Psychological Interventions and Health Outcomes in Heart Disease

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Key points:

- Introduction
- Psychological Factors and Cardiovascular Risk
- Mechanisms Linking Stress to Cardiac Dysfunction
- Acute and Chronic Stress in Cardiovascular Events
- Atrial Fibrillation and Emotional Health
- Therapeutic and Preventative Strategies

Introduction

Heart disease is a major cause of death and a significant cause of rising health care expenditures in developed countries. Of the most common types of heart disease, forecasts indicate that heart failure (HF) will grow 48% by 2030 [27,28,29] totaling more than 8 million adults with this illness.[1]

Depression's Impact on Heart Failure and Coronary Artery Disease

Numerous studies have shown that depression is prevalent in patients with HF and contributes importantly to morbidity and mortality. Likewise, depression has a large effect on outcome in Coronary Artery Disease (CAD) patients.[1,11,6,7,8]

Anxiety and Its Effect on CAD and HF

Studies of the association between anxiety, CAD, and HF are not as voluminous as studies of depression, although one of the first described phobic anxiety as a risk factor. An additional study revealed that anxiety was linked with a 41% elevated risk of incidence and mortality in CAD and a 35% elevated risk for HF.[1,11,6,7,8]

Chronic Stress and Cardiovascular Disease (CVD)

Chronic psychological stressors have a strong association with ischemic or coronary heart disease. Prefrontal and limbic areas of the brain analyze events and create emotional reactions, dictating behavioral and physiological responses.[1,6,11,7,8]

Autonomic Dysfunction and Heart Rate Variability (HRV)

Carney et al. discovered that chronic stress compromises HRV and autonomic control. Zafeiropoulos et al. showed that chronic stress enhances sympathetic tone, heart rate, and cardiovascular reactivity, which causes an increased susceptibility to arrhythmias and cardiac injury [1,9,10]

Sympathetic Nervous System (SNS) and Vagal Dysfunction:

Enhanced SNS activity due to depression results in vagal dysfunction. The vagus nerve has an important protective function in vascular health by releasing acetylcholine, which suppresses pro-inflammatory cytokines released by splenic macrophages.[30,31,32,33] The CARDIA study identified an inverse correlation between vagal nerve function and inflammatory markers of atherosclerosis. Vagal dysfunction decreases myocardial ischemic tolerance and

decreases the efficacy of ischemic preconditioning interventions.[1,13]

Hypertension and Atherosclerosis

Hypertension is the most potent risk factor for CVD. Atherosclerosis is most commonly seen in high-pressure sites of the vascular tree. Increased blood pressure causes vascular remodeling, enhanced arterial wall thickening, and circumferential elongation, contributing to:

- Endothelial dysfunction through reduced nitric oxide synthase expression.
- Oxidative injury of the arterial walls. [1,14]

Mechanisms of Myocardial Protection:

Acetylcholine and muscarinic receptor agonists prevent the myocardium from ischemic damage[34,35,36,37] by:

- Regulating the activity of reactive oxygen species (ROS).
- Modulating the activity of ATP-gated K+ channels.
- Increasing nitric oxide production, which enhances myocardial vasodilation and perfusion.

Chronic Stress and Hypertension – Jackson Heart Study (2019)

Seventy-seven African Americans participated in a 7-year study that revealed those with high stress levels had a 37% higher risk of hypertension than those with low stress levels. Levine's study proved that catecholamine release due to stress results in renal, splanchnic, and cutaneous vasodilation, which reduces organ perfusion and activation of the renin-angiotensin-aldosterone system (RAAS).[38,39]

RAAS activation increases secretion of aldosterone, which causes water retention and elevated blood pressure.[2,15,16,17,18,19,20]

Stress-induced Takotsubo Cardiomyopathy

Takotsubo cardiomyopathy, first described by Ramaraj in 2007, is a heart condition directly linked to intense emotional or physical stress. It occurs due to high levels of catecholamines**,** which trigger inflammatory cytokines and cause endothelial injury.[2,21,22,23,24]

- Impact of Stress & COVID-19:

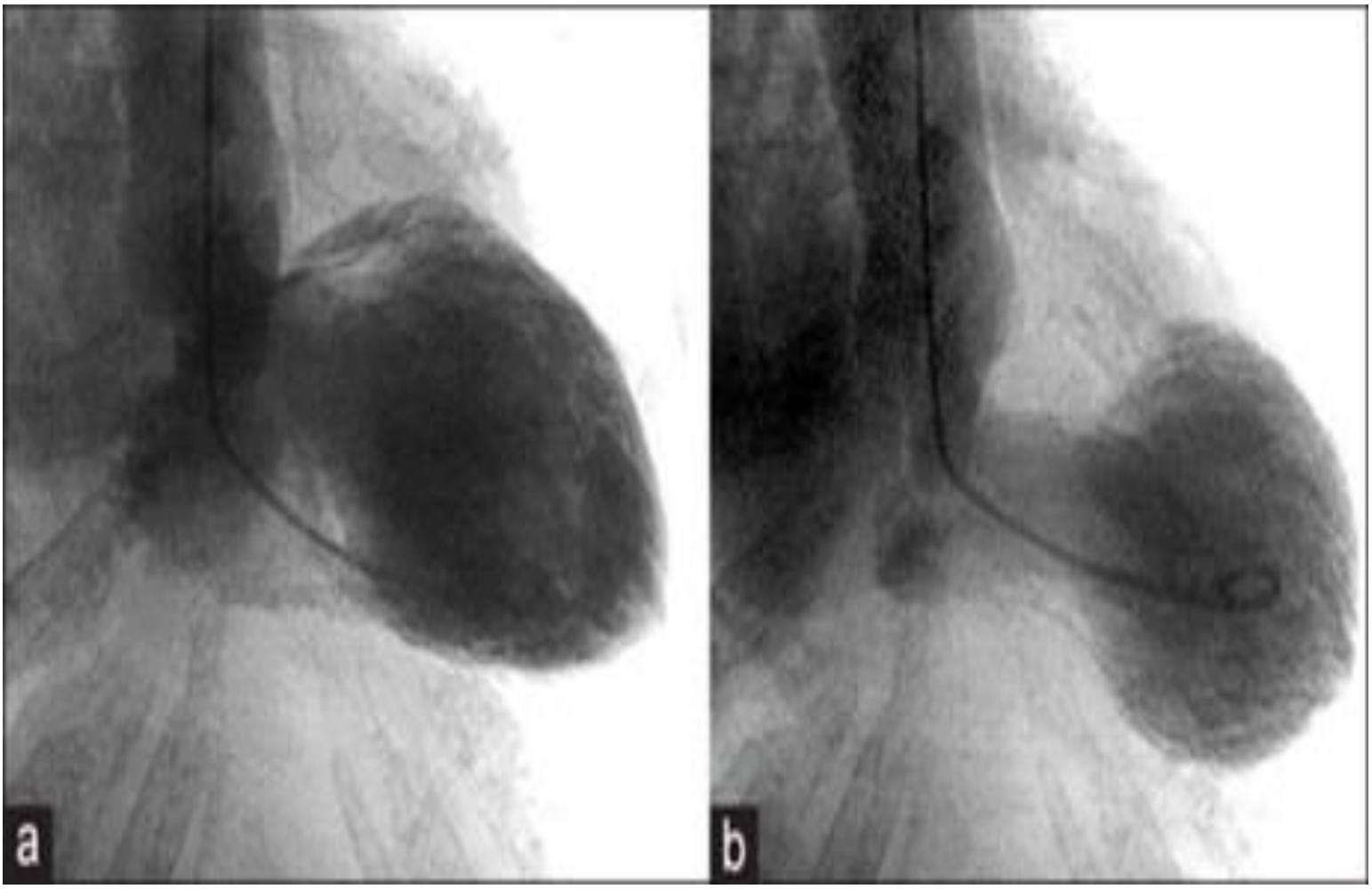
  The condition became more prevalent during the COVID-19 pandemic, as Al Houri et al. suggested that psychological stress, fear, and anxiety contributed to its development.

- Clinical Features:
  A hallmark of the condition is "transient left ventricular apical ballooning"[43,44], visible on ventriculography. This leads to left ventricular dysfunction, outflow obstruction, and mitral regurgitation, which can cause heart failure symptoms like hypotension, syncope, and cardiogenic shock**.**
- Gender Differences & Research Needs:

  Studies by Natale et al. Indicate that postmenopausal women are most affected, suggesting a possible hormonal influence.

