Anxiety and coronary artery disease

Coronary artery disease is the leading cause of death and a major cause of disability in both men and women, globally. During recent years, the impact of psychosocial distress on coronary artery disease morbidity and mortality has received a great deal of attention. Specifically, increased prevalence of anxiety is documented in patients with coronary artery disease and anxiety exerts negative acute and long-term effects on the outcome of the disease. Health professionals tend to focus on the treatment of coronary artery disease, underestimating problems arising from the mental dimensions. This review explores the relationship between anxiety and coronary artery disease.

1. INTRODUCTION

Coronary artery disease is the leading cause of death and a major cause of disability in both men and women in the US and other developed countries. By 2025, coronary artery disease is expected to be the top cause of death throughout both the developed and developing countries. It is estimated that 80% of the global burden of cardiovascular disease is incurred in low- and middle-income countries and that 30% of deaths globally and 42% in the EU result from coronary artery disease.

Considerable advances during recent decades in the field of cardiovascular medicine, including progress in diagnostic tools and improvement in interventional treatment, have led to prolongation of the life expectancy of patients with coronary artery disease. In the past, the main concerns in everyday clinical practice were management of the acute disease and prevention of death. Now that the effects of demographic and clinical characteristics on the onset and outcome of coronary heart disease have been established, the evaluation of these factors is included in routine clinical practice and in primary and secondary prevention. Recent research has highlighted the impact of psychosocial distress on coronary artery disease morbidity and mortality, which is recognized as being almost equal to that of demographic factors and risk markers, although further studies are needed in this area.

Coronary artery disease, acute and chronic, triggers a variety of psychological responses that may affect the biological outcome of the disease. As a growing body of evidence documents a significant association between psychological stress and cardiac illness, the treatment of psychological distress has been brought to the forefront of clinical practice and care. There is, accordingly, growing interest in screening for psychological distress in order to identify patients who require psychological intervention to enable them take responsibility for their health management.

2. ANXIETY AND CORONARY ARTERY DISEASE

Anxiety is an unpleasant emotion that affects about 24.9% of the population at some time in their lives, with a reported worldwide prevalence of 16.6%. A high prevalence of anxiety is documented in patients with coronary artery disease. Specifically, 70–80% of individuals who have suffered an acute heart attack experience anxiety, which persists long-term in about 20–25% of cases. Anxiety presenting shortly after the acute coronary syndrome may persist up to 2 years later at clinically significant levels.

Prevalence rates of anxiety among patients with stable coronary heart disease range from 16% to 42%, while rates in patients shortly after acute myocardial infarction
range from 20% to 50%,\textsuperscript{11,12} with up to one quarter experiencing symptoms of anxiety at least as intense as those of the average inpatient on a psychiatric unit.\textsuperscript{13}

Anxiety exerts significant acute and long-term influence on outcomes following the acute coronary syndrome.\textsuperscript{2,13} It has been estimated that anxiety triples the risk for all-cause mortality following myocardial infarction and almost doubles the risk for reinfarction in the ensuing 5 years.\textsuperscript{11} In addition, anxiety is an independent predictor of adverse cardiovascular events and can impede recovery, while treatment of anxiety may improve cardiac symptoms.\textsuperscript{2}

Hospitalized patients who experience anxiety are more likely to develop new episodes of arrhythmia or ischemia during their hospitalization.\textsuperscript{14} Patients in hospital manifest anxiety immediately after the heart attack, which peaks on the second day and usually subsides after the first few days.\textsuperscript{2} The in-patient incidence of anxiety among patients with acute coronary syndrome approaches 50% in the coronary care unit.\textsuperscript{11} In a Greek population study, 25.5% of 702 patients hospitalized with coronary artery disease experienced moderate levels and 32.7% high levels of anxiety.\textsuperscript{15}

Similarly, anxiety is a common condition in the primary care setting, affecting at least 10% of primary care patients with coronary artery disease,\textsuperscript{16} while with regard to heart failure, anxiety ranges from 29% to 45% of patients.\textsuperscript{17}

