How Anxiety, Depression and Stress Affect Heart Disease

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Most common psychiatric disorder in CAD 15-20%

Occurs in up to 30% after CABG and up to 20% in CHF

MDD is an independent risk factor for CAD with a risk of 1.5-2x.

MDD gives a 3-4x risk of death after MI

In CAD with depression, MDD is a better predictor of death than physiologic measures and have poorer QOL and more functional disability.

DEPRESSION STATISTICS

MDD also effects QOL in CHF

MDD also is associated with nicotine addiction, affects compliance and causes alterations in platelet aggregation, reduced HRV

Risk of CHD 60% higher in depressed patients

Clinical depression better predictor of CHD than depressive symptoms

However one study (Nicholson, 2006) could not establish that MDD was an independent risk factor.
MDD is 3x more common in patients after an MI
15-20% Patients with MI are depressed
12 months prevalence of MDD is 9.3% in those with CHD compared to 4-8% without comorbid illness. (7.9-17% in those with other conditions)

MDD increases risk of death due to cardiac events up to 10 yrs after diagnosis of CAD
Depression is an increased predictor of death at 6 mos (HR 5.74) and at 18mos (OR 3.44-7.82). It is as predictive as LVD after MI and smoking

High Levels of Phobic Anxiety are associated with an elevated risk of CHD death but not nonfatal MI and may be more related to sudden CHD death in men.
Phobic anxiety was also associated with an increase risk (1.50X) risk of SCD and fatal CHD (1.31x) but not nonfatal MI in women.
Increased risk of MI (1.7-2.54x) in men with high levels of worry about social situations
**ANXIETY STATS**

In normative aging study, RR of fatal CHD: 1.94 and SCD: 4.46 in men with 2 or more anxiety symptoms.

Worry about finances increased risk of combined CHD and angina by 20%.

Total worry increased risk of CHD and angina (1.4).

One study found GAD and MDD increased the risk of CHD and those with GAD were 3.1x more likely to take an antihypertensive.

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In another study, obsession had a relationship to ischemic heart disease.

Again in this study, phobic anxiety was predictive of fatal ischemic heart disease.

Anxiety has been shown to have a relationship to HTN.

Anxiety is an independent predictor of heart disease and is independent of depression.

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**MECHANISMS OF ANXIETY IN FATAL HEART DISEASE**

Phobic anxiety might exaggerate hormonal responses to MI or induce fatal arrhythmias.

People with phobic anxiety may have a greater vulnerability to a triggering event.

Anxiety may give decreased vagal tone and increased sympathetic response.

People with high levels of anxiety have reduced heart rate variability which has been shown to predict SCD in the elderly and in patients with failure.
**MECHANISMS OF HOW ANXIETY CAUSES HEART DISEASE**

- Acute anxiety attacks may trigger fatal ventricular arrhythmias.
- SCD incidence increases in earthquakes or wars.
- Anxiety may lead to diabetes, HTN, and high cholesterol through elevated catecholamine levels.
- Phobic anxiety may lead to unhealthy lifestyle habits such as smoking and inactivity.

**MECHANISMS OF ANXIETY**

- Anxiety induced hyperventilation could induce coronary spasm.
- Frequent VPBs identified as anxious.
- Causes are similar to those identified in depression.
- Anxiety increases sympathetic arousal and increase BP chronically.
- Anxiety decreases HRV and baro-reflex control.

**MECHANISMS OF HOW DEPRESSION CAUSES HEART DISEASE**

- Reduced HVR (increased sympathetic activity and decreased vagal activity).
- Hypothalamic-pituitary adrenal axis dysfunction
- Depression affects immune function which is a risk factor for ASHD.
- Increased factor 4 and B-thrombo-globulin.
- Impaired Vascular function.
**MECHANISMS OF DEPRESSION**

Increased CRP, IL-6, ICAM-1 and fibrinogen levels
Depression increases WBC which predicts heart disease possibly increasing vascular resistance through vasoactive substances or toxic substances and also may impair tissue perfusion
MI decreases regulation of DLPFC which decreases mood which further increases cardiac events
Chronic fatigue increases cytokines

