Letter by Verkissen and Kop Regarding Article, “Risk of Acute Myocardial Infarction After the Death of a Significant Person in One’s Life: The Determinants of Myocardial Infarction Onset Study”

To the Editor:

The death of a significant person can be an important precipitating factor for acute myocardial infarction (MI). Mostofsky et al1 recently reported that grief over the death of a significant person is associated with a marked increased risk of MI in the subsequent days (hazard ratio, 21.1; 95% confidence interval, 13.1–34.1). This finding is consistent with previous prospective investigations showing that adverse life events such as the death of a loved one are associated with increased risk of cardiovascular disease–related mortality.2,3

The interpretation of the findings by Mostofsky et al requires further consideration because of the reliance on case-crossover methodology.4 One caveat is that only 19 of 1985 patients were exposed to the death of a significant other within 24 hours before the onset of MI-related symptoms. This number is too small to support generalization to the general population at risk of MI. Moreover, this particular precipitant occurs in <1% of the patients, which limits the clinical implications of the findings. The wide 95% confidence interval (13.1–34.1) further indicates a lack of precision of the risk estimate. More reliable associations were found when the 24-hour pre-MI period was compared with the 3 to 7 days preceding MI, but with substantially lower risk estimates (hazard ratio, 3.6; 95% confidence interval, 2.0–6.7).

Another limitation concerns retrospective measures that are inherent to the case-crossover design, but problematic when self-report is involved. Reliance on retrospective self-report measures increases the risk of bias by decaying memory for more distant events and search for meaning by patients experiencing an adverse event. Both factors result in an a priori higher likelihood of finding elevated risks for more proximate exposures. The authors selected a control period of 1 to 6 months before the MI because this period “is recent enough that patients are likely to correctly report the loss of a significant person in one’s life” (p 492) without a clear rationale or reference to support this particular interval. Sensitivity analyses with different control periods resulted in a substantially lower risk estimate. Furthermore, no efforts were made to examine the role of emotional states or other triggers that have been documented in previous reports from this study. The exposure mostly involved distant relatives or friends (153/193; 79%) and not direct family, which makes the study vulnerable to recall bias. In addition, no verification of the exposure was obtained (eg, by death certificates or medical chart review of the deceased).

The association between bereavement and cardiovascular risk may indeed have important implications for clinical practice, and the detailed clinical description of