Patients with coronary artery disease, particularly after myocardial infarction, are at risk of developing post-traumatic stress disorder (PTSD) with prevalence rates varying between 4% and 24% one month after the event. Patients with PTSD often show poor adherence to medical advice, possibly due to their underestimation of the risk of future myocardial infarction recurrence or to their development of denial behavior towards the trauma of hospitalization.\textsuperscript{18,19}

In addition to their recording elevated levels of overall anxiety as measured on anxiety scales, anxiety disorders are more common in cardiac patients than in the general population. Generalized anxiety disorder is present in up to 24% of patients with cardiac disease.\textsuperscript{13}

In addition, there is a high incidence of comorbidity between panic disorder, a psychiatric condition with recurrent panic attacks, and heart disease, which is associated with a higher overall morbidity, functional deficits, increased cardiovascular risk and poor adherence to cardiac rehabilitation or exercise programs. The panic attacks may cause the patient with coronary artery disease to seek care, but can also provoke a cardiac event, and panic disorder has been found to be an independent risk factor for subsequent coronary events.\textsuperscript{20–22}

The symptomatology of panic disorder may often mimic a non-existent cardiac disease or, alternatively, conceal an actual episode of heart disease, leading to diagnostic ambiguities. Panic disorder, however, cannot account for abnormal findings on the electrocardiogram (ECG) and or changes in enzyme biomarkers, although it may mimic the clinical presentation of an acute coronary syndrome, to such an extent that it is clinically indistinguishable, necessitating further exploration. This frequently leads to costly and unnecessary medical examinations and prolonged mismanagement of the underlying panic. Chest pain, which characterizes both coronary artery disease and panic disorder, is a common symptom that leads patients to substantial use of health resources in both the community medical setting and the emergency department.\textsuperscript{20–22}

Given that acute coronary syndrome is a life-threatening disease that demands prompt treatment, it is understandable that most physicians consider it as a possible diagnosis in any patient presenting with acute symptoms of chest pain or discomfort, palpitations, nausea or abdominal distress.\textsuperscript{20–22}

Anxiety is also prevalent in chronic coronary disease, at rates ranging from 28% to 56% in patients with heart failure, and it is associated with adverse outcomes, such as cardiac re-admission.\textsuperscript{23–25} Heart failure is a complex disease affecting several dimensions of daily life and often demanding high consultation frequency in general practice.\textsuperscript{26} It is associated with significant physical, psychological and lifestyle changes that often lead to increased mental health difficulties. The impact of anxiety can reduce the ability of patients to cope with their physical symptoms and adhere to medical treatment.\textsuperscript{26} One potential contributor to anxiety in the chronically ill such as those with heart failure is anxiety sensitivity. Higher sensitivity is associated with poorer energy, mental capacity and social functioning and may be a correlate of poorer adjustment to chronic illness.\textsuperscript{27} It is of note that the number of studies exploring the association between anxiety and heart failure is limited while greater emphasis has been placed on the role of depression.

The co-occurrence of anxiety and depression is important, with 57.5% of individuals who present with major depression also meeting the 12-month criteria for an anxiety disorder.\textsuperscript{26,29} Anxiety and depression frequently go together in patients suffering acute coronary syndrome, comprising a common psychological factor that influences heart disease.\textsuperscript{20–22} Anxiety tends to follow threats or traumatic events, whereas depression follows loss.\textsuperscript{22}

In initially healthy individuals, anxiety contributes to the development of cardiovascular disease.\textsuperscript{2,13} Specifically,
anxious persons are at higher risk of cardiac episodes and cardiac death, independently of demographic variables, biological risk factors and health behaviors.\textsuperscript{2,3} Anxiety may be more strongly associated with the onset of cardiac disease than depression. In particular, worry, which is a component of anxiety, appears to be especially associated with cardiac disease.\textsuperscript{13} Chronic worrying about social, financial, and health problems is associated with various features of coronary heart disease including angina and non-fatal and fatal myocardial infarction. Situations leading to intense anger are also potent triggers of myocardial ischemia.\textsuperscript{24} The ways in which negative emotions may exacerbate symptoms of disease are either by direct physiological effects or through poor compliance with recommended medical treatment.\textsuperscript{2}

