Triggers of Acute Cardiovascular Events and Potential Preventive Strategies: Prophylactic Role of Regular Exercise

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Abstract: There is now considerable evidence to suggest that acute myocardial infarction, sudden cardiac death, and stroke can be triggered by physical, chemical, and psychological stressors, including heavy physical exertion and situations that create heightened emotional stress. The increased risk appears to be largely limited to a susceptible subset of the population, that is, individuals with known or occult cardiovascular (CV) disease. In this article, we summarize the evidence supporting the impact of selected triggers in the pathogenesis of acute CV events, as well as the potential role of various preventive strategies, especially regular exercise training and improvements in cardiorespiratory fitness to reduce the CV risk imposed by various triggers.

Keywords: acute cardiovascular event; exercise; physical activity; exercise training

Introduction
Considerable evidence indicates that acute cardiovascular (CV) events, including acute myocardial infarction (AMI), sudden cardiac death (SCD), and stroke, can be triggered by physical, chemical, and psychological stressors, including acute intense physical exertion and situations of considerable emotional stress. This risk may be particularly high for individuals with known CV disease (CVD) or high CVD risk. In this article, we review the evidence supporting the role of various triggers in CV events, as well as the evidence supporting potential preventive strategies. In particular, we review the role of regular exercise training (ET) and improvements in cardiorespiratory fitness (CRF) to reduce the risk imposed by these specific CV triggers.

Physical Stress
Although considerable epidemiologic evidence suggests that regular endurance ET/physical activity (PA), moderate-to-high levels of CRF, or both, may help to protect against the development of CVD and its adverse clinical sequelae, exertion-related CV events have been reported in the medical literature and the lay press, suggesting that vigorous PA (≥ 6 metabolic equivalents [METs]; 1 MET = 3.5 mL O₂/kg/min) may actually trigger cardiac arrest or AMI in persons with known or occult CVD. Several hypotheses have been suggested as triggering mechanisms for plaque rupture, acute coronary thrombosis (Table 1), or threatening ventricular arrhythmias (Figure 1).

The cause of exertion-related CV complications is largely associated with the patient's age. Structural CV abnormalities, including hypertrophic cardiomyopathy (HCM) and malformations of the coronary arteries, are the major causes of SCD in younger patients. However, atherosclerotic CVD is the most common autopsy finding in individuals aged > 40 years. Thus, it is the combination of vigorous physical
exertion and a diseased or susceptible heart, rather than the exercise itself, that seems to present the hazardous milieu for CV events during or soon after strenuous ET.

The relative risk (RR) for AMI and SCD across various types of PA, performed at mild-to-moderate intensities, is similar to that expected with chance alone. In persons with known or occult CVD, vigorous PA, such as jogging or running, seems to be associated with a greater incidence of acute CV events compared with periods of light or no PA.\textsuperscript{12} The absolute risk that a nonfatal or fatal CV event will occur during or soon after vigorous PA has been estimated to be between 1 in 500,000 hours and 1 in 2.6 million hours of ET.\textsuperscript{10} Thus, isolated bouts of vigorous PA may transiently increase the risk of CV complications; however, the absolute risk associated with each episode of ET is extremely low.\textsuperscript{13} Although CV events are more frequent in the morning, several reports\textsuperscript{14-16} now suggest that ET performed in the morning induces no higher RR than ET performed at other times of the day.

Numerous independent studies have reported that AMI and SCD can be triggered by vigorous PA, and that the risk increases with decreasing frequencies of regular ET and vice versa. Accordingly, the estimated RR (95% confidence interval [CI]) of ET-related primary cardiac arrest, SCD, or nonfatal AMI ranges from 2.1 (95% CI, 1.1–3.6) to 56 (95% CI, 23–131). The RR seems to be especially high for susceptible individuals, that is, habitually sedentary individuals with underlying CVD who were performing unaccustomed vigorous PA.\textsuperscript{11} For example, the Determinants of Myocardial Infarction Onset study\textsuperscript{14} found that the likelihood of a sedentary person experiencing an exertion-related AMI was nearly 50 times that encountered by individuals who perform ET \( \geq 5 \) per week (Figure 2). Exercise training for just 1 or 2 times per week reduced the risk for exertion-related AMI by \( > 80\% \).

