MAYO CLINIC

Exercise Counteracts the Cardiotoxicity of Psychosocial Stress

Evan L. O'Keefe, MS; James H. O'Keefe, MD; and Carl J. Lavie, MD

Abstract

Physical inactivity and psychosocial stress are prevalent in residents of the United States. The purpose of this article is to review the interaction between these 2 conditions and examine the effects of exercise on stress and cardiovascular (CV) health. A query of scientific references between 1974 to 2018 was performed using the PubMed search engine accessing the MEDLINE database using the search terms *psychosocial stress*, *CV disease* (*CVD*), *physical activity*, *exercise*, *cardiac rehabilitation*, and *team sports*. Psychosocial stress is a strong independent risk factor for adverse CV events. Conversely, people who experience CV events subsequently have drastically elevated rates of new-onset mental health disorders, including depression and anxiety. Psychosocial stress and CVD often trigger self-reinforcing feedback loops that can worsen mental health and cardiac prognosis. Exercise predictably improves CV health and prognosis and also is effective at lowering levels of psychosocial stress. Group exercise in particular seems to provide social support while at the same time boosting fitness levels and, thus, may be the single most important intervention for patients with concomitant CVD and emotional stress. Collaborative physical activity, such as group exercise, team sports, interactive physical play, and cardiac rehabilitation programs, have the potential to improve mental health and CV prognosis.

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From Ochsner Clinical School, The University of Queensland School of Medicine, New Orleans, LA (E.L.O., C.J.L.); University of Missouri—Kansas City and Saint Luke's Mid America Heart Institute (J.H.O.); and Department of Cardiovascular Diseases, John Ochsner Heart and Vascular Institute, New Orleans, LA (C.J.L.).

Human existence is, by nature, sometimes a struggle—survival of the fittest where life and death competition is grist for the evolutionary mill of natural selection. In the past century, however, that struggle for survival has been transformed entirely. What once played out largely outside in a natural setting is now taking place indoors in man-made urban surroundings; walking and physical work have been generally supplanted by vehicular travel and cognitive tasks; and violence, starvation, and infection have been superseded by noncommunicable diseases such as diabetes, obesity, and cancer. This cultural evolution has ushered in a general decline in physical fitness while simultaneously triggering a steep rise in the incidence of cardiovascular (CV) disease (CVD) and mental illness (Table).[1-6]

Evidence indicates that psychosocial stress, often associated with depression, anxiety, and hostility, is a strong independent risk factor for CVD events and that the mind-heart connection likely accounts for a substantial portion of the attributable risk of CVD.[7,8] A large and accumulating body of research suggests that psychosocial stress not only precipitates acute adverse CV events such as myocardial infarction (MI) and stroke but also perpetuates chronic CVD,[9] with a clinical effect comparable to other major CVD risk factors, such as smoking, low physical activity, and hypertension (HTN).[10-13] On the other hand, after being diagnosed as having CVD or diabetes mellitus individuals subsequently experience drastically elevated rates of new-onset mental health disorders.[14,15] Some studies suggest that up to half of all patients early after MI or coronary artery bypass surgery experience symptoms of depression.[16,17] Moreover, psychosocial stress can catalyze a downward spiral of worsening morbidity and can shorten life expectancy.[15,18-20] This article explores the evidence suggesting bidirectional feedback-loop relationships between psychosocial stress and CVD; it also explores how physical activity, group

exercise, and interactive physical play can potentially confer beneficial effects that largely neutralize the adverse effects of psychosocial stress.

STRESS TRIGGERS CV EVENTS

In the hours to days after the 9/11 attacks on the Twin Towers of the World Trade Center, New York City citizens experienced a 2.3-fold increase in ventricular fibrillation and ventricular tachycardia.[21] Similar elevations in risks of sudden cardiac death and acute MI were documented in the Taiwanese survivors after their deadly 1999 earthquake,[22] as well as in the Israeli survivors of the 18 Iraqi missile attacks during the Persian Gulf War.[23] Even in the context of healthy coronary arteries, psychosocial stress can cause strikingly abnormal electrocardiographic changes usually associated with myocardial ischemia despite the absence of clinically detectable congestive heart disease (CHD).[24,25] Moreover, simply answering "yes" to the question, "During the last month have you felt so sad, discouraged, hopeless, or had so many problems that you wondered if anything was worthwhile?" signifies a 5-fold risk of developing significant CHD.[26]

The possible pathophysiologic mechanisms by which psychosocial stress triggers acute CV events include sympathetic surges that lower the arrhythmic threshold, spike the blood pressure, increase inflammation, and cause hypercoaguability.[27] In addition, psychosocial stress has been shown to often provoke high-risk, maladaptive behaviors and to impair general functioning.[16] For example, psychosocial stress may instigate self-destructive behaviors, including substance abuse, noncompliance with medication, and failure to maintain a wholesome diet and prudent lifestyle.[13,16,28]