Specifically, anxiety impairs energy and cognition, is related with poor uptake of self-care behavior, and is considered to be a predictor of poor adherence to lifestyle change recommendations and compliance with medical treatment. Patients with high levels of anxiety have been reported to have difficulty in making lifestyle changes and coping with challenges, and encounter more problems during cardiac rehabilitation.\textsuperscript{2,5,12,35,36}

Finally, anxiety is associated with recurrent adverse cardiac events, impaired psychosocial functioning and poor quality of life.\textsuperscript{2,3} It is of note that that anxiety may hinder psychosocial adjustment to the chronicity of cardiovascular disease or delay physical recovery after an acute event.\textsuperscript{2}

The most important benefit to health care professionals is not simply the knowledge about anxiety prevalence, but rather a deeper understanding of the causes of anxiety in this vulnerable population, leading to early detection and effective treatment.\textsuperscript{2,6,12,13}

2.1. The phenomenon of anxiety

Anxiety is a basic human experience that occurs in all pathological and non-pathological situations. Anxiety may follow any human activity and presents at all phases of the development of the personality. Specifically, anxiety is attributed to the perceived inability to predict, control or achieve the desired results when confronted with distant or potential threats that depend on the type of stimulus and the interpretation given by each individual. Anxiety constitutes a form of social adjustment, since individuals under the impact of anxiety try to harmonize their needs with the demands of society.\textsuperscript{2,6,37−39}

Anxiety occurs as a response to perceived risk, real or imagined, arising from internal or external sources. This warning signal prepares the individual to defend from a threat or to flee (“fight” or “flight”); an adaptive psychological and physical response to prepare the individual for better performance. At this stage, anxiety has a protective role that enhances normal functioning and triggers responses that provide protection from threats. Conversely, anxiety becomes maladaptive, with negative consequences for the individual, when it is of a high level or persists to such a degree that it limits the effective functioning of the individual in everyday life.\textsuperscript{2}

Anxiety is seen as a negative emotion, accompanied by distinct psychological and somatic attributes. The manifestation of anxiety involves psychophysiological reactions that are sometimes obvious, such as pain, sweating, tachycardia, and sometimes non-obvious, such as raised blood pressure, changes in blood levels of cortisol and adrenaline and lipids, etc. The individual who perceives these changes may seek solutions, such as taking medication or applying other control methods. Otherwise, the psychophysiological arousal persists, leading to the development of symptoms, arising mainly from the cardiovascular, gastrointestinal, urogenital and immune systems. The individual subsequently becomes dominated by negative thoughts and an inability to maintain everyday activities, and presents increased tone of the autonomic nervous system, resulting in impaired functionality. The whole situation becomes “a vicious circle” since the physical symptoms are perceived as a threat to health that provokes anxiety, which in turn triggers more physical symptoms.\textsuperscript{37−39}

Anxiety should be distinguished from fear. The central features of both fear and anxiety are anticipation of and preparation for future threats that endanger the integrity of the organism. Although these two defensive responses serve as warning signals and prepare the individual for either flight or fight, they are distinct phenomena; fear is related to an impending identifiable danger whereas anxiety is related to a potential unseen, or symbolic threat. Other differences are related to the duration; anxiety is characterized by longer duration because the threat is unknown and therefore the individual cannot avoid it, while fear lasts as long as the risk is present.\textsuperscript{37−39}

Anxiety encompasses a number of disorders, including panic disorder, phobic anxiety, generalized anxiety, anxiety reactions and chronic anxiety with a variety of manifestations. All anxiety reactions have similar cognitive, neurobiological and behavioral components.\textsuperscript{2,3}

A wealth of literature confirms the relationship between anxiety and cardiovascular diseases. Anxiety is to some extent considered to be a normal response, with a beneficial effect on coronary heart disease, mainly at the onset because it prompts the individual to seek medical help quickly or to alter risk factors and actively participate in the therapeutic regime. Conversely, persistent and severe anxiety is associated with an adverse outcome of coronary disease.\textsuperscript{37−39}
Over the past decades various theories have been put forward to explain the association between anxiety and coronary artery disease. Such mechanisms can be categorized into two sequences, explained respectively by neurohormonal and behavioral pathways. With regard to the neurohormonal pathway, the most widely accepted link between anxiety and coronary disease is activation of the sympathetic nervous system giving rise to impaired vagal control, reduction in the heart rate variability, elevated levels of proinflammatory cytokines and hypercortisolemia from activation of the hypothalamic-pituitary axis. In addition, atherogenesis is promoted by recurrent activation of the neurohormonal system, with subsequent endothelial injury and atherosclerosis.  

