Journal of the American College of Cardiology Vol. 56, No. 1, 2010

Published by Elsevier Inc.

ISSN 0735-1097/$36.00
doi:10.1016/j.jacc.2010.04.013

QUARTERLY FOCUS ISSUE: PREVENTION/OUTCOMES

Editorial Comment

What Does Heart Disease Have to Do With Anxiety?*

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This issue of the *Journal* features 2 unusual reports concerning anxiety as risk factors for subsequent cardiac disease. I say "unusual reports" because they do not focus on how current anxiety levels are related to current cardiac symptoms. Rather, they focus on the extent to which anxiety symptoms forecast cardiac disease far into the future.

See pages 31 and 38

The meta-analysis by Roest et al. (1) suggests that anxiety symptoms predict incident cardiac events, years in advance of their onset. Combining reports from 20 studies that encompassed approximately 250,000 individuals, the authors found that anxious persons were at increased risk for coronary heart disease (CHD) many years in the future. It was not that an anxious person today had a myocardial infarction tomorrow but rather that anxiety symptoms predicted CHD onset—on average, 11 years into the future. The report describes clearly and succinctly virtually every step of the analysis. Moreover, the findings are not limited to American observations but, rather, included studies from Norway, the Netherlands, Russia, Sweden, Japan, and the United Kingdom. Interestingly, the risk gradient persisted in analyses that adjusted for demographic and risk-promoting (e.g., smoking) behaviors. That is, the future cardiac risks associated with anxiety were not explained by sedentary lifestyle, poor education, and so forth.

The report by Janszky et al. (2) also found that anxiety disorders predicted future coronary disease. The authors examined data from a cohort of approximately 50,000 Swedish men who were examined for military service and who were subsequently followed for an average of 37 years. Although depression was not a predictor for subsequent coronary disease in this sample, anxiety disorders were significantly predictive of subsequent coronary disease, even after controlling for baseline differences in blood pressure, smoking, and the like. That this was a nationwide sample of men reporting for mandated military service examination extends the generalizability of the findings. In addition, the study did not rely just on self-report measures of anxiety. Rather, individuals who reported psychiatric symptoms were secondarily screened by a psychiatrist, and an anxiety diagnosis was made only when the recruit met International Classification of Diseases-8th Revision criteria for anxiety neurosis.

What is one to make of such findings? What is it about anxiety that makes it so toxic to the cardiovascular system? That answer, alas, cannot be provided by these studies. One wonders about mediating physiology. Obvious candidate mediators include sympathetic nervous system activity and various inflammatory markers, but anxiety's physiological reverberations are extensive indeed. Recent studies, for instance, raise the question of whether sleep interruption (a common accompaniment of anxiety) might contribute to diverse manifestations of cardiovascular disease (CVD) (3) or whether diverse mood factors affect endothelial function (4). Alternatively, one wonders about underlying factors common to both CVD and anxiety. The uncomfortable fact is that there is a substantial amount of unexplained variance in the incidence of CHD, despite considering traditional risk factors such as smoking and high cholesterol. New risk factors need to be carefully scrutinized for clinical utility. It might be one thing if the new risk factor is rarely encountered, but if the risk is both statistically significant and commonly encountered, then it might be all the more important to study. In this regard, anxiety disorders are as prevalent as hypertension. The lifetime prevalence of anxiety disorders is approximately 28% (5). Anxiety disorders are a major affliction of the young, but even in older individuals, they are common disorders, with an estimated 12-month prevalence of 10% (6). Regardless of their high prevalence and possible cardiac risk, anxiety disorders are associated with considerable suffering, disability, and impaired quality of life. Their impact on global functioning is roughly akin to that of low back pain or leg ulcers. When anxiety coexists with depression, the corresponding impact on quality of life is even worse, along the lines of the impact of chronic obstructive pulmonary disease (7).

It is odd that anxiety symptoms can be such a strong beacon, lighting the way to future coronary disease decades in advance. Cardiologists are certainly cognizant of anxiety's

*Editorials published in the *Journal of the American College of Cardiology* reflect the views of the authors and do not necessarily represent the views of *JACC* or the American College of Cardiology.

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effects on transient physiology (blood pressure, palpitations, angina). But it is intriguing indeed to note that one single assessment of anxiety casts such a long shadow decades into the future.

In the meantime, how should these observations guide practice? These observations on anxiety come at a time when psychiatry is once again redrawing diagnostic guidelines in the Diagnostic and Statistical Manual. For decades, the Diagnostic and Statistical Manual has differentiated between anxiety disorders and depressive disorders; yet increasingly, clinicians are pointing out that these disorders rarely occur in isolation and that the distress associated with them increases synergistically when both sets of symptoms coexist in the bosom of 1 unfortunate patient.

The studies in this issue of the *Journal* suggest that, by the time patients with symptoms of CHD present themselves to a cardiologist, early-life anxiety might have already taken its toll. Anxiety hurts. It hurts subjectively, and these studies suggest that anxiety hurts physiologically. Physicians are frequently timid about assessing emotional symptoms. It is odd that we thread catheters, ablate lesions, and give rectal exams but are uncomfortable asking our patients about their lives. Assessment tools like the Prime-MD (8) are readily available, with their easy-to-ask questions such as "have you been bothered a lot by 'nerves' or feeling anxious or on edge?" Such questions open the door. Findings such as those described in these articles suggest that including this information in our clinical assessments might be relevant for the diagnosis (and prevention) of CVD.

I well remember my gross anatomy days, when we dissected confidently, intent upon following anatomical structures and disregarding fat tissue as having little meaning or importance. We now appreciate how important fat is, even though it lacks the structural "integrity" of a muscle group. Emotional factors are even harder to grasp. They don't show up, even amorphously in a cadaver but are enormously influential in terms of their impact on functioning. That emotional factors affect the heart is obvious. How they do so and how to mitigate these effects remains to be discovered. These studies did not address treatment strategies, and thus it remains to be determined whether treatments aimed at alleviating anxiety (e.g., medications, psychotherapy, stress reduction, lifestyle alteration) would reduce the cardiovascular risk (Is our fate sealed as soon as we have an early-life anxiety disorder?), but until proven otherwise, the wise clinician might "assume" that treatment of anxiety disorders might have benefits beyond immediate symptomatic and functional improvement.

Acknowledgments

The author thanks Sidney Zisook, Matthew Allison, and Murray Stein for helpful comments.

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Key Words: anxiety ■ coronary heart disease ■ depression ■ meta-analysis ■ myocardial infarction.