This excessive adrenergic tone makes psychosocial stress one of the most pervasive and pernicious risk factors for CVD.[8] Chronic imbalance of the autonomic nervous system with sustained sympathetic nervous system prominence and insufficient vagal tone causes elevation of heart rate (HR), delayed HR recovery, loss of normal beat-to-beat variability in HR, and blunted peak exercise HR, all of which increases risk of CVD and all-cause mortality.[8] Chronic imbalance of the autonomic nervous system also predisposes to inflammation, endothelial dysfunction, hypercoagulability, platelet activation, insulin resistance, coronary spasm, left ventricular hypertrophy, and cardiac arrhythmias.[8,9,13,29-32]

The landmark INTERHEART study, after collecting and analyzing data from more than 50 countries and 11,000 patients, found that psychosocial stress is the third most important modifiable risk factor for CHD and MI, ranking behind only lipids and smoking (Figure 1).[7] In addition, the INTERHEART study showed that psychosocial stress accounts for approximately one-third of the attributable risk of CHD.[7] This means that psychosocial stress is a stronger risk factor for CHD than many other widely recognized CVD risk factors, including obesity, diabetes mellitus, HTN, poor diet, and sedentary lifestyle.[7,13,33] In the total group of patients with previously diagnosed CHD, those who self-reported high levels of psychosocial stress had a 5-fold increased risk of major CVD events within 6 months, a 4-fold increase in medical costs, and a 2.5-fold increased risk of additional hospitalizations.[34] The mind-heart connection is so profound that severe emotional trauma experienced as a child can predispose to CHD as an adult, decades later.[35] The

ARTICLE HIGHLIGHTS

- Psychosocial stress is an independent risk factor for adverse CV events.
- Cardiovascular disease elevates rates of new-onset mental health disorders.
- Both psychosocial stress and CVD often trigger self-reinforcing feedback loops that worsen both prognoses.
- Exercise predictably improves CV health and effectively lowers levels of psychosocial stress.
- New evidence suggests social exercise involving interactive physical play may be the single most important intervention for patients afflicted by concomitant CVD and emotional stress.

TABLE. Overview of CVD, Mental Illness, and Physical Inactivity

CVD in America
Approximately 1 in 3 American adults, >80 million people, have CVD, and half of those affected are not yet 60 years old.
CVD has been the leading cause of death in the United States since the early 1920s, when it surpassed pneumonia, tuberculosis, and dysentery, the 3 most common causes of death until then.
Mental illness in America
Depression is the third leading cause of chronic disability.
Mental health and behavioral disorders are among the top 5 contributors to the global burden of disease.
Physical inactivity in 2018
Physical inactivity is currently the fourth leading cause of death worldwide.
During the past 50 y, there has been a persistent decrease in adults working in occupations requiring at least moderate levels of physical activity.

CVD = cardiovascular disease.

severity of psychosocial stress lies on a continuum, with robust evidence indicating the existence of a dose-response relationship between psychosocial stress and premature mortality.[33,36-38]

In the INTERHEART study,[7] psychosocial stress was assessed using 4 simple questions asking participants about their subjective perception of stress at work, stress at home, financial stress, and major life events they may have experienced in the past year. Two other questions assessed their locus of control and the presence of depression. Other more detailed assessments of self-reported measures of experienced stress are often deployed in psychological research on stress and its consequences.[39]

DEPRESSION AND CVD

Depression is one of the most prevalent forms of psychosocial stress, and it has been consistently identified as a strong independent risk factor for CVD.[40] Agatisa et al[41] studied individuals with a history of major recurrent depression and reported an increased relative risk of 2.7 for severe coronary calcification and 3.4 for severe aortic calcification. Other studies confirm that chronic depression independently increases the risk of CVD development by