- Treatment & Future Directions:

  Takotsubo cardiomyopathy is treated similarly to myocardial infarction (MI), but its exact cause and best treatment strategies remain unclear, highlighting the need for further investigation.
  [2,40,41,42]



(Common presentation of takotsubo cardiomyopathy observed with ventricular apical ballooning in end-diastolic (a) and end-systolic (b) frames of left ventriculography. Figure taken from Impact of Chronic Psychological Stress on Cardiovascular Disease Risk: A Narrative Review)

Atrial fibrillation:

Recent studies have identified the important role played by psychosocial parameters in atrial fibrillation (AF) such as depression, anxiety, anger, stress, PTSD, Type D personality, and socioeconomic status. A meta-analysis ratified that anxiety, depression, anger, and job stress enhance AF risk, whereas psychological trauma and postoperative anxiety are also associated with AF development.[45,46]

AF patients have greater emotional distress compared to the general population, resulting in poor quality of life, higher symptom burden, and greater risk of complications such as stroke and significant bleeding.[25,26]

The 2020 ESC guideline recognized that Type D personality is related to higher anxiety, depression in AF patients.[3]

Autonomic nervous system dysfunction

Depression is also one of the main risk factors for Coronary Heart Disease (CHD) because it has effects on the Autonomic Nervous System (ANS).[52] Depression results in overactivation of the sympathetic branch and parasympathetic dysfunction, causing elevated heart rate, elevated blood pressure, oxygen demand of the myocardium, and increased likelihood

of arrhythmias, ventricular fibrillation, and sudden cardiac death. Furthermore, increased levels of catecholamines in depression worsen progression of CHD by inducing vasoconstriction,[47,48,49] coronary spasms, and myocardial stress. Studies indicate that autonomic dysfunction due to depression reduces

myocardial tolerance to stress and impaired recovery after MI, which is evidence of the synergistic influence of HPA axis dysregulation.[4]

Dysfunction of the Hypothalamic-pituitary-adrenal axis (HPA)

Depression stimulates the HPA axis, leading to increased cortisol, elevating heart rate, blood pressure, inflammation, and metabolic risks such as insulin resistance and hypercholesterolemia that all contribute to CHD.[52]

Cortisol also inhibits growth and gonadal hormones that further impair cardiovascular well-being. Furthermore, depression also activates the sympathetic nervous system, which raises angiotensin-II and glucocorticoids, thereby further augmenting blood pressure and oxygen demand. Research verifies that glucocorticoids impair heart cells and deteriorate CHD prognosis.[50,51]

The combined action of HPA axis and sympathetic overactivity greatly enhances CHD risk in depressed individuals.[4]

Acute Stress And Cardiac Event

Acute stress, including natural disasters, and terrorist attacks, is closely associated with heightened cardiac events.[53,54,55] In a population of 95,647, mortality risk was 2-3 times greater in the immediate period following bereavement, which normalized after a month. Severe stressors such as the 1994 Los Angeles earthquake witnessed sudden cardiac deaths increase more than fivefold, and missile attacks in Israel during the 1991 Gulf War also resulted in an increase in fatalities. Moreover, anger attacks (≥5 on a 7-point scale) over doubled the risk of myocardial infarction, drawing attention to acute emotional distress as a major cardiac trigger.[5,53,54,55]

Pathophysiological Mechanisms

Acute stress, in contrast to chronic stress, is simpler to model and can be investigated under controlled laboratory conditions in both animals and humans. Advanced methods such as radionuclide imaging and measurement of coronary endothelial function have advanced the knowledge of how acute stress exacerbates CAD.[64]

These studies improve our understanding of the mechanisms through which acute stress evokes deleterious cardiovascular consequences among CAD patients.[5]

Chronic and Subacute Life Stress

Occupational stress is widely researched in the context of CAD, with emphasis on job strain (high demand, low control). A 6-year follow-up study of 1,928 men reported that job strain raised cardiovascular mortality risk fourfold.[62,63]

More recent models associate high work demand & low reward with cardiac events and progression of carotid atherosclerosis. Low job control in itself also foretells subsequent cardiac events. Subacute life stress (aggregate of stressful events during months) has been associated with acute MI. The Recent Life Change Questionnaire revealed that high levels of stress in the recent 6 months were prevalent in MI and sudden cardiac death.[60,61]

It indicates a potential, strong correlation of chronic work stress, life stress, and development of atherosclerosis.