Concerning the behavioral pathway, individuals with anxiety disorders are prone to unhealthy types of lifestyle behavior, such as physical inactivity, smoking and inappropriate diet, which promote the development of coronary artery disease. With respect to unhealthy diet, the response to acute stress includes changes in dietary habits, loss of appetite and reduction in food intake, whereas chronic stress is associated with increase in food intake involving changes in the amount and quality of food and frequency of meals. A possible explanation for this is that stressed individuals resort to food as a surrogate solution to their problems.

3. ASSESSMENT OF ANXIETY

Underestimation of the role played by anxiety in the development and outcome of cardiac diseases may be one reason why they continue to be the leading cause of death in most developed countries. In everyday clinical practice involving non psychiatric patients are treated the exploration of anxiety is not emphasized, thus placing patients at risk for the consequences of untreated anxiety. Health professionals may fail to manage anxiety effectively since they rarely incorporate it in their routine assessments, for various reasons. Firstly, they consider it to be a natural response to the disease, secondly, they pay more attention to the treatment of coronary disease and thirdly, under the pressure of work they do not devote sufficient time to assessing anxiety symptoms. Last but not least, health professionals are not adequately educated to recognize anxiety symptoms. From the nursing viewpoint the most important indicators for the assessment of anxiety are restlessness, increased heart rate and blood pressure, agitation, increased respiratory rate, and increased diaphoresis, although in acutely ill patients increased heart rate and blood pressure may not reflect level of anxiety accurately. Not surprisingly, the distinction between “normal” and pathological anxiety is difficult as anxiety is in various ways. For instance, it is frequently described as “feeling uncomfortable” or as a “physical discomfort” due to overactivity of the autonomic nervous system. Additionally, anxious thoughts or behavior may reflect the presence of anxiety.

The period during hospitalization is the best for anxiety diagnosis because all patients have the same probability of early diagnosis, treatment and effective management. As the average length of stay of patients with acute coronary disease is decreasing, screening opportunities for identifying symptoms of anxiety are becoming less. Psychological distress should be re-evaluated at the discharge of the patients from hospital. Patients identified as anxious and depressed and those with history of depression should receive appropriate psychological intervention. Before discharge it is difficult to predict which patients will to adjust to the disease over the following months. Quite often, patients do not experience symptoms of anxiety until several weeks after their discharge, when the impact of coronary disease on their life becomes apparent.

More significantly, follow-up of patients with anxiety symptoms is equally limited. Unfortunately, one study showed that almost two thirds (65.2%) of all hospital inpatients with abnormal scores on the hospital anxiety and depression scale (HADS) are not identified by their attending physicians as suffering from psychological problems. Similarly, in primary care, the recognition of anxiety disorders remains poor with only one third of cases labeled as such by their general practitioners. In medical care settings there are many barriers to recognition and treatment of anxiety, caused by factors related to the patient (e.g., negative patient expectations about treatment), the care provider (e.g., limited mental health knowledge, lack of curiosity about the role of psychosocial factors in their patients’ illness) and the system (e.g., restricted availability of mental health resources). Although in the primary care setting, family physicians usually develop long-lasting relationships and mutual trust with their patients, due to sustained close contact, comorbidity in patients with heart failure is often neglected. The integration of psychiatric services into primary care settings can improve recognition and treatment of psychiatric disorders for large populations of patients. The absence, however, of academic centers where evidence-based forms of anxiety treatment are provided illustrates the difficulty in effective screening and diagnosis and intervention.

Finally, striking differences are recorded in the prevalence of anxiety in patients with coronary artery disease.
that can probably be attributed to the use of different diagnostic tools, or to methodological inadequacies or to various aspects of the measurement of psychosocial factors in clinical practice. The growing understanding of the importance of anxiety in coronary artery disease creates a demand for a globally accepted instrument which will permit comparisons between populations and nations and adequate dissemination of the findings of research on the link between psychosocial factors and outcomes.