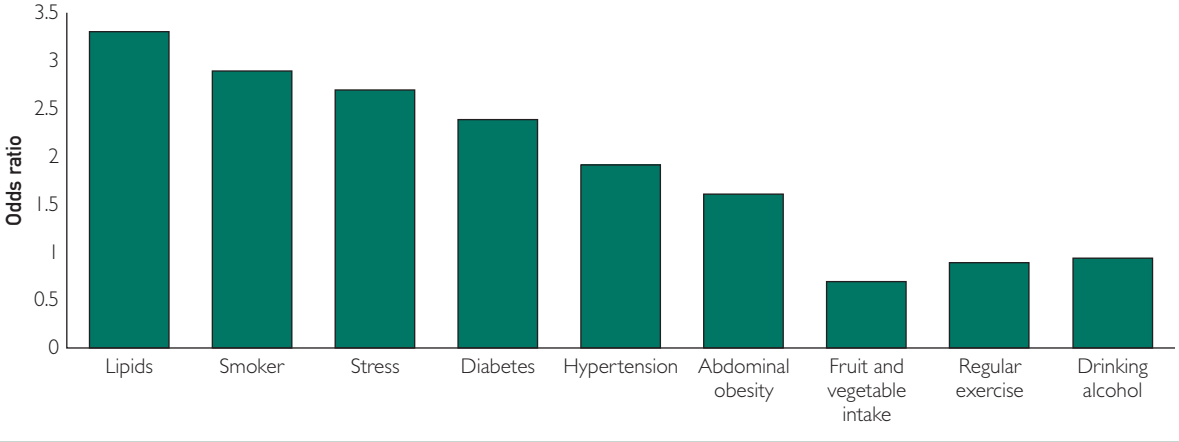

FIGURE 1. The odds of experiencing a myocardial infarction for individuals in the INTERHEART study. An odds ratio greater than 1 indicates an increased risk of heart attack, and an odds ratio less than 1 indicates a reduction in heart attack risk. Adapted with permission from *Lancet*.[7]

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approximately 2-fold compared with nondepressed matched cohorts.[26,42,43] Correspondingly, depression is also an independent risk factor for the development of HTN, type 2 diabetes mellitus, and adverse CHD events.[10-13,44-46]

In addition to its tendency to disturb autonomic nervous system balance, depression can also cause dysfunction in the hypothalamus-pituitary-adrenal (HPA) axis.[47,48] Such irregularities in the HPA axis are correlated with many of the disturbances that compose the metabolic syndrome—elevated blood pressure, truncal obesity, hypertriglyceridemia, and hyperglycemia.[49,50] Furthermore, patients with major depression often exhibit persistently elevated baseline levels of cortisol.[51]

Severe depression accompanied by a sense of hopelessness is an especially lethal condition that predisposes to sudden cardiac death and CV mortality.[52,53] In patients free of CHD at baseline, Penninx et al[43] found that those with major depressive disorder were 3.9 times more likely to die of CVD causes compared with those without major depressive disorder at baseline. Middle-aged and older individuals are approximately twice as likely to fall victim to premature mortality and CVD death if they are concomitantly experiencing high levels of depressive symptoms.[54] A Norwegian epidemiologic study reported that depression is as potent as smoking as a risk factor for all-cause mortality.[55] Although antismoking campaigns, graphic warnings, taxation, and smoking bans/restrictions now help the general public to understand and avoid the dangers of tobacco, depression continues, unfortunately, to undermine the well-being of our population, and, tragically, the CV toxicity of major depressive disorder remains largely unrecognized by health care providers and patients alike.

ANXIETY AND CVD

Evolutionarily intended as an early warning signal to keep us safe, anxiety now endures predominantly as a chronic maladaptive emotional response that not only fails to protect us from danger but also can paradoxically induce mental and physical disease. Cardiovascular disease often induces high levels of anxiety in afflicted patients,[12,18,31] and, inversely, long-term excessive anxiety is associated with increased risk of CVD.[12,13,56]

Patients who reported high anxiety also recorded increased body weight, percentage body fat, and triglyceride levels and also showed trends for higher low-density lipoprotein to high-density lipoprotein (HDL) ratios and triglyceride to HDL ratios, as well as lower HDL levels.[18] Accordingly, several studies have suggested that patients with CVD are at least 2-fold more likely to experience future adverse CVD events if they struggle with concomitant anxiety.[57,58] Likewise, for the post-MI patient, the psychological strain induced by severe anxiety is associated with a worse prognosis and increased mortality.[59,60] By disturbing both the sympathetic nervous system and the HPA axis, anxiety reduces HR variability and impairs vagal tone, which can increase vulnerability to sudden cardiac death.[13,18,56,61,62]

However, the evidence for anxiety-causing CVD remains speculative, with some notable studies reporting an inverse relationship between heightened anxiety levels and reduced CVD mortality rates.[63,64] Similarly, Parker et al[65] found that increased anxiety correlated with improved outcomes after an acute coronary syndrome. However, the health consequences of psychosocial stress seem to be highly variable with respect to individual susceptibilities, types of stressors, and coping mechanisms used.[66] An apt example is illustrated by the highly variable rates of CHD among caregivers. The psychological strain experienced by caregivers is often substantial and long term, yet those caregivers engaged in an emotionally fulfilling relationship have no associated increase in mortality.[67] It is only caregivers providing for others in the context of a hostile or emotionally distant relationship in whom increased risk for early mortality is observed.[67]