To put these data in perspective, it is important to consider that the absolute risk associated with each bout of ET is extremely low, the RR is inversely related to the habitual level of PA, and the long-term cardioprotective effect of regular PA is substantial. Based on data from the Onset study,\textsuperscript{14} the risk of AMI associated with each bout of PA is approximately doubled for an individual who participates in vigorous 1-hour sessions of ET \( \geq 5 \) days per week. However,
Triggers of Acute Cardiovascular Events

Figure 2. Relative risk of acute myocardial infarction associated with vigorous physical exertion (≥ 6 METs) according to habitual frequency (sessions/week) of vigorous exertion. The T bars indicate the 95% confidence interval limits. The dotted line indicates the baseline risk.

2 heavy snowfalls that occurred in the greater metropolitan Detroit, MI area, it was found that of those who experienced SCD due to atherosclerotic CVD (N = 271), 36 people (33 men, 3 women) were engaged in manual (n = 32) or automated (n = 4) snow removal, representing the largest number of exertion-related deaths reported to date after heavy snowfalls.25

Extreme ET—Too Much of a Good Thing?
The graded benefit of regular ET/PA for CV risk is well-established. Observational and epidemiologic studies have, for the most part, focused on moderate-to-vigorous levels of PA. Nevertheless, an increasing number of middle-aged and older adults may undertake ET in excess of these intensities, at maximal or near-maximal levels, sometimes for short bursts or extended durations.27 However, few data are available as to whether the risk-benefit ratio is maintained among those participating in regular intense ET, as is commonly associated with triathlons and marathon running. Numerous reports in the medical literature and the lay press raise the possibility that more extreme ET may actually trigger acute CV events, especially in individuals with known or occult CVD or structural CV abnormalities (eg, HCM).

Reports documenting the favorable risk factor profiles and superb cardiac performance of marathon runners have led to speculation that marathon running may promote "immunity to coronary heart disease (CHD)."28 Among individuals who exceed contemporary PA recommendations, antidiabetic, antihypertensive, and low-density lipoprotein cholesterol-lowering medications are inversely related to vigorous PA and CRF.29 These data, coupled with the recent finding that regular ET prevents cellular senescence,30 have led an increasing number of adults to the conclusion that "more ET is better."

Marathon running has increased in popularity in the last 3 decades with participation increasing from 25,000 runners in 1976 to approximately 2 million in 2010. It is estimated that approximately 6 to 8 marathon runners will die while running each year in the United States due to the combination of known or occult CVD and superimposed physical and/or environmental stresses (eg, cold, heat, humidity, altitude).21 In 2009, 3 runners died within 15 minutes of each other while competing in the Detroit Free Press/Flagstar Marathon.32 Prolonged-endurance ET has been reported to have adverse CV consequences. Marathon running causes acute dilation of the right atrium and right ventricle, reduction of right ventricular ejection fraction, and release of cardiac troponin I and B-type natriuretic peptide—possible harbingers...
of long-term sequelae, including fibrosis. If the current mantra “exercise is medicine” is embraced, then indications and contraindications require clarification, and under- and overdosing are possible.

The potential CV risks of unconventionally vigorous ET, especially over short bursts or extended durations, should be weighed against the benefits. In sedentary populations, the risk of exertion-related CV events is highest due to the greater incidence of atherosclerotic CVD and the greater RR of ET. Contemporary guidelines recommend that most adults engage in moderate-intensity ET for ≥ 30 min·d⁻¹ on ≥ 5 d·wk⁻¹ for a total of ≥ 150 min·wk⁻¹; vigorous-intensity-endurance ET for ≥ 20 min·d⁻¹ on ≥ 3 d·wk⁻¹ (≥ 75 min·wk⁻¹), or a combination of moderate- and vigorous-intensity ET to achieve a total energy expenditure of ≥ 500 to 1000 MET·min·wk⁻¹. Although additional benefits occur with increasing MET minutes per week, a recent meta-analysis showed that people who had PA levels lower than the minimum recommended amount also had significantly lower risk for CHD. At considerably higher ET levels, only limited data are available regarding the risk–benefit ratio. Accordingly, in some individuals, there is the potential for a plateau or even a decline in benefit at more extreme levels of endurance ET, with a heightened risk for AMI and/or SCD.

