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Anger, ventricular arrhythmias and sudden death

Abstract

Recent studies provide clear and convincing evidence that anger contributes significantly to the pathogenesis and expression of coronary artery disease. Several investigations have linked anger attribute to several aspects of coronary artery disease including: 1. - Association with coronary risk factors (lipid levels, cardiovascular reactivity and blood pressure) 2. - Coronary disease pathogenesis, morbidity and mortality 3. - Triggering of acute coronary syndromes 4. - Progression of coronary atherosclerosis induced by anger 5. - Ventricular arrhythmias and sudden death. Evidence from prospective epidemiological and clinical studies, supported by experimental studies lend to a casual association between anger and ventricular arrhythmia and sudden cardiac death

Cardiovascular disease and the impact of pshycological factors

Recent studies provide clear and convincing evidence that psychosocial factors contribute significantly to the pathogenesis and expression of coronary artery disease (CAD) (1) This evidence is composed largely of data relating coronary disease risk to five (5) specific psychosocial domains (1-3): 1) depression 2) anxiety 3) personality factors and trait. Anger, the focus of the present study is the most important of them 4) social isolation 5) chronic life stress.

Anger is a relatively stable personality trait that is manifested in the frequency, intensity and duration of the anger experience (4). Persons with high compared with low trade anger have rage and fury more often, more intensely and with longer lasting episodes (4).

Pathophysiological mechanisms underlying the relationship between these entities and coronary heart disease can be divided into behavioral mechanisms (4). Whereby psychosocial conditions contribute to a higher frequency of adverse health behaviors, such as smoking and poor diet, and direct pathophysiological mechanism, such as neuroendocrine and platelet activation (1).

Studies have linked anger attribute to several aspects of CAD including (2,3):

1. Association with coronary risk factors including LDL, HDL, triglycerides levels, cardiovascular reactivity and blood pressure (5,6)
2. The association between anger and CAD pathogenesis, morbidity and mortality (1,2,7)
3. Triggering of acute coronary syndromes onset by episodes of anger (8)
4. Progression of coronary atherosclerosis induced by anger, independent of medication or other risk factors (9)
5. Ventricular arrhythmia and sudden death (10)

Anger and coronary heart disease

The deleterious effects of anger and cardiovascular health are increasingly gaining attention in the research literature (2,3). Evidence for an anger-CAD association has been derived from studies that use different measures of anger, different CAD end points and different study design (2). The prospective association between anger and CAD was described initially by investigators from the Framingham Heart Study (7), who reported that anger independently predicted the eight-year incidence of CAD. More recently, Williams et al (2) reported in the ARIC study that high trait anger was associated with and increased risk for CAD morbidity and death independent of the established biological risk factors. There was a dose-response relation between level of anger and CAD risk (2).

Anger, ventricular arrhythmias and sudden death

The emotional state of anger has been implicated in the precipitation of myocardial ischemia, myocardial infarction and life-threatening ventricular arrhythmias, including sudden cardiac death (8,10-12). In a recent and excellent article, Hemingway et al (13) reviewed evidence from prospective epidemiological and clinical studies, supported by experimental studies, that suggest a link between psychosocial factors such as anger, anxiety, depression, hostility/type A behavior, social supports and work characteristics and ventricular arrhythmias, sudden death and cardiac autonomic function. Overall, 88/96 (92%) of identified published studies investigating psychosocial and social aspects of arrhythmic risk were positive (13). This remarkable consistency across different populations and study designs, lends cautious support to a casual association (13).

Indirect and circumstantial evidence has strongly suggested that psychological stress may be an important factor in the development of malignant ventricular arrhythmias and sudden death (10-13). Sympathetic arousal can trigger arrhythmic events (10). Ventricular tachycardia, like sudden death, occurs more frequently in the morning, at the time of peak of catecholamine level and lowest vagal tone as demonstrated in patients with implantable cardioverter defibrillators (ICDs) (10,14). Ventricular tachycardia occurs more frequently on Monday in working patients with ICDs, suggesting a role for stress (15). In addition, atrial and ventricular ectopy and nonsustained arrhythmias increase during the stress of being in-call in house officers (16) and during exposure to a hostile environment in animals (17). Mittleman et al (8) reported an important association between outbursts of anger and nonfatal myocardial infarction and sudden death. Reich et al (18) determined that anger precede episodes of arrhythmias in 15 % of patients with recurring life-threatening arrhythmias. In a recent article Kovach et al (12) reported that provocation of an intense anger like state in six canines increases the magnitude of T-wave alternans to a greater degree than does a brief period of myocardial ischemia. Superimposition of the anger like response during occlusion-induced myocardial ischemia potentiates the increase in the magnitude of T wave alternans elicited by myocardial ischemia alone, further magnifying the risk of ventricular arrhythmias in this setting (12). The cardioselective beta-1 adrenergic blocker metoprolol blunts the magnitude of this increase in behavioral stress-induced alternans, suggesting that adrenergic factors are, in part, responsible for T-wave alternans during the anger like response (12). However, arousal-induced increases in heart rate are likely to contribute in the setting of myocardial ischemia (12). An alternative explanation is that factors in addition to sympathetic nerve activity contributed to the development of T-wave alternans during the anger

state (12). One likely possibility is that aggressive arousal result in a decrease in cardiac vagal tone. This might conduce to the residual sinus tachycardia as well as to T-wave alternans (12).

The population of patients with ICDs provides a unique opportunity to evaluate the effects of mental stress on human arrhythmias. Lampert et al (14) reported that mental stress (anger recall and mental arithmetic) shortens cycle lengths and renders induced ventricular tachycardia more difficult to terminate. These alterations in ventricular tachycardia characteristics were associated with increased norepinephrine levels, which are known to rise during mental stress, but with no evidence of ischemia on ECG or left ventricular ejection fraction (14). In these patients with defined arrhythmic substrate, anger destabilized the circuit, creating a potentially more dangerous arrhythmia. This suggest that psychological stress may facilitate sudden cardiac death by increasing the lethal potential of arrhythmias in susceptible patients (14)

We examined a series of 57 consecutive victims of sudden death. Among them, we found anger as the most frequent trigger mechanism preceding the final event (19)

Pathophysiologic mechanism of the influences of anger on ventricular arrhythmias and sudden death

The precise biological mechanism and process by which anger influences ventricular arrhythmia and sudden death is yet to be clarified (8,10-14). There are two mainly hypothesis. One possibility is that anger is related to tonic reflex sympathetic-parasympathetic balance (10-13). This may affect arrhythmic risk directly by lowering the threshold for ventricular arrhythmia (13). Another possibility is that heightened sympathetic arousal and catecholamine secretion induced by anger are damaging to the heart and its vasculature and also play a role in the development of atherosclerosis lesions (2,3,13)

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