Unique Female Indicators of Coronary Heart Disease: Do They Exist?

To the Editor:

In the article “Women’s early warning symptoms of acute myocardial infarction,” Dr Jean McSweeney and coworkers2 renewed the attention to prodromal symptoms of acute coronary events. In 1975, Alonzo et al2 observed that “unusual fatigue and weakness” were the most prevalent symptoms of myocardial infarction, followed by dyspnea and angina. Many authors replicated those findings and added loss of energy, increased irritability, and sleep disturbances to the list. According to McSweeney et al, “it is unknown whether prodromal symptoms themselves predict future [coronary heart disease] events.”1 This statement is in contrast with the fact that 6 epidemiological studies have shown that these prodromal symptoms increase the risk of coronary events in both healthy populations and those with heart disease.3,4 Pathophysiological mechanisms that may underlie this increased risk include viral reactivation, increased inflammation, disturbances in coagulation and fibrinolysis, and hypoactivity of the hypothalamic-pituitary-adrenocortical (HPA) axis (lowered ACTH and cortisol).5 Hypoactivity of the HPA axis activates inflammation. These observations fuel the debate as to whether or not these prodromal symptoms reflect depression (ie, a mental disorder). The frequently observed association between depression and future coronary events might be due to the fact that these prodromal symptoms are markers of inflammation and/or viral reactivation. McSweeney et al2 made a valuable contribution by replicating old observations, including the fact that both sexes present prodromal symptoms in a slightly different way. However, there is no reason to believe that there are unique female indicators of coronary heart disease as they suggest, because the same symptoms have been found to predict coronary events in men.

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Response

We welcome the interest of van Diest et al in our work1 and this opportunity to respond to their comments. We appreciate the contributions of early investigators who demonstrated the importance of prodromal symptoms, including fatigue. It is unfortunate that the scientific community has not pursued this line of research, as there are many unanswered questions and the clinical utility of prodromal symptoms in predicting future coronary events remains unclear.

Van Diest et al take exception with our statement that “it is unknown whether prodromal symptoms themselves predict further [coronary heart disease] events.” They contend that epidemiological studies referenced in their letter have shown that prodromal symptoms increase the risk of subsequent coronary events in healthy populations and those with heart disease. In fact, the number of such studies is limited, each had relatively small sample sizes, and some included only men or small numbers of women. However, the most important limitation of the body of work they referenced, as well as our own, is that these studies are retrospective and/or cross-sectional in nature. As a result, we can only say that prodromal symptoms are associated with risk of subsequent coronary events. It remains unknown whether any group or single prodromal symptom predicts future cardiac events until prospective, longitudinal studies are conducted.

Van Diest et al additionally express concern over what they believe is our suggestion that the prodromal symptoms we reported are unique to women. It is not our contention that fatigue or the other prodromal symptoms we reported are necessarily unique to women. We offered a profile of prodromal and acute symptoms from our findings and discussed this profile in light of common clinical beliefs about coronary heart disease symptoms, beliefs based largely on research conducted in men. Because we only studied women, we are unable to compare prodromal and acute symptoms between men and women. Nonetheless, our findings are important because they provide from a large cohort a profile of prodromal and acute symptoms that women experience with an acute myocardial infarction. This profile indicates that women have prodromal and acute symptoms that differ markedly from what is thought of as “typical” presentation. This is clinically relevant because clinicians rely on typical presentations to increase their index of suspicion for cardiac disease.

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