HOSTILITY AND CVD

Psychosocial stress stemming from individual character traits also plays a detrimental role in health outcomes. A large body of evidence

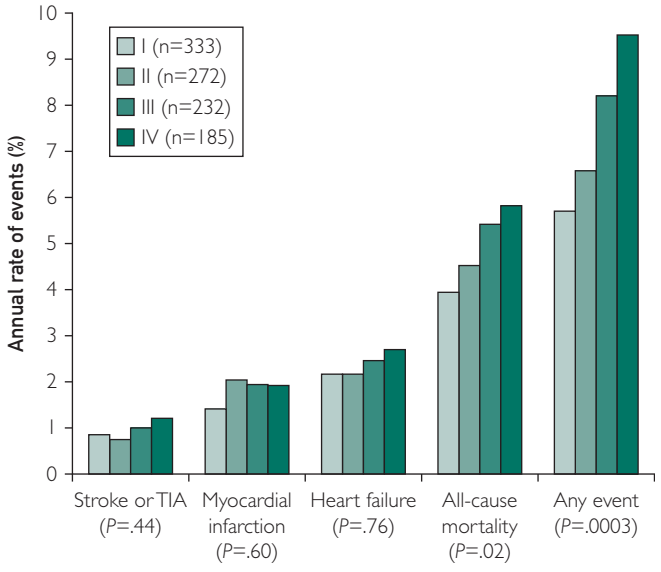

FIGURE 2. Age-adjusted annual rates of adverse events as a function of hostility. Quartile I (lightest shade of green) is the least hostile group, with each sequential quartile increasing in level of hostility. Increased levels of hostility were significantly associated with rates of all-cause mortality and any event, which is a composite of stroke or transient ischemic event (TIA), myocardial infarction, heart failure, and death. Data from *Am J Cardiol*.[81]

indicates that hostility is a particularly toxic emotion that encompasses several negative emotions, including anger, resentment, cynicism, and mistrust.[20] In contrast to most chronic illnesses and noncommunicable diseases, hostility arises disproportionately in adolescents and younger adults rather than in older individuals. Using psychometric testing, Lavie and Milani[31] found that compared with elderly patients with CHD, younger patients with CHD had a 94% increase in hostility, a 52% increase in anxiety, and a 24% increase in depression.

As previously stated, psychosocial stress directly induces a host of physiologic derangements via the sympathetic nervous system and the HPA axis, including elevated blood pressure during waking hours and sometimes during sleep. Hostility and other types of adverse psychosocial stress are linked to elevations in resting HR and amplified elevations in blood pressure, often in response to even mundane, generally nonthreatening environmental stimuli.[8] Individuals with high levels of hostility tend to respond to stress with exaggerated adrenergic responses, which not only can increase blood pressure but also can cause coronary vasoconstriction, increase inflammation, and activate platelets, all of which could trigger MI, stroke, or CV death.[68] In addition, psychosocial stress leads to hypercortisolemia and higher levels of circulating catecholamines[69] and lower levels of vagal tone, particularly in the CV system.[70] Importantly, in addition to these involuntary responses, psychosocial stress can indirectly degrade health and well-being by triggering maladaptive coping strategies and self-destructive behaviors. Indeed, hostility has been linked to poor diet, obesity, sleep disturbances, and abuse of alcohol, tobacco, and other addictive substances, and it can lead to unhealthy levels of social isolation.[71,72]

Hostility has been associated with elevated risks of HTN, coronary artery calcification,[73] coronary atherosclerosis,[74] peripheral atherosclerosis,[75,76] dyslipidemia, and obesity, as well as elevated levels of tumor necrosis factor α[77] and platelet reactivity.[78] High levels of hostility have also been linked to a 4-fold increased incidence of symptomatic CHD and a 5-fold increase in adverse CVD events.[12,79,80] Hostility as a CVD risk factor is especially prevalent in younger males, where psychosocial stress and high levels of hostility are associated with increased risks of all-cause mortality and CVD (Figure 2).[81,82]

CVD INCITING MENTAL ILLNESS

Cardiovascular disease and psychosocial stress often coexist in bidirectional, self-catalyzing relationships whereby adverse CVD events such as MI, heart failure, arrhythmias, and stroke often worsen or even cause psychiatric issues, such as major depression or generalized anxiety disorder. Regardless of demographic characteristics, clinically unrecognized depression is prevalent in CVD.[83] The psychosocial stress associated with depression can lead patients to "catastrophize" their condition, which can cause them to become hypervigilant about their health. In turn, this can predispose to unnecessary visits to the emergency department, an increased use of outpatient services, and increased hospitalizations.[83] Psychosocial stress, particularly depressive symptoms, also