Sexual Activity
Sexual activity is often equated with an aerobic requirement of 2 to 4 METs. In an early report in the home setting, the associated cardiac demands were modest for middle-aged long-married individuals with and without CHD, with heart rates reaching an average of 117 bpm. More recent studies using ambulatory ECG monitoring in men with CHD (N = 88) reported similar results, with heart rates generally ranging from 118 to 127 bpm during sexual intercourse. ECG signs of myocardial ischemia occurred in 31% of the study population, and in 78% of these individuals, ischemia was manifested as asymptomatic ST-segment depression. It should be emphasized, however, that cardiac demands in longstanding relationships tend to become less demanding over time. Moreover, exercise-based interventions have been shown to be helpful in reducing coital symptoms and heart rates.

The role of recent sexual activity as a trigger of AMI has been examined in both the Onset and Stockholm Heart Epidemiology Programme (SHEEP) studies, with similar results. In the Onset study, sexual activity was reported within 2 hours of AMI by 27 of 858 patients (3%), with a RR of 2.5 (95% CI, 1.7–3.7). However, the RR of AMI following sexual activity decreased from 3.0 to 1.9 to 1.2 for patients who engaged in vigorous PA (≥ 6 METs) once or not at all, twice, or ≥ 3 times per week, respectively (p = 0.01). The absolute risk of sexual activity was extremely low (1 in 1 million for an apparently healthy individual). In the SHEEP study, only 5 of 399 patients (1.3%) without premonitory symptoms reported sexual activity during 2 hours before the onset of AMI symptoms. The RR of AMI was 2.1 (95% CI, 0.7–6.5) during 1 hour after sexual activity: however, the risk among habitually sedentary patients was 4.4 (95% CI, 1.5–12.9). In both the Onset and SHEEP studies, as well as a recent systematic review and meta-analysis, regular PA was associated with decreasing risk for AMI after sexual activity, suggesting that the cardioprotective mechanisms may be similar to those operating in ET. The bottom line is that patients should have greater fear of physical inactivity than sexual activity. However, extramarital sex may be more demanding from a CV perspective. According to 1 study, 80% of deaths associated with sexual intercourse occur in hotel rooms “in relations with lovers” rather than wives. It was suggested that alcohol and other changes in the environment may serve to enhance arousal and the associated somatic and cardiac demands.

Chemical Stress
Illicit Drugs
There is considerable evidence to suggest that chemical stressors, including illicit drugs, can increase the risk of AMI in individuals without CHD and, more frequently, in patients with known or occult coronary atherosclerosis. For example, users of cocaine demonstrate a 23.7-fold increase (95% CI, 8.5–66.3) in the risk for AMI in the 60 minutes immediately following cocaine use, compared with self-matched control periods using a case-crossover study design. Similarly, the risk for AMI was elevated 4.8 times versus control conditions (95% CI, 2.4–9.5) in the hour after smoking marijuana. These findings persisted after excluding individuals who simultaneously engaged in other potentially AMI-triggering activities. For both cocaine and marijuana use, the heightened risk seemed to decline rapidly and was not significantly elevated beyond the first hour.

Air Pollution
In recent years, a growing body of epidemiologic and clinical evidence has led to a heightened concern about the consistent associations between active and passive cigarette smoking, short-term elevations in environmental air pollution, and increases in acute CV events, including myocardial
ischemia and infarction, ventricular arrhythmia, heart failure exacerbation, and stroke. Even a very short period of passive smoke exposure has persistent vascular consequences, such as depressed endothelial progenitor cell activity, endothelial dysfunction, and blocked nitric oxide production. According to city-wide smoking bans have unequivocally reduced the incidence of hospitalizations for acute coronary syndromes (ACS). Several environmental air pollutants are of special interest, including carbon monoxide, nitrogen oxide, sulfur dioxide, ozone, lead, secondhand smoke (the single largest contributor to indoor air pollution), and particulate matter (PM), which are principally fine particles < 2.5 μm in diameter. The latter, which is associated with increased hospitalization and mortality from CVD, can be generated from vehicle emissions, tire fragmentation and road dust, industrial combustion, metal processing, construction and demolition activities, residential wood burning, pollutants, molds, and forest fires.

