitalarias, Villa San Benedetto Menni Hospital, FoRiPsi, 22032 Albese con Cassano, Como, Italy
[b] Department of Psychiatry and Neuropsychology, Faculty of Health, Medicine and Life Sciences, Maastricht University, 6200 Maastricht, The Netherlands
[c] Department of Psychiatry and Behavioral Sciences, Leonard Miller School of Medicine, Miami University, 33136 Miami, USA
[d] Center for the Psychology of Learning and Experimental Psychopathology, Department of Psychology, University of Leuven, Tiensestraat 102, P.O. Box 3726, 3000 Leuven, Belgium
[e] Laboratory of Panic and Respiration, Institute of Psychiatry, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil
[f] National Health Service, Department of Mental Health, Psychiatric Service of Diagnosis and Treatment, Hospital "G. Mazzini", ASL 4, Teramo, Italy
[g] Department of Education Science, University of Catania, Catania, Italy

ARTICLE INFO

Article history:
Received 8 October 2015
Received in revised form
4 January 2016
Accepted 6 January 2016
Available online 13 January 2016

Keywords:
Panic
Cardiac risk
Cardiac disease

ABSTRACT

Background: The recognized relationship between panic disorder (PD) and cardiac disorders (CDs) is not unequivocal. We reviewed the association between PD and coronary artery disease (CAD), arrhythmias, cardiomyopathies, and sudden cardiac death.
Methods: We undertook an updated systematic review, according to PRISMA guidelines. Relevant studies dating from January 1, 2000, to December 31, 2014, were identified using the PubMed database and a review of bibliographies. The psychiatric and cardiac diagnostic methodology used in each study was then to very selective inclusion criteria.
Results: Of 3044 studies, 14 on CAD, 2 on cardiomyopathies, and 1 on arrhythmias were included. Overall, the studies supported a panic–CAD association. Furthermore, in some of the studies finding no association between current full-blown PD and CAD, a broader susceptibility to panic, manifesting as past PD, current agoraphobia, or subthreshold panic symptoms, appeared to be relevant to the development of CAD. Preliminary data indicated associations between panic, arrhythmias, and cardiomyopathies.
Limitations: The studies were largely cross-sectional and conducted in cardiological settings. Only a few included blind settings. The clinical conditions of patients with CDs and the qualifications of raters of psychiatric diagnoses were highly heterogeneous. CDs other than CAD had been insufficiently investigated.
Conclusions: Our review supported a relationship between PD and CDs. Given the available findings and the involvement of the cardiorespiratory system in the pathophysiology of PD, an in-depth investigation into the panic–CDs association is highly recommended. This should contribute to improved treatment and prevention of cardiac events and/or mortality, linked to PD.

Contents

* Correspondence to: Villa San Benedetto Hospital, Hermanas Hospitalarias, via Roma 16, 22032, Albese con Cassano, Como, Italy.
E-mail address: caldiroladaniela@gmail.com (D. Caldirola).

http://dx.doi.org/10.1016/j.jad.2016.01.003
0165-0327/

1. Introduction

Panic disorder (PD) is a highly prevalent (lifetime prevalence is 3–4%), debilitating psychiatric disorder (Kessler et al., 2012). Unexpected panic attacks (PAs) are a core symptom of PD. These are sudden episodes of intense fear and discomfort, associated with a surge of somatic symptoms such as chest pain, palpitations, dyspnea, and breathlessness (American Psychiatric Association, 2013). Understandably, patients are often frightened of dying from a heart attack during a PA. It has been demonstrated that more than 20% of patients who refer to heart first aid are not suffering from a cardiac problem but from PD (Soares-Filho et al., 2014). Typically, these patients undergo cardiac examination with negative results and receive reassurance that their heart is fine. Having just experienced an event that felt life-threatening, patients often meet this reassurance with skepticism (Starcevic and Berle, 2006). While they may accept that there is no evidence of an acute cardiac problem at that present moment, they wonder if cardiac problems will appear over time. This is important for two reasons. First, the constant anxiety of anticipating a further PA, and the enduring fear and doubt about the possibility of having a cardiac problem considerably affects patients' quality of life and daily functioning, leading to a high rate of health care consumption (Batelaan et al., 2007). Second, a central position of cognitive therapy, one of the main forms of psychological treatment for PD, is that patients with PD tend to misinterpret benign bodily symptoms as potentially fatal or dangerous events. Thus, cognitive therapy aims to help patients overcome such “misguided”, fearful beliefs, including those related to cardiac symptoms (Austin and Richards, 2001; Clark et al., 1999). However, if PD is a risk factor for subsequent cardiac events, such cognitive interventions may be excessively reassuring.