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can be associated with a learned helplessness, which often increases days spent in bed and long-lasting functional disability.[84]

Compared with the general public, depression is approximately 3 times more common in patients with CHD, heart failure, or acute MI.[83,85] Cardiovascular disease is accompanied by major depression disorder in approximately 25% of patients, with estimations of minor depression and elevated depressive symptoms afflicting almost half of all patients with diagnosed CVD.[16] Major depression occurs with a prevalence rate of approximately 6% to 7% in the general population, yet, in cohorts of patients with heart failure or diabetes mellitus with poor glycemic control, the rates of diagnosed depression range from 20% to 40%.[86,87] This body of evidence indicates that in patients with chronic CVD, depression is being grossly underaddressed.

EXERCISE EFFECTS ON CVD

The adoption of a consistent exercise regimen is one of the most effective steps that a patient struggling with psychosocial stress can take to reduce mental suffering and physical disability. Increased physical activity, regular exercise, and improved levels of cardiorespiratory fitness have the power to ameliorate many of the adverse physiologic effects of psychosocial stress. Cardiorespiratory exercise training programs have been shown to improve autonomic nervous system function,[88] inflammation,[89] metabolic syndrome,[14,90] blood rheology,[91] brain plasticity, mood, and cognition.[92] Evidence indicates that this exercise training–induced realignment of blood rheology and the autonomic nervous system could, in part, result from improvements in psychological and behavioral factors.[91] Typically, an exercise regimen over time lowers stress, improves functionality, and reduces subsequent rehospitalization costs.[93]

Exercise training improves many of the systemic derangements associated with depression, including improvements in HR variability, baroreflex reactivity, QT prolongation, autonomic balance, inflammation, hypercoagulability, and endothelial function.[94] Yet, it is in the most crucial category of all—mortality rates—where patients stand to benefit the most from increased physical activity.[83] Compared with inactive patients, those with consistent levels of adequate physical activity after experiencing an MI have half the risk of dying during follow-up.[95] Individuals with heart failure had a 59% lower incidence of mortality if they participated in exercise cardiac rehabilitation. The cumulative data indicate that increased physical activity, exercise training, and formal cardiorespiratory exercise training each seem to decrease morbidity and markedly improve patient well-being and overall survival rates.[32,83,96,97]

EFFECT OF EXERCISE ON STRESS

Exercise training reduces cortisol levels, HR, and anxiety responses to stress.[98] Furthermore, improved cardiorespiratory fitness reduces reactivity of the autonomic nervous system to psychosocial stress.[98]

The Aerobics Center Longitudinal Study reported that low levels of negative emotions were associated with a 30% lower risk of all-cause mortality. Even more impressively, when low levels of negative emotions were coupled with high cardiorespiratory fitness,

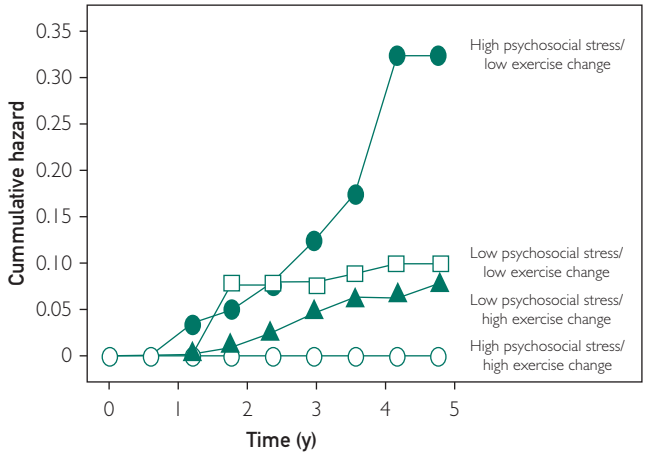

FIGURE 3. Actuarial cumulative hazard plot for survival time based on changes in exercise capacity (high exercise change vs low exercise change) after exercise training split by baseline psychosocial stress (high psychosocial stress vs low psychosocial stress; n=522). Individuals with high psychosocial stress who did not increase their exercise were at markedly higher risk for mortality during follow-up. In contrast, those with high psychosocial stress who increased their exercise had the lowest risk of mortality. Reprinted with permission from *Am J Med*.[106]