In 2004, the first American Heart Association (AHA) scientific statement on air pollution and CVD concluded that exposure to PM air pollution contributes to CV morbidity and mortality, with specific reference to 3 lines of research. First, population-based studies in numerous cities across the United States and in many cities worldwide have reported an increased mortality rate from cardiac causes on the day following high levels of PM air pollution. Second, several investigations have documented that high levels of PM air pollution are associated with increased admissions to hospitals for angina pectoris and related cardiac causes among Medicare beneficiaries. Third, an especially well-designed study using a case-crossover approach linked high levels of PM air pollution in the greater Boston, MA area to an increased risk for AMI. However, a similar study conducted in Seattle, WA did not find an association between high levels of PM and the occurrence of out-of-hospital primary cardiac arrest.

Recently, the AHA updated its previous statement, based on new evidence linking PM levels of exposure to acute CV events, and concluded that the overall evidence is consistent with a causal relationship between PM < 2.5 μm exposure and CV morbidity and mortality. Possible putative biologic mechanisms linking ambient PM air pollution to AMI and threatening ventricular arrhythmias include abrupt increases in heart rate and blood pressure, fibrinogen, and blood coagulation; arterial vasoconstriction; inflammatory mediators (e.g., C-reactive protein, lipoprotein-associated phospholipase A2); endothelial injury/dysfunction; and decreases in heart rate variability. A meta-regression analysis of potential triggers of nonfatal AMI to calculate population-attributable fractions concluded that air pollution and other well-accepted triggers such as vigorous PA, alcohol, and coffee are of similar magnitude (5%–7%). The authors concluded that omnipresent air pollution exposure and the associated population risks may have considerable public health relevance, highlighting the potential cardioprotective benefits of lowering PM levels to current Environmental Protection Agency standards.

Although regular PA is an important component of a healthy lifestyle, outdoor ET, especially in highly populated urban areas, can increase exposure to unhealthy airborne pollutants. Accordingly, individuals with chronic diseases, the elderly, pregnant women, individuals with known or suspected CVD, individuals with diabetes mellitus, or individuals with pulmonary disease should limit outdoor activities when pollution levels are high. Moreover, runners and walkers should be counseled to avoid main roads, perform ET in the early morning hours (when PM concentrations are lowest), and refrain from performing ET in smog or areas of high traffic congestion. The Environmental Protection Agency provides daily information about ozone and PM levels for > 150 cities.

Psychological Stress

There is mounting evidence to suggest that psychological stressors can trigger the onset of acute CV events. Sympathetic nervous system stimulation emanating from acute stress can lead to a cascade of physiologic responses, including increases in the double product and proarrhythmogenic state, vasoconstriction, worsening endothelial function and injury, platelet activation, and hemostatic alterations. Clinical consequences may include the development of myocardial ischemia, manifested as significant ST-segment depression, angina pectoris, or both. Threatening ventricular arrhythmias, more vulnerable coronary plaques, and the potential for thrombosis. These changes form the milieu for the triggering of AMI and SCD.

Epidemiologic studies have suggested that the occurrence of acute CV events is not random over time; the incidence of AMI and cardiac arrest is highest in the early morning hours, and β-blocker therapy attenuates this morning increase in risk. These data and other population studies now provide support for the hypothesis suggesting that exposures that increase sympathetic activity have the potential to trigger acute CV events. Emotional and stress-related psychological exposures that are associated with an acute, transient increase in the risk for CV events include
earthquakes, sleeping deprivation, sporting events, outbursts of anger, and discrete episodes of anxiety. More recently, natural disasters, such as Hurricane Katrina, and stock market crashes have been linked to a heightened risk of acute CV events.