**MECHANISMS OF DEPRESSION**

Poor health behaviors such as drinking and smoking, poor diet, no exercise
Decreased adherence to medications
Triple the risk of non-compliance with medical treatment regimens
Decreased baroreflex sensitivity

**MECHANISMS OF DEPRESSION**

Fatigue due to depression increases cardiac risk through decreased activity and exhaustion increases risk for recurrent MI and future MI
Decreased blood flow and glucose in depressed subjects to cortical, limbic, brainstem and DLPFC, ACC and parahippocampal areas to OFC, hippocampal and hypothalamic and thalamic areas changes autonomic tone
Decreased Baro-reflex sensitivity which increases the risk for V-Fib
Decreased threshold for V fib is a primary mechanism for SCD
CO-MORBID ILLNESSES THAT LOOK LIKE DEPRESSION OR ANXIETY

Dementia
Frontal Deficits
Drug effects
Apathy
Abulia
Atrial fibrillation mimicking anxiety
Fatigue

MEDICATION ISSUES IN CAD

Decreased absorption due to decreased intestinal blood flow, gut wall edema
Decreased excretion due to decreased renal blood flow
Decreased metabolism due to decreased hepatic blood flow
Drug interactions between psychiatric and cardiac drugs
Reduced albumin and increased A-1 acid glycoprotein with cardiac cirrhosis

PSYCHIATRIC EFFECTS OF CARDIAC DRUGS

Alpha blockers: depression, sexual dysfunction
Amiodarone: mood d/o due to thyroid dysfunction, delirium
ACE: mood elevations, increased Li levels
Anti-arrhythmics: hallucinations, confusion, delirium
B-blockers: fatigue, sexual dysfunction
Digoxin: VHD, delirium, depression
Diuretics: anorexia, weakness, apathy d/t electrolyte disturbances, increased lithium
CARDIAC EFFECTS OF PSYCHIATRIC DRUGS

Prolonged QTc with antipsychotics:
Mellaril > Geodon > Seroquel > Risperdal > Abilify
No documented cases of Torsades with Geodon!
QTc prolonged with TCAs, SSRIs, CBZ, Cymbalta, Lithium
Prozac, Paxil, Zoloft, Cymbalta, Wellbutrin, Nefazodone, Lex starring Trazodone
frequently inhibit other drugs that raise QTc

CARDIAC EFFECTS OF PSYCH DRUGS

Amantadine and CHF
Stimulants and arrhythmia and HTN
TCA and arrhythmia - quinidine like effect
Provigil and tachycardia and HTN
SSRIs, Wellbutrin and Effexor with HTN/Tachy
MAOIs and other antidepressants-HTN, alone Hypotension
Low potency FG’s and Most SGAs-hypotension

CARDIAC EFFECTS OF PSYCH DRUGS

Tegretol-AV block-Type Ia effect
Viagra-hypotension, myocardia ischemia
Lithium-bradycardia, sinus node dysfunction
What really is stress?
"Stress" would effect the heart by the same mechanisms as depression and anxiety.
Catecholamines and Hypothalamic-pituitary axis abnormalities would be the main mechanisms behind "stress" effects on the heart.
Takotsubo Cardiomyopathy would be the primary example.

Stress-and-Heart-Disease

Takotsubo Cardiomyopathy
Stress-induced cardiomyopathy, also called apical ballooning syndrome, broken heart syndrome, and takotsubo cardiomyopathy. Characterized by transient systolic dysfunction of the apical and/or mid segments of the left ventricle that mimics myocardial infarction (MI), but in the absence of obstructive coronary artery disease.