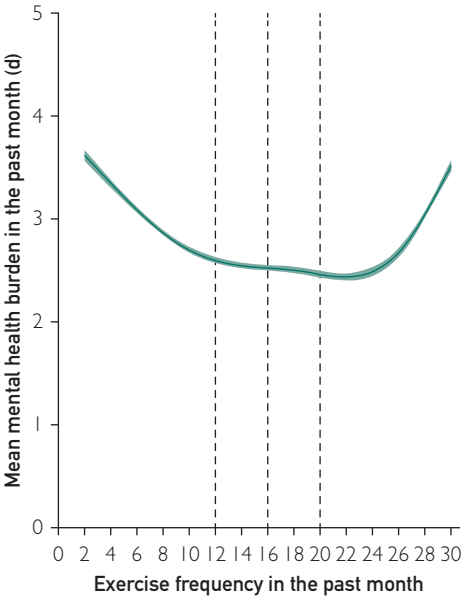

FIGURE 4. Mental health burden as a function of exercise frequency. People who exercised 12 to 24 times per month had the lowest mental health burden. Frequencies of less than 3 per week (12 sessions per month) or more than 6 per week (24 sessions per month) were associated with worse mental health. Reprinted with permission from *Lancet Psychiatry*.[108]

all-cause mortality dropped by 63%.[99] Exercise not only mitigates CVD risk factors but also curbs emotional distress, anxiety, hostility. and depression.[15,19,100,101] Although psychosocial stress disproportionally afflicts younger patients with CVD,[82,102] Lavie and Milani[31] reported that these same individuals have the most to gain. After formal cardiac rehabilitation programs, the younger cohort had the greatest improvements in both body mass index and oxygen consumption, in addition to 50% to 80% reductions in hostility, anxiety, and depression.[31]

Recent studies suggest that in patients of all ages who have experienced an MI, exercise has the ability to treat existing depression or prevent future depression.[103-107] Moreover, 57% of exercise training participants who exhibited significant improvements in oxygen consumption demonstrated parallel reductions in their levels of depression.[104] A substantial body of research now supports the assertion that for depression, exercise is as effective as antidepressant medications.[83,105]

Milani and Lavie[106] also reported that in 522 patients, nearly all mortality during follow-up occurred in the cohort of patients with high psychosocial stress who failed to increase their exercise capacity (Figure 3). Furthermore, the cohort of patients with heart failure with persistent depressive symptoms after formal cardiorespiratory exercise training have a 4-fold higher mortality rate compared with their nondepressed counterparts.[32,83] Yet, even individuals with persistent depression after successfully completing cardiorespiratory exercise training had half of the all-cause mortality rate as depressed patients who dropped out of exercise training.[83]

THE POWER OF PHYSICAL PLAY

Studies show that the stress reduction benefits of physical activity are magnified when exercise is performed in social settings such as group workouts, team sports, and interactive play.[107] A recent, very large cross-sectional study found that people who exercised regularly had approximately 43% fewer days of poor mental health compared with matched sedentary individuals.[108] The mental health improvements were strongest for those who exercised 30 to 45 minutes per session, 3 to 5 times per week. Group sports such as soccer, basketball, volleyball, and other popular team sports showed the strongest associations with good mental health.[108] As with other studies on the topic of exercise and health, more is not always better; the mental health benefits of exercise were markedly diminished in those who exercised more than 24 times per month, or longer than 90 minutes per session (Figure 4).[108]

A large longitudinal prospective study of Danish adults showed that the leisure-time physical activities that are most effective for improving life expectancy are those that require 2 or more individuals to play together, such as racquet sports, golf, and soccer (Figure 5).[109] These physical activities that require interactive play increased life expectancy much better than solitary exercises such as running and workouts on a treadmill or elliptical trainer.

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INTERVENTIONS TO IMPROVE STRESS AND CV HEALTH

Thus, CVD is both a cause and a result of psychosocial stress. Exercise, especially when performed in interactive sports or social settings, increases life expectancy and markedly improves overall health and well-being.[108,109] Thus, increased physical activity is a potent, natural, and practical therapy for alleviating stress and improving overall prognosis (Figure 6). In addition to standard CVD pharmacology, the following 3-pronged approach is aimed at bolstering psychological health while also promoting CV wellness and longevity.

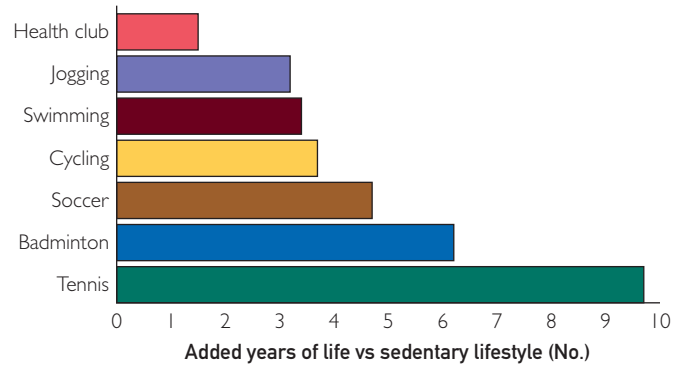

FIGURE 5. Survival improvement calculated using multivariable Cox proportional hazards regression analysis adjusted for age, sex, educational level, income, alcohol intake, tobacco smoking, diabetes, and weekly volume of other leisure-time physical activities. Compared with sedentary lifestyle (control group), all the different leisure-time physical activities significantly improved survival time except health club activities (treadmill, elliptical trainer, weights, etc). Adapted with permission from *Mayo Clin Proc.*[109]