Earthquakes
Numerous studies have examined the rates of acute CV events soon after earthquakes. Perhaps the most thorough analyses have been those performed after the massive Northridge, CA earthquake that occurred on January 17, 1994. In this unusual situation, millions of people were awakened simultaneously at 4:31 AM by a life-threatening catastrophic event—1 of the strongest earthquakes recorded in a major North American city (Los Angeles County). A review of the county coronor's records for the week before the earthquake, the day of the earthquake, the days after the earthquake, and the corresponding control periods in the 3 previous years suggested that the associated emotional stress probably triggered a disproportionate number of SCDs, from a daily average of 4.6 in the preceding week to 24 SCDs on the day of the earthquake. Only 3 of these cases occurred during associated heavy physical exertion (eg, running from a shaking house or clearing heavy earthquake debris); thus, the remaining deaths were likely triggered by extreme emotional stress. Most of these individuals (96%) had either risk factors for or a history of atherosclerotic CVD. An autopsy on the remaining fatality disclosed HCM. It was concluded that extreme emotional stress may precipitate fatal cardiac events in individuals who are at increased risk for such events.

Alteration of Sleep Patterns
A substantial number of CV events occur early in the night when patients are asleep, followed by a trough before waking. Varied sleep states are associated with modulations in autonomic tone, neuroendocrine function, and inflammatory cytokine release. Disturbed sleep patterns have been associated prospectively with increased CV mortality, and sleep apnea is positively related to AMI, worsome arrhythmias, stroke, congestive heart failure (CHF), hypertension, and structural cardiac abnormalities. Chronic insomnia and sleep debt are also associated with shifts in the pattern of interleukin-6 production and with compensatory increases in sympathetic tone and cortisol production in the evening.

In 2008, investigators described the impact of shifts to and from daylight-saving time on the incidence of AMI, transitions that can disrupt chronobiologic rhythms and influence the duration and quality of sleep. In the spring, there was a 5% to 10% increase in the incidence of AMI for the first 3 weekdays after the transition to daylight-saving time. In the fall, there was a pronounced decrease in AMIs on the Monday after the switch to standard time. The researchers suggested that the most plausible explanation for these findings is the adverse effect of altered sleep patterns on CV health. This adverse effect includes increasing the activity of the sympathetic nervous system, which accelerates heart rate and increases the level of cytokines, immune cells that trigger inflammation and damage arteries.

Sporting Events
Recently, investigators hypothesized that in a country such as Germany, where soccer is particularly popular, World Cup matches involving the national team might arouse heightened emotions sufficient to trigger an increase in the incidence of cardiac emergencies. The Fédération Internationale de Football Association World Cup, held in Germany from June 9 to July 9, 2006, provided an opportunity to test this hypothesis. On days of matches involving the German team, the incidence of cardiac emergencies was 2.7 times that of the control period (95% CI, 2.3–3.0; P < 0.001). However, the incidence was 3.3 (95% CI, 2.8–3.8) and 1.8 (95% CI, 1.4–2.3) for men and women, respectively. Among spectators with CV events on the days of matches played by the German team, the proportion with documented CHD was 47.0%, as compared with 29.1% of individuals with events during the control period. The authors acknowledged, however, that beyond the associated emotional stress, the exact circumstances contributing to the CV events were not known. Superimposed physical exertion, lack of sleep, overeating, heavy alcohol ingestion, cigarette smoking, environmental stressors (eg, temperature, humidity, barometric pressure) and failure to comply with a prescribed medical regimen, may have also played a role. However, other studies have found no increase in CV events on the days of major sporting events.