Takotsubo Cardiomyopathy
The Japanese name for an octopus trap, which has a shape that is similar to the apical ballooning configuration of the left ventricle (LV) in systole.
In the more commonly described "typical" type of stress-induced cardiomyopathy, the contractile function of the mid and apical segments of the LV are depressed, and there is compensatory hyper-kinesis of the basal walls, producing a balloon-like appearance of the distal ventricle with systole. Less commonly the ventricular hyper-kinesis is restricted to the mid-ventricle ("atypical") with relative sparing of the apex. About a third of cases involve both right and left ventricles.
TAKOTSUØ CARDIOMYOPATHY

Women account for 80 to 100 percent of cases, with a mean age of 61 to 76 years. Frequently but not always triggered by an acute medical illness or by intense emotional or physical stress (eg, death of relatives, particularly if unexpected, domestic abuse, arguments, catastrophic medical diagnoses, devastating financial or gambling losses, natural disasters).

Postulated mechanisms include catecholamine excess, coronary artery spasm, and microvascular dysfunction. Alternatively, there may be dynamic mid-cavity or left ventricular outflow tract obstruction which may contribute to apical dysfunction. Analogous permanent (rather than transient) apical outpouchings develop in patients with hypertrophic cardiomyopathy and mid-ventricular obstruction.

May be caused by diffuse catecholamine-induced microvascular spasm or dysfunction, resulting in myocardial stunning, or by direct catecholamine-associated myocardial toxicity. In some patients with stress-induced cardiomyopathy, the only apparent stressor is exposure to catecholamine or beta-agonist drugs in routine clinical doses.

Plasma norepinephrine have been noted to be elevated in studies. Elevated catecholamine levels and reversible left ventricular ballooning have also been observed in a rat model of immobilization-induced stress.
The following observations support the hypothesis of vascular dysfunction that may be catecholamine-induced:

- The occasional finding of multifocal coronary vasospasm on coronary angiography.
- Transient myocardial perfusion abnormalities that resolve with improvement in the myopathy.
- The presence of abnormal TIMI frame counts on angiography. The TIMI frame count is the number of cine frames required for dye to first reach standardized distal coronary landmarks.

Other evidence of catecholamine-induced myocardial effects:

For the limited available endomyocardial biopsy data, findings have ranged from no evidence of myocarditis to ischemic fibrosis with or without acute cellular infiltration to mononuclear infiltrates with contraction band necrosis. In a series of eight patients, acute biopsies obtained during the period of left ventricular dysfunction revealed intercellular accumulation of glycogen, many vacuoles, disorganized cytoskeletal and contractile structures, contraction bands and increased extracellular matrix proteins. These alterations resolved nearly completely after functional recovery. In a mouse model, it has been demonstrated that a high level of epinephrine is negatively inotropic due to a switch from beta-2 adrenoreceptor mediated Gs protein signaling, which is positively inotropic, to Gi protein signaling which is negatively inotropic. It is speculated that the greater effect at the apical myocardium may be due to a higher density of beta-adrenoreceptors at this location.

TAKOTSUBO CARDIOMYOPATHY

1.7 to 2.2 percent of cases presenting with suspected ACS. A similar prevalence of 1.2 percent was reported from a registry of 3265 patients with troponin-positive ACS.
Stress-induced cardiomyopathy is typically triggered by an acute medical illness or by intense emotional or physical stress, although a triggering event is not always present. Proposed pathogenic mechanisms include catecholamine excess, multivessel coronary artery spasm, and microvascular dysfunction.

Stress-induced cardiomyopathy may account for approximately 2 percent of suspected acute coronary syndromes.

Common presenting features include ECG abnormalities (often anterior ST elevations), elevated cardiac biomarkers, substernal chest pain, and dyspnea. Proposed diagnostic criteria include presence of transient regional wall motion abnormalities (typically not in a single coronary distribution), absence of angiographic evidence of obstructive coronary disease or acute plaque rupture, presence of new ECG abnormalities or modest troponin elevation, and absence of pheochromocytoma or myocarditis.

Acute complications of stress-induced cardiomyopathy include acute heart failure, tachyarrhythmias, bradyarrhythmias, cardiogenic shock, and transient LVOT obstruction. In-hospital mortality is approximately 2 percent. Patients who survive the acute episode typically recover normal LV function within one to four weeks.

TAKOTSUBO CARDIOMYOPATHY

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Up To Date, Takotsubo Cardiomyopathy, 2012