ENHANCED CARDIAC REHABILITATION

Cardiac rehabilitation that uses a program to emphasize interpersonal support for stress reduction has been shown to bestow synergistic CV health benefits beyond those provided by solitary exercise.[110] Furthermore, group exercise seems to provide social support while at the same time improving fitness levels, and thus may be the single most important intervention for patients afflicted by concomitant psychosocial stress and CVD because it has the potential to improve outcomes for both conditions.[97,111] Of concern, patients presenting with persistently high estimated cardiorespiratory fitness matched with persistently high depressive symptoms demonstrate no attenuation in mortality risk.[112] In essence, unremittingly high levels of psychosocial stress can thwart some of the health benefits of long-term exercise training.

With this in mind, we recommend that the standard cardiorespiratory exercise training regimen should be revamped with increased emphasis on interpersonal interaction during and after the formal exercise classes. Cardiac rehabilitation exercises in general are predominantly solitary activities, such as walking on a treadmill or strength training. The physical activities performed during cardiac rehabilitation training could be easily transitioned to be interactive group exercise sessions.

LIFESTYLE MODIFICATION

Behavioral cardiology has gained traction due to myriad CVD risk factors that stem from psychosocial stress and self-destructive lifestyles. For example, an inadequate social support network has been implicated in increasing mortality rates in patients with CVD. Specifically, psychosocial stress factors such as social isolation[113] as well as living alone,[114] lacking a confidant,[115] low emotional support,[116] lack of available support,[117] and low perceived support[118] all increase long-term mortality rates. Other subjective contributors to adverse clinical outcomes include excessive job strain[7,119,120] and a low socioeconomic status, particularly when linked with poor health habits, indigent housing conditions, and financial instability.[104] Furthermore, evidence suggests that a strained marital relationship also adversely affects CV health.[120,121] Unfortunately, various types of psychosocial stress tend to cluster together in a vulnerable person and precipitate cumulative effects.[122] Ruberman et al[113] reported that in post-MI patients, high levels of life stress and social isolation were each individually associated with a 2-fold increase in subsequent CVD events, but when those insults occurred simultaneously, the individual's CV risk was magnified 4-fold.

Research shows that approximately 95% of Americans believe in God or some

spiritual higher power. Faith and hope confer beneficial effects on the mind-heart axis as well as the CV system, especially when combined with attendance at regularly scheduled in-person gatherings.[123] In part, a person's outlook on life is volitional so that one can consciously choose to adopt a more optimistic attitude, a friendlier and more trusting manner, and an altruistic demeanor, all of which are associated with improvements in mental health and physical well-being.[124] Notably, the presence of a pet (particularly a dog) in the home or regularly tending a garden are 2 additional methods of lowering stress and improving long-term CV health and overall well-being.[125,126]

Heat therapy, such as sauna bathing, seems to lower the risk of fatal CV events and has also been used to reduce subjective stress.[127] Meditation, tai chi, and yoga have also been found to be effective for lowering stress, although definitive studies have not been performed to prove that these interventions improve CV outcomes.[128,129]

PHARMACOLOGIC INTERVENTION

A recently published randomized trial suggested that a selective serotonin reuptake inhibitor might improve long-term outcome after an acute MI. Of 300 patients with depression after recent acute MI, 6 months of treatment with escitalopram compared with placebo resulted in a reduced risk of major adverse CV events after follow-up of 8 years.[130] The selective serotonin reuptake inhibitor class of antidepressant medication has been found to be safe for patients with CVD and could prove useful as an adjunct in some individuals, although further randomized trials are needed to clarify this potential indication.