Some historical studies have suggested an association between PD, arrhythmias, idiopathic cardiomyopathy, sudden cardiac death (Chignon et al., 1993; Coryell et al., 1986; Kahn et al., 1987; Katon, 1986). Several have also found a relationship between PD and coronary artery disease (CAD). PD prevalence ranged from 11% to 53% in patients with documented CAD (emergency rooms (ERs)/outpatient cardiology clinic) (Fleet et al., 2000; Huffman and Pollack, 2003; Jeejeebhoy et al., 2000), and prevalence was higher in patients presenting with atypical chest pain (Fleet et al., 2000). Among patients with PD who referred to ERs for chest pain, the chance of having CAD was 26% (Lynch and Galbraith, 2003). Conversely, other studies failed to find an association between PD and CAD in patients presenting with chest pain to ERs or cardiology settings (Katerndahl, 2004, 2008a,c). This discrepancy may be explained by the methodological limitations of several of the studies, including low sample sizes; failure to use sensitive, standardized tests for cardiac diagnoses; the use of self-report measures to evaluate PD; and a lack of examination or adjustment for other comorbid psychiatric disorders that could have been associated with cardiac risk. A recent meta-analysis investigating the relationship between different anxiety disorders and CAD showed an association between PD and CAD but underscored the high levels of heterogeneity relating to methodological differences among studies (Tully et al., 2014).

Overall, there is support for a connection between PD and cardiac disorders (CDs), but this is not unequivocal.

Given the importance of this issue for both patients with PD and clinicians, we performed an updated systematic review that considered the association between PD and CDs. To avoid the previously mentioned limitations and provide novel information, we used very selective criteria, regarding the methodology of psychiatric and cardiac diagnoses, to determine which studies should be included in the review, we considered arrhythmias, cardiomyopathies, and sudden cardiac death, in addition to CAD, and we employed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

2. Methods

This systematic review was performed according to the PRISMA guidelines (Liberati et al., 2009). The protocol for this review was not previously registered. A PubMed database search of scientific literature, written in the English language, dating from January 1, 2000, to December 31, 2014, was performed using the following search terms: ((panic or anxiety disorder) AND (cardiac disease OR cardiovascular disease OR coronary artery disease OR coronary heart disease OR heart disease OR acute coronary syndrome OR myocardial infarction OR myocardial ischemia OR heart failure OR heart attack OR sudden cardiac death OR arrhythmia OR cardiac dysrhythmia OR atrial fibrillation OR supra ventricular tachycardia OR hypertensive heart disease OR cardiomyopath* OR valvular heart disease OR tako* OR broken heart syndrome)). We also used the reference lists of relevant studies and pertinent review articles to gain access to additional literature. Of 3044 records identified in the search, 14 studies on CAD, 2 on cardiomyopathies, and 1 on arrhythmias were included in the review (Fig. 1, PRISMA flow diagram).

Studies were admitted to the review if they had included participants with principal diagnosis of PD that had been a result of a structured, clinician-administered interview conducted according to DSM-III/DSM-III-R criteria [Association, 1980 #124; Association, 1987 #125], DSM-IV/DSM-IV-TR [Association, 1994 #126; Association, 2000 #127] or ICD-9/ICD-9-CM [Centers for Disease Control and Prevention, #209; Centers for Disease Control and Prevention, #210] and 10 [Centers for Disease Control and Prevention, #211] criteria (for population-based studies, diagnosis of PD that was a result of clinical unstructured interviews was accepted, but only if the diagnosis was in accordance to the diagnostic criteria listed above); participants > 18 years of age; a control group of participants with no mental illness (where applicable); and if an explicit statement had been made that the diagnosis of CDs had been obtained using medical examination with sensitive, standardized tests and/or standardized criteria; if they had been peer-reviewed.

The PRISMA flow diagram (Fig. 1) provides detailed information regarding the selection process of the studies. Each step of the