Comorbid Effects of Anxiety and Panic Disorder on Cardiovascular Diseases and Its Management Approach: A Review

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Abstract: Recent data indicate that psychological and emotional disorders may play an important role in the natural history of cardiovascular diseases. Studies indicate that anxiety and panic disorders in cardiac patient influence mortality and morbidity. Panic disorder, a subtype of anxiety disorder, has been associated with increased risk of fatal myocardial infarction and sudden cardiac death in epidemiological studies. Anxiety and panic attacks may accelerate different direct and indirect pathways involved in the pathogenesis of cardiovascular disorders such as lifestyle risk factors, hypertension, myocardial perfusion, autonomic nervous system or hypothalamus-pituitary-adrenal axis, and other inflammatory processes. Panic disorder seems to correlate particularly with sudden death: which suggests that it may be considered one of the main inducers of life-threatening arrhythmias, rather than to be linked to the development and progression of ischemic heart diseases.

Keywords: Panic disorder, anxiety, cardiovascular diseases, epidemiology, pathophysiology, treatment.

I. Introduction

Anxiety: Anxiety disorders are classified under Neurotic, stress-related and somatoform disorders, divided under many subcategories like generalized anxiety disorders, panic disorders and attacks, phobic anxiety disorders. Anxiety disorders include disorders that share features of excessive fear and anxiety and related behavioral disturbances. Fear is the emotional response to real or perceived imminent threat, whereas anxiety is anticipation of future threat. 1 Such situations create a confusing situation as symptomatology correlates cardiovascular disorders, generally of sudden onset. Sometimes the level of fear or anxiety is reduced by pervasive avoidance behaviors. 2

Panic Disorder: Panic attacks feature prominently within the anxiety disorders as a particular type of fear response. Panic attacks are not limited to anxiety disorders but rather can be seen in other mental disorders as well. Thus, while the anxiety disorders tend to be highly comorbid with each other, they can be differentiated by close examination of the types of situations that are feared or avoided and the content of the associated thoughts or beliefs. 3

Anxiety in general, and specific disorders, such as generalized anxiety disorder or panic disorder, have been independently associated with increased risk of fatal myocardial infarction and sudden cardiac death in epidemiological retrospective population studies and prospective trials, both in healthy subjects. 3

Co morbidity Effects of Anxiety & Panic Disorder on Cardiovascular Diseases

Recently, acute and chronic mental stress and many psychiatric disorders have been accepted as a cause of cardiovascular disease. 4, 5 In post-myocardial infarction patients a higher level of anxiety is found as an important predictor of cardiovascular outcome. 6 Panic disorder, a subtype of anxiety disorder, poses difficulty in diagnosis due to considerable overlap in symptoms between panic symptoms and cardiac symptoms. 7 Previous studies demonstrated an increased prevalence of panic disorder in patients with coronary artery disease 8. Epidemiological studies reveal patients with panic disorder possessed higher risk of fatal myocardial infarction and sudden cardiac death compared to normal population. In addition, increased risk of a fatal events were found in presence of higher levels of anxiety. 3, 9

Although panic disorder is usually more common in people without CAD than with CAD, it is still seen in a significant portion of those with CAD 10, 11, 12, 13, 14. In fact, studies suggest more panic disorder in patients with CAD than without it among cardiac patients referred for esophageal motility studies 15. 16

Panic disorder is associated with several cardiac abnormalities. 16 In addition to patients with panic disorder having elevated standing heart rates, 10% were found having arrhythmias. 17 Panic disorder is
associated with increased left ventricular mass and diameter, and patients with panic disorder have poorer cardiovascular fitness as demonstrated by lower maximum oxygen consumption and decreased exercise tolerance.

Patients presenting to the emergency department with panic attacks were found to have increased levels of B-type natriuretic peptide. Conflicting studies concerning an association with idiopathic cardiomyopathy have been reported. Case reports also have linked panic disorder to a descending aortic aneurysm and pulmonary hypertension secondary to an atrial septal defect with pulmonic valve disease. However, strong association is found between panic disorder and mitral valve prolapse (MVP). The panic-MVP relationship has been well documented, but MVP may not likely to be the source of chest pain. The presence of MVP doesn’t alter psychiatric comorbidity or treatment response, but the source of the linkage needs further research. There is no supporting evidence for a MVP-to-panic sequence as proposed. Indirect linkages via autonomic vulnerability or dysfunction have also been proposed. Likely explanation might be that the decreased left ventricular volume due to tachycardia seen in panic disorder produces the MVP. Studies suggesting that the MVP disappears with remission of the panic disorder supports this sequence. Thus, anxiety and panic disorders have been linked to several forms of cardiac disorders. In fact, this association is seen in studies from the United States and around the world. Although a relationship with MVP is relatively common, an association with CAD would be the most significant.