Assessment of anxiety involves exploration of the following: (a) Biological causes, (b) psychiatric causes, and (c) psycho-social mechanisms.

Firstly, it is necessary to address the biological causes that trigger anxiety through neurophysiological mechanisms. Secondly, the possibility that the anxiety is a symptom of a psychiatric disorder needs to be explored. For example, in patients with established psychiatric disorder, anxiety may be the manifestation of disorganization because of hospitalization or a symptom of depression, as in more than 50% of patients with depression there is coexistent anxiety disorder. In addition, phobias are frequent in hospital because of either the environment (simple phobia), or the presence of strangers (social phobia). Recording of the family and personal history provides valuable relevant information. Documentation of any existing psychiatric history is not enough as psychiatric evaluation, but psychiatric consultation should be requested to explore anxiety disorders. One concern of the psychiatrist examining the patient with cardiovascular disease is careful diagnostic evaluation to exclude the possibility that the anxiety is caused by physiological problem, cardiovascular drugs, substance toxicity or alcohol or drug withdrawal.11,13

The possibility of excessive alcohol consumption requires medical attention, because this is frequent in individuals experiencing anxiety and also has detrimental effects on the outcome of coronary artery disease.51,52

It is not rare that anxiety and cardiac symptoms coexist, suggesting the possibility of substantial overlap which may create diagnostic problems. Patients with psychiatric disorders may experience symptoms from the cardiovascular system and heart disease may present in patients with psychiatric symptoms. Recognition of the one disease entity, however, should not discourage evaluation of other because of the potential consequences if it is left undetected. In addition, diagnostic uncertainty is often associated with medication, such as in the case of psychotrophic drugs that cause ECG abnormalities and symptoms from the cardiovascular system, while certain cardiovascular drugs can cause psychiatric symptoms.20–22

Taking into account all of the above, it is understandable why the evaluation of anxiety in cardiac patients is difficult.

Diagnostic ambiguities are common concerns for physicians in the primary care setting, the emergency department and the cardiology clinic and intensive care unit. Collaboration between the cardiologist and the psychiatrist is essential for provision of effective comprehensive treatment to patient with cardiovascular disease and anxiety.

Given that anxiety is a complex dynamic expression of biological, psycho-social and psychiatric factors, health care professionals should not underestimate the importance of anxiety but rather identify individuals for whom early and accurate assessment of anxiety is particularly critical. The use of protocols in daily clinical practice that allow for efficient and systematic screening and evaluation of anxiety in cardiac patients helps patients to avoid the devastating effects of anxiety on cardiac health. It is of fundamental importance to develop forms of intervention to ensure that the patients identified receive basic, but critical treatment for their anxiety, and most significantly, it is important to take all clinical steps to bridge the gap between knowledge about the effects of anxiety and provision to patients of optimal care.13

Enhancing the awareness about anxiety among health professionals working with non-psychiatric patients would benefit thousands of patients around the world and drastically minimize the economic, medical, individual and social burden of coronary artery disease. Following this line of thought it is certain that the mental health training of frontline practitioners to improve their skills in differential diagnosis, identification of overlap of anxiety symptoms with physical symptoms and mental health issues, such as the ability to address patient concerns and provide comfort in openly discussing anxiety, will significantly improve the outcome of the disease.13

4. TREATMENT OF ANXIETY

In general, treatment of anxiety disorders typically involves a combination of medication and psychotherapy.

Regarding the pharmacological treatment of anxiety, the main categories of drugs used are benzodiazepines, antidepressants and beta-blockers.11,13

Benzodiazepines are a safe and effective treatment for the reduction of acute anxiety and for some anxiety disorders (e.g., panic disorder) with or without depression. These agents have several beneficial physiological effects, including immediate lowering of the catecholamine level and decreasing coronary vascular resistance.

They can be administered to patients with ongoing or
recent myocardial ischemia for whom anxiety is contributing to elevation of the heart rate and blood pressure, or other physiological disturbances. Benzodiazepines may be administered either in a single dose or as systematic treatment. Their administration (dose and frequency) is determined by the type of drug and the patient’s clinical response. They are well tolerated in small doses and have rapid onset of action. Caution is required when they are administered with other drugs and particularly substances that have sedative properties (e.g., alcohol, sedatives, antipsychotics), or when administered to elderly persons with renal insufficiency. The benzodiazepines that are most commonly used in clinical practice are lorazepam (Tavor), diazepam (Stedon), alprazolam (Xanax), bromazepam (L Roxotanil) and chlorazepam (Tranxene).