Anger/Anxiety
On an individual basis, isolated episodes of anger have been reported to immediately precede the onset of AMI in 2 independent studies. In the Onset study, which used 2 types of self-matched control data based on a case-crossover design, the RR of AMI in the 2 hours following an anger episode (categorized as very angry, furious, or enraged) was 2.3 (95% CI, 1.7–3.2). The RR was significantly lower (P < 0.05) among regular users of aspirin (1.4; 95% CI, 0.8–2.6) than among nonusers (2.9; 95% CI, 2.0–4.1). In the SHEEP
study, outbursts of anger were associated with a 9-fold RR (95% CI, 4.4–18.2) of AMI for a 1-hour period after the confrontation.72 In addition, the Onset study demonstrated that discrete episodes of anxiety could also trigger the onset of AMI (RR, 1.6; 95% CI, 1.1–2.2).73 More recent studies have shown that anxiety worsens prognosis in patients with known CHD,82 and that chronic job strain is an independent predictor of recurrent CV events in patients who had a recent AMI.83

Impact of Hurricane Katrina on Acute CV Events

Gautam et al.73 from Tulane Medical Center in New Orleans, LA, reported a dramatic 3-fold increase in patients who presented with AMI during the 2 years following February 2006 (when Tulane reinstated complete on-site cardiac catheterization services post-Hurricane Katrina): the increased incidence of acute CV events persisted for the 2-year period. These data suggest that a natural disaster such as a hurricane may heighten emotional stress and the incidence of AMI over time. At Ochsner Medical Center in New Orleans, LA (which remained open before, during, and immediately after Hurricane Katrina), we analyzed 1500 consecutive symptomatic patients the year before and year after Hurricane Katrina and found no increase in the incidence of ACS or the absolute number of ACS patients treated.84 Nevertheless, patients who presented with ACS to Ochsner after Hurricane Katrina were, on average, 3 years younger (P < 0.01), with a greater proportion of patients < 55 years (P < 0.01) and a smaller proportion of patients > 65 years (P < 0.01).85 Our data, therefore, also suggest that a natural disaster, such as a major hurricane, may selectively increase the risk for AMI and ACS, especially in younger patients.

Impact of Stock Market Declines on Acute CV Events

Fiuzat et al.75 from the Duke Databank for Cardiovascular Disease, evaluated major CV events, including AMI, from January 2006 to July 2009 in patients undergoing angiography for evaluation of CHD. Of 11 590 patients in the study cohort, 2465 had an AMI during this period. During the plummeting stock market values from October 2008 to April 2009, there was a pronounced increase in the AMI rate (P = 0.003), which remained significant after adjusting for seasonal variations in risk (P = 0.02). This was the first report to suggest an association between stock market crashes and the risk for major CV events.

Prevention of Acute Triggers

Given the considerable evidence to suggest that triggering of acute CV events is a legitimate and serious concern, a question remains regarding whether we can attenuate the adverse impact of potential triggers. Toft et al.86 suggested that prevention of acute CV events at times of increased risk can be designated as “triggering acute risk prevention” (Table 2). Their potential therapeutic strategies included prophylactic pharmacotherapies, such as aspirin, ß-adrenergic blocking agents, angiotensin-converting enzyme inhibitors, and statins. Others have also suggested that patients at risk take cardioprotective medications (eg, aspirin, short-acting ß-blockers) before engaging in activities suspected of triggering CV events.87 Additional preventive strategies include counseling habitually sedentary patients with known or suspected CHD to avoid unaccustomed heavy physical exertion and high-risk activities (eg, snow removal) and practices (eg, illicit drug use), implementing anger management interventions, and strict enforcement of environmental regulations/public policy regarding air pollution. However, an increasing number of studies now suggest that perhaps the most powerful intervention to prevent acute CV events from some triggers involves engaging in regular PA and/or

Table 2. Strategies for Triggered Acute Risk Prevention

- Long-term general prevention (ie, lowering baseline CV risk)
- Long-term trigger-specific prevention therapy, especially regular physical activity and exercise training, as well as mental stress-reducing exercises and anger-management interventions
- Modification or avoidance of the trigger, if a person has a low absolute risk of CV events, avoidance is not necessary
- Cardioprotective medications (eg, aspirin, ß-adrenergic blockers, statins, angiotensin-converting enzyme inhibitors, nitrates) that may reduce the link between the trigger and its potential pathophysiologic consequences
- Improvements in medical infrastructure (including improvements and availability of electronic medical records)
- Specific recommendation for population stressors and natural disasters
- Counseling units, habitually sedentary patients to avoid unaccustomed heavy physical exertion and high-risk activities (eg, snow removal)
- Advisement of all patients to avoid prolonged periods of sleep deprivation and illicit drug use (eg, marijuana, cocaine)
- Strict enforcement of environmental regulations/public policy regarding air pollution; limit outdoor activities when pollution levels are high
- Recognition that exercise overdoing is possible, potentially triggering acute CV events in those with known or occult CVD
- Whenever possible, ensuring that immediate emergency assistance (ie, AEDs, CPR-trained personnel) is available