Omega-3 fats, particularly those derived from marine life, are critically important for optimal functioning of the brain[131] as well as the CV system.[132] Approximately 90% US adults are deficient in omega-3, and this predisposes to adverse CV events, depression, and other mental disorders.[133] Increased omega-3 content in the cell membranes and

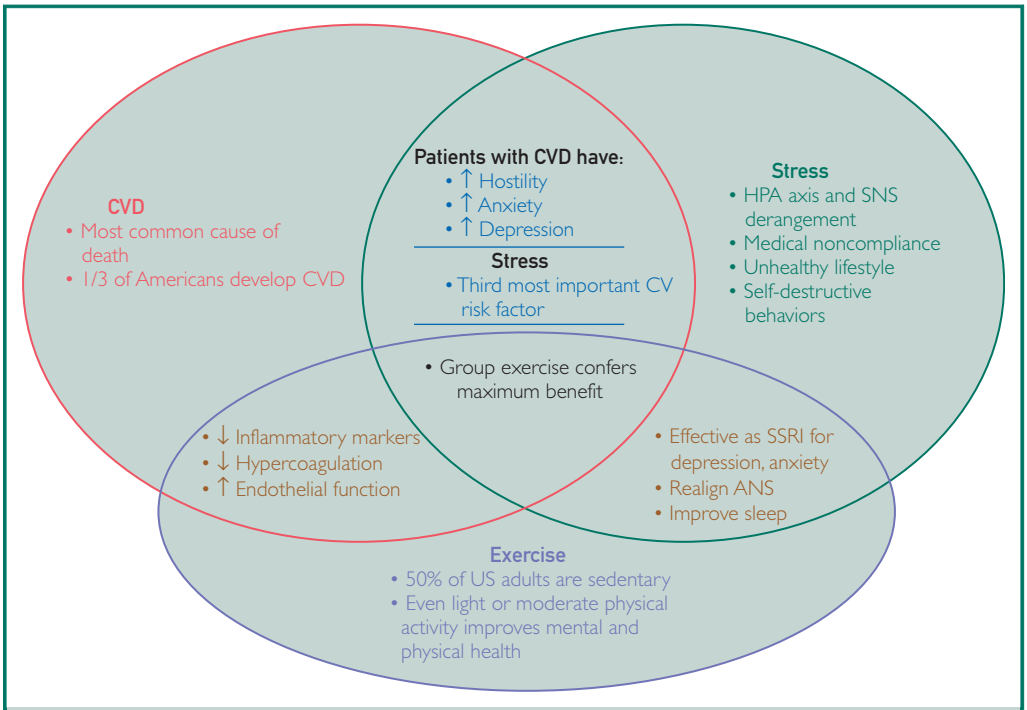

FIGURE 6. The complex interactions among stress, cardiovascular (CV) disease (CVD), and exercise. ANS = autonomic nervous system; HPA = hypothalamus-pituitary-adrenal; SNS = sympathetic nervous system; SSRI = selective serotonin reuptake inhibitor.

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blood induced by eating fish or consuming omega-3 supplements may, in part, exert cardioprotective effects via improvement in mood and overall brain functioning.[131,132,134]

β-Blockers can be useful in treating some specific types of stress, such as panic attacks and performance anxiety. β-Blockers have been found to be as effective as benzodiazepines for the treatment of panic disorder and do not carry the high risk of sedation, cognitive impairment, dependence, and tolerance seen with benzodiazepines.[135] Propranolol also seems to be useful for the treatment of performance anxiety, wherein the β-blocker blunts the adrenergic hypersensitivity, thereby diminishing the fear response.[135] β-Blockers do not treat the underlying psychological causes of anxiety but can help reduce physical manifestations of excess adrenergic tone such as tremor, sinus tachycardia, diaphoresis, and dizziness. By decreasing the body's physical reactions to stress, β-blockers can help lessen the subjective sense of anxiety during stressful times.

CONCLUSION

Psychosocial stress and CVD often coexist in bidirectional self-reinforcing associations that can exert toxic effects on long-term mental and physical health. It is our strong assertion that cardiorespiratory exercise training programs and increased physical activity, especially when performed in socially interactive settings, such as interactive play, have the potential to reduce the burden of noncommunicable diseases in general and specifically to reduce psychosocial stress while at the same time improving CV prognosis. Much of the data on this topic are observational, and, thus, randomized controlled trials are necessary to prove which types of interactive exercise are most beneficial for mental and CV health.

Abbreviations and Acronyms: **ANS** = autonomic nervous system; **CHD** = congestive heart disease; **CV** = cardiovascular; **CVD** = cardiovascular disease; **HDL** = high-density lipoprotein; **HPA** = hypothalamus-pituitary-adrenal; **HR** = heart rate; **HTN** = hypertension; **MI** = myocardial infarction; **SNS** = sympathetic nervous system; **SSRI** = selective serotonin reuptake inhibitor

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Correspondence: Address to Carl J. Lavie, MD, FCCP, Medical Director, Cardiac Rehabilitation, Director, Exercise Laboratories, John Ochsner Heart and Vascular Institute, Ochsner Clinical School - The University of Queensland School of Medicine, 1514 Jefferson Hwy, New Orleans, LA 70121-2483 (clavie@ochsner.org).

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