

Correlation Between Stress, Cardiovascular Disease and Depression

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CORRELATION BETWEEN STRESS, CARDIOVASCULAR DISEASE AND DEPRESSION

Chronic stress results in failures of homeostasis leading to various diseases such as atherosclerosis and depression³. Interleukin (IL)-6 is a stress substance biomarker linked to arteriosclerosis and depression. IL-6 and CRP, the two important biomarkers of systematic inflammation, are considered indicative and potentially predictive for atherosclerosis³.

Large bodies of evidence indicate that stress can activate inflammatory response in brain as well as peripherally³. IL-6 is a cytokine featuring pleiotropic activity; it induces synthesis of acute phase proteins such as CRP⁴. C-reactive protein (CRP) is produced by the liver. Its level rises when there's inflammation in your body. A study found that elevated levels of C-reactive protein were linked to a three times greater risk of a heart attack⁵. Levels of the pro-inflammatory marker C-reactive protein (CRP) are increased in individuals with posttraumatic stress disorder (PTSD). Furthermore, single nucleotide polymorphisms (SNPs) in the *CRP* gene are associated with CRP levels, risk for cardiovascular disease⁸.

Large bodies of clinical trial pointed out that chronic stress, whether early life stress or adult stress has long been linked to increased coronary heart disease (CHD) risk³. Cardiovascular diseases (CVD) remain among the 2 leading causes of death in the United States since 1975 with 633,842 deaths or 1 in every 4 deaths, heart disease occupied the leading cause of death in 2015 followed by 595,930 deaths related to cancer. CVD is also the number 1 cause of death globally with an estimated 17.7 million deaths in 2015, according to the World Health Organization (WHO). The burden of CVD further extends as it is considered the most costly disease even ahead of Alzheimer disease and diabetes with calculated indirect costs of \$237 billion dollars per year and a projected increased to \$368 billion by 2035⁶.

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CAD results from decreased myocardial perfusion that causes angina due to ischemia and can result in myocardial infarction (MI), and/or heart failure. It accounts for one-third to one-half of all cases of cardiovascular disease⁶. Plaque buildup, or fatty deposits, in your arteries is called atherosclerosis. Plaque may partially or totally block blood flow through large- or medium-sized arteries anywhere in the body, including in the heart, brain, pelvis, legs, arms or kidneys. This can lead to conditions such as Coronary Artery Disease (plaque in arteries in or leading to the heart and Angina (chest pain from reduced blood flow to the heart muscle)⁷. Atherosclerotic cardiovascular disease (ASCVD) involves plaque buildup in artery walls, which includes conditions such as acute coronary syndrome and peripheral artery disease, and can cause a heart attack, stable or unstable angina, stroke, transient ischemic attack (TIA) or aortic aneurysm⁷.

An estimated 21.0 million adults in the United States had at least one major depressive episode. This number represented 8.3% of all U.S. adults. Major depression is defined as a period of at least two weeks when a person experienced a depressed mood or loss of interest or pleasure in daily activities, and had a majority of specified symptoms, such as problems with sleep, eating, energy, concentration, or self-worth². Depression is 3 times more common in patients after a heart attack than in the general population, with 15% to 20% of heart attack victims qualifying for a diagnosis of major depressive disorder, and a far greater proportion experiencing increased levels of depressive symptoms¹. Several characteristics that have been found in depressed persons that could account for a poorer prognosis after a heart attack, including not taking medications as prescribed, continuing to smoke, less physical activity, increased stress hormone levels, increased blood sugar and lipid levels, increased tendency of blood to clot and increased inflammatory levels¹.

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In recent years, anti-inflammatory drugs, such as canakinumab and colchicine, have shown an ability to reduce the incidence of cardiovascular events in secondary prevention. Colchicine could be a potential candidate for use in clinical practice given its safety and low price⁹. The widely available therapeutic has several anti-inflammatory effects however that have proven effective in a broad spectrum of cardiovascular diseases as well. It is considered standard-of-care therapy for pericarditis, and several clinical trials have evaluated its role in pericarditis, post-operative- and post-ablation atrial fibrillation, post-pericardiotomy syndrome, coronary artery disease, percutaneous coronary interventions, and cerebrovascular disease¹¹. Canakinumab (ACZ885, Ilaris) is a human anti-IL-1 β monoclonal antibody developed by Novartis. Its mode of action is based on the neutralization of 1 β signaling, resulting in suppression of inflammation in patients with disorders of autoimmune origin¹⁰. Anti-inflammatory drugs may have synergistic effect with conventional antihypertensive drugs on the prevention and treatment of stress-related CVD³.

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