Adapted from Circulation.88

Abbreviations: AED, automated external defibrillator; CPR, cardiopulmonary resuscitation; CV, cardiovascular; CVD, cardiovascular disease.

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ET, which is associated with improvements in CRF, as well as the avoidance of unhealthy behaviors.

In our experience with ET-based, phase 2, cardiac rehabilitation (CR) programs, > 50% reductions in major psychological risk factors, including depression, anxiety, and hostility, were observed. In fact, the improvements in depression were associated with a 3-fold reduction in overall mortality during a 3-year follow-up. Depressed patients with CHD who did not attend CR programs had a nearly 30% mortality during 3-year follow-up, compared with approximately 8% mortality among their counterparts who completed a CR regimen. Whether patients demonstrated modest or moderate improvements in CRF following CR programs, the prevalence of depression fell markedly, as did the mortality risk compared with those who showed no improvements in CRF. More recently, we reported that almost all of the benefits obtained from ET after major CV events were derived from improved CRF in a cohort of patients with high psychosocial stress. Similarly, depressed patients with CHD and HF had a particularly high mortality risk during a 3-year follow-up, which was dramatically reduced following ET-based CR programs.

Collectively, these data and other recent reports highlight the salutary impact of ET-based CR, improved CRF, or both, on psychological risk factors and prognosis in patients following major CV events. It seems likely that similar mechanisms would be involved in prophylactically treating patients with known or suspected CHD who may be exposed to triggers of acute CV events. Two meta-analyses have now shown that regular engagement in ET is associated with a decreased overall risk of CV events by up to 50%, presumably from multiple mechanisms, including antiatherosclerotic, anti-ischemic, antiarrhythmic, antithrombotic, and psychologic effects (Figure 3). Because > 40% of the risk reduction associated with ET cannot be explained by changes in risk factors, a cardioprotective “vascular conditioning” effect has been proposed, including enhanced nitric oxide vasodilator function, improved vascular reactivity, altered vascular structure, or combinations thereof. Another possible mechanism might be through adaptations in autonomic control. As a consequence of endurance ET, sympathetic drive at rest is reduced and vagal tone is increased, with potential cardioprotective effects on blood pressure, thrombosis, and other factors associated with CHD risk.

**Conclusion**

Substantial data indicate that acute CV events may be triggered by emotional stress, heavy PA, sexual activity, population stresses (eg, natural disasters, such as Hurricane Katrina and earthquakes; stock market crashes), sleep deprivation, illicit drug use, and air pollution. Mechanisms for acute triggering may involve biomechanical, prothrombotic, vasoconstrictors, and arrhythmogenic stimuli, mediated in large
Triggers of Acute Cardiovascular Events

part by transiently heightened effects of the sympathetic nervous system.

Following natural disasters, public health strategies should embrace CVD prevention and encourage survivors to implement comprehensive risk reduction interventions, including a program of regular ET. Having a more robust electronic medical record system for clinics, hospitals, and pharmacies, with secondary access points available in the event that the initial access point becomes damaged or non-accessible, would also be helpful.

Although there are many potential interventions to reduce the risk of acute triggers, which have been previously summarized in greater detail, we believe that prophylaxis for many acute CVE associated with triggers should include regular PA/ET, which is readily accessible and beneficial for both physical and mental health.

It is exercise alone that supports the spirit and keeps the mind in vigor.

—Cicero

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Conflicts of Interest Statement
Barry A. Franklin, PhD and Carl J. Lavie, MD have no disclosures relative to this article.

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Barry A. Franklin and Carl J. Lave


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Triggers of Acute Cardiovascular Events