Antidepressants constitute another medication category that was developed to treat depression but may be effective for anxiety disorders. These include certain selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants (TCAs), monoamine oxidase inhibitors (MAOIs), and the newer atypical antidepressants. Antidepressants achieve their full effect in relieving anxiety symptoms usually after weeks; it usually takes about 4 to 6 weeks before symptoms start to fade, and for this reason they are co-administered with benzodiazepines.11,13 The safety of antidepressants is also a factor that should be considered before prescribing these medications to vulnerable patients (i.e., those with unstable symptoms or with recent myocardial infarction).13

Beta blockers are mainly used in treatment of high blood pressure and certain heart problems. Although drugs in this category do not affect the emotional symptoms of anxiety, they relieve the physical symptoms of anxiety such as rapid heart rate, trembling voice, etc., by controlling the effects of the stress hormone norepinephrine. Buspirone is a newer anti-anxiety drug that relieves anxiety by increasing serotonin and decreasing dopamine in the brain. Buspirone is an effective treatment of anxiety and is not addictive, not sedative, has minimal withdrawal effects and causes no impairment of memory or coordination impairment, but its action takes two weeks to be effected.11,13

Insomnia, which often accompanies anxiety, should be treated, because poor quality of sleep exacerbates the patient’s psychopathology. Specifically, older patients often deny feeling anxious or depressed and are more likely to present with insomnia, irritability, agitation and multiple somatic complaints.22

Psychotherapy involves sessions with a trained mental health professional, such as a psychiatrist or psychologist, designed to elucidate the etiology of the anxiety disorder and provide help in dealing with its symptoms. Psychotherapy is individualized, short-term (not exceeding six months) and focuses on the modification of dysfunctional emotions and behavior. Mild anxiety in particular may be treated with psychotherapy. The ultimate goal of psychotherapeutic intervention is to deal with chronic or life-threatening disease that may impair even the most resilient coping strategies and overwhelm the most abundant interpersonal resources.5,11,13 A prerequisite for effective management is a positive therapeutic relationship with the health professionals.17

Specific forms of interventions, such as cognitive-behavioral stress management, can have a positive effect on the quality of life of patients with chronic disease, resulting in decrease of perceived stress, improvement in perceived social support, facilitation of problem-focused coping and positive change in cognitive appraisal. The cognitive part of this approach helps people to change the thinking patterns that have been supporting their fears, and the behavioral part helps people to change the way they react to anxiety-provoking situations. Psychosocial interventions can also decrease the patients’ overuse of medications and utilization of the health care system.5,13

It is recognized that transition to life after hospitalization is not easy as patients often feel unprepared, lack the requisite knowledge and may be confused about what to expect during recovery at home after a cardiac event.20 Rehabilitation programs that involve psychological intervention to alleviate distress, in conjunction with coronary risk behavior intervention exert a positive influence on both the physical and psychological outcome, while lack of psychosocial intervention is associated with higher rates of mortality and recurrent myocardial infarction.5,17 Anxiety appears to reduce participation in rehabilitation programs, and therefore intervention to improving the anxiety level before participation in exercise or cardiac rehabilitation is of fundamental importance.13

Recognition that anxiety is a response to disease, provision of information to primary care patients about the symptoms of anxiety and hospital counseling, including encouraging patients to express their emotional state or adopt a more positive attitude to the disease, all contribute significantly to the effective management of the disease and improvement in the quality of life of cardiac patients. When anxiety is attributed to normal adaptation to the disease, informing and reassuring the patient is a matter of high priority.

5. CONCLUSIONS

Understanding the significant relationship between anxiety and coronary artery disease should prompt health
professionals to systematic efforts to identify anxiety among their patients with cardiovascular disease.

Effective management of anxiety should be a goal in the management of all critical care patients, since it positively influences disease outcome and contributes significantly to the improvement of the quality of life of the patients.

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