Another study found an association between panic attacks and both ischemic and non-ischemic chest pain among women undergoing holter monitoring. In fact, in a large managed care database, an association between diagnoses of panic disorder and coronary heart disease was found even after controlling for covariates. Similarly, women enrolled in a different study demonstrated an association between panic attacks and coronary heart disease. If this association is true, myocardial ischemia could cause panic attacks via increased catecholamines or cerebral carbon dioxide levels secondary to lactate.

Finally, a relationship between panic disorder and CAD could exist through a relationship between panic disorder and cardiac risk factors. While a separate study reported mild association with hypertension, diabetes, obesity, or hyperlipidemia, other studies reported no association with BMI and reported no association with hypercholesterolemia. People with panic disorder frequently have a family history of CAD and have a higher number of risk factors than controls.

First, panic disorder is linked to elevations in both systolic and diastolic blood pressures. Hypertension is found to be associated with both panic disorder and panic attacks, which was consistent across primary care and cardiology settings. This association may explain why 9% to 32% of patients with chest pain and normal results of coronary angiograms have hypertension.

Second, anxiety and panic disorders are associated with lipid abnormalities. Specifically, total cholesterol levels are increased in those with panic disorder. This is supported by studies documenting elevated cholesterol levels in 8% to 55% of patients with chest pain and normal coronary angiograms. In addition, the presence of panic attack in patients with chronic obsessive-compulsive disorder was associated with elevated triglyceride and decreased high-density lipoprotein (HDL) levels. Conflicting gender differences in lipid patterns have been found. In one study, women with panic disorder frequently have elevated low-density lipoprotein (LDL) levels with decreased HDL levels, while male patients frequently have elevated triglyceride levels. However, one study found elevated LDL levels in men in response to pentagastrin-induced panic attacks but not in women. But associations between panic disorder and lipid abnormalities are not always found and, if found, are primarily seen in psychiatric settings and in studies with small sample sizes.

**Management Approach To Anxiety Disorders And Cardiovascular Diseases**

Proper management of anxiety disorders and cardiovascular events is of utmost importance in clinical setting. Traditionally, anxiety and panic disorders are treated with either cognitive behavioral therapy (CBT), pharmacotherapy (antidepressants, high-potency benzodiazepines), or both. A recent survey of family physicians found that, of their patients with panic disorder who were not referred to mental health providers, 73% received selective serotonin reuptake inhibitors (SSRIs), 23% received high-potency benzodiazepines, and 18% received CBT. Comparison of CBT in primary versus secondary care settings found a more rapid response in primary care settings. In fact, previous studies have shown that, after 20 minutes of instruction in the emergency department, exposure therapy decreases depression, avoidance, panic attack frequency, and emergency department visits. Thus, CBT may be useful in the management of panic disorder in the presence of CAD.

Pharmacotherapy for panic disorder in CAD patients is more complicated. Although TCAs are effective in panic disorder, their cardio toxicity precludes them as first-line agents in the presence of CAD. In fact, tricyclics use has been linked to the development of MI. In addition, imipramine therapy for panic disorder increases cardiovascular mortality risk secondary to increased blood pressure and heart rate.
Benzodiazepines can also be considered. Alprazolam treatment of panic disorder actually decreases total cholesterol and catecholamine response to exercise. In addition, although alprazolam does not decrease the frequency or severity of angina attacks in CAD patients taking propranolol, it does decrease symptom severity and reduce nitroglycerin use. Other potential cardiovascular benefits of low-dose benzodiazepines include decreased myocardial contractility and increased blood flow. In fact, benzodiazepines were found to delay onset of exercise treadmill test-induced ischemia and to reduce MI rate in patients with CAD. However, benzodiazepines should generally not be used in elderly patients or those with a history of substance abuse or personality disorders.

II. Conclusion

Although both are independent etiology of chest pain, panic disorder and coronary artery disease may coexist, particularly in primary care settings. The panic attacks may cause the patient with coronary disease to seek care but could also provoke a cardiac event, if co-morbid. Distinguishing between the 2 disorders can be difficult when based on clinical criteria alone. If one condition is recognized, a search for the other is to be done in particular patient subgroups. All patients with co-morbid panic disorder and CAD should be treated with exercise and smoking cessation. Treatment with a “safe” antidepressant, high potency benzodiazepines, or CBT depends on the presence of co-morbid anxiety, panic disorder and cardiovascular risk factors.

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