Pathophysiological Mechanisms

Chronic stress directly affects physiology through the elevation of arterial blood pressure and neurochemical arousal. Comparable neurochemical activation has also been detected in subacute stress conditions, further establishing the connection between stress and cardiovascular dysfunction.[60,61,62,63]

Promotion of Arrhythmogenesis

Research has repeatedly demonstrated that there is a strong association between behavioral stress and arrhythmogenesis[65,66] especially in the case of coronary artery disease (CAD). Lown et al. Say that three fundamental conditions are responsible for the development of arrhythmia:

- Myocardial electrical instability
- An acute provocative event (usually mental stress)
- A chronic state of mind (like depression or hopelessness).

Animal experiments by Verrier et al. Proved that stress markedly decreases the heart's electrical stability, rendering it more vulnerable to arrhythmias. In such experiments, stressed dogs—either by aversive conditioning (transthoracic shocks) or natural rage-like reactions (withholding of food)—had a 40% decrease in ventricular fibrillatory threshold.[67,68]

This indicates that their hearts were much more likely to get arrhythmias during stress.

In addition, β-adrenergic blockers were shown to block stress-induced arrhythmias, indicating that these actions are sympathetic nervous system mediated. Additional studies validated that anger and emotional distress are especially effective inducers of cardiac rhythm abnormalities. Together, these studies highlight that psychological and emotional stressors directly contribute to enhancing arrhythmic risk,[71] especially through excessive sympathetic activation.

Emotional Stress and Coagulation Abnormalities

Emotional stress has been known to induce coagulation abnormalities and predispose towards cardiovascular events. Recent evidence demonstrates that both experimentally induced acute psychological stress as well as endogenous stressors (e.g., earthquakes)[53,54,55] can result in platelet abnormality, hemoconcentration, and altered blood viscosity. Plasma volume losses due to stress have been demonstrated, which potentially lead to raised blood viscosity—a recognized risk factor for cardiac events. Animal studies are in agreement that acute stress is able to induce coagulation changes, whereas human studies indicate that such abnormalities can last for weeks following a severe stress episode. For instance, following the Hanshin-Awaji earthquake, patients with hypertension had temporary elevation of blood pressure, hematocrit, fibrinogen, and other hemostatic factors, which normalized after 4 to 6 months. It is not established if stress-evoked[5,53,54,55] platelet activation and hemoconcentration are mediated through identical mechanisms. Nonetheless, another study established that platelet activation was associated with catecholamine levels while hemoconcentration was related to blood pressure alterations, an indication of the different underlying processes. These studies highlight the interrelationship between emotional stress, coagulation of the blood, and cardiovascular morbidity.[72]

Acute Stress and Endothelial Dysfunction

Animal research demonstrates that acute stress induces coronary endothelial abnormalities,[73,74] from dysfunction to actual endothelial damage and necrosis. For instance, borderline hypertensive rats subjected to stress exhibited impaired arterial dilation and an attenuated response to nitric oxide, which suggests that stress impairs coronary relaxation. Experiments in monkeys and rabbits validated that sympathetic activation injures endothelial integrity. Stress-exposed rabbits had significant endothelial damage, but this was prevented by β-blockers, which points to the adrenergic stimulation. Likewise, social stress-exposed monkeys had more damaged endothelial cells, and once more, β-blockers avoided this effect.[75]

These observations create a direct connection between behavioral stress, neuroendocrine activation, and atherosclerosis in the early stages. From these animal studies, scientists hypothesize that acute or subacute psychological stress in humans might also induce transient endothelial dysfunction,[76] possibly accounting for the fact that psychological symptoms precede myocardial infarction.

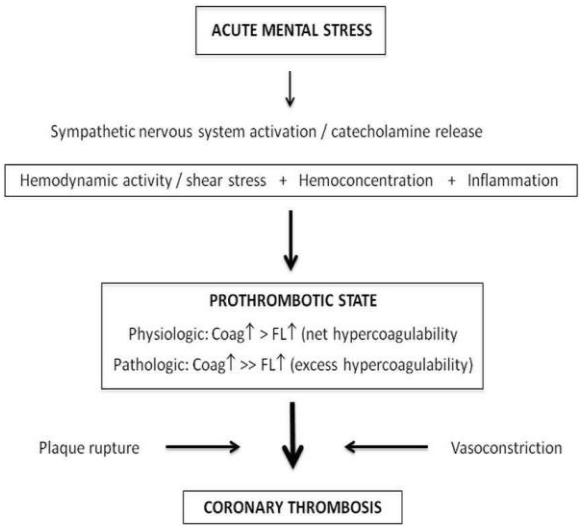


Figure taken from ScienceDirect.com

Therapeutic Implications

Acute and chronic psychosocial stress are both involved in the development of coronary atherosclerosis,[77] which is why CAD-prone patients need behavioral interventions. Acute stress cannot be avoided, but the prevention and treatment of CAD can perhaps prevent its detrimental effects. Chronic stress is, however, clinically manageable with perhaps the potential to diminish its contribution to disease evolution. In view of this promising hypothesis, psychosocial intervention has had limited clinical evidence. In our opinion, the issue of studying and integrating psychosocial interventions into clinical practice would benefit from the following measures:

- Physicians need to highlight psychosocial risk factors during patient counselling. If doctors recognize these problems, patients are more apt to take them seriously and alter their behaviour. However, if physicians do not take these concerns seriously, patients will tend to minimize their significance. Increased physician awareness of psychosocial aspects of CAD risk and disease development is necessary for enhancing patient outcomes.[78]
- Upcoming behavioural intervention trials need to be structured to complement current medical treatment, including lipid-lowering treatment and lifestyle change. Trials would measure the additional benefit of psychosocial stress interventions in the reduction of CAD risk.[79]

  As large-scale trials are costly and time-consuming, other early evaluation techniques—such as endothelial function tests, carotid ultrasound[80] for Recent animal research indicates that stress reduction can enhance coronary endothelial function. Studies in monkeys on an atherogenic diet revealed that those with early stress but subsequent stability had less endothelial dysfunction than those under continuous stress.[73,74,75,76]

  This suggests that chronic stress damages endothelial function, but its removal can reverse the damage. Acute and chronic psychosocial stress can cause coronary endothelial dysfunction. More evidence suggests that coronary disease is related to inflammation, which is mediated by biomechanical (shear stress) and biochemical (cytokines, growth factors) stimuli. Additional prospective research is required to determine how psychosocial stress leads to inflammation and whether behaviour modification can alter these effects.[83]

- The efficacy of behavioural interventions in cardiac patient[84,85] requires further assessment and translation to clinical

practice. Physicians tend to underestimate psychosocial risk factors because of lack of awareness, unreliable measurement tools, inadequate training in behavioural skills, and time pressure. Moreover, reimbursement problems and methodological constraints in research have added to the scepticism. Yet, meta-analyses demonstrate significant health outcomes when psychosocial interventions are superimposed upon usual cardiac care. To enhance efficacy, subsequent efforts need to target.[84,85]

Personalized Treatment Plans – Because a variety of psychosocial factors are linked with CAD, treatments must be individualized. For example, patients who are depressed or socially isolated might respond to cognitive therapy and group therapy. Trials such as ENRICHD and SADHART are already evaluating targeted interventions.[86]

Combining Lifestyle and Psychosocial Stress – Psychosocial determinants affect unhealthy lifestyle behaviours (e.g., smoking, unhealthy diet) and can block behaviour change. On the other hand, health behaviours such as exercise not only benefit physical health but also decrease psychological distress (e.g., depression).[87,88]

The integration of behavioural interventions into cardiac treatment might result in more cost-saving interventions. Because changing behaviour is difficult, predictive factors of success or failure in changing health behaviour should be researched. Motivation theories of psychology, applied within business contexts, could also be used to enhance patient compliance and psychosocial functioning in CAD treatment.[89]

- Organizational support is the key to developing interdisciplinary collaboration in biobehavioural medicine. Researchers across disciplines have made a contribution towards understanding psychosocial risk factors in cardiovascular disease.[1,11,6,7,8]
- Organizations such as the American Heart Association and American College of Cardiology can serve an important function to advance formal communication and collaboration across disciplines. By promoting collaborative research work, interventions for psychosocial risk factors can be facilitated through a synergistic process.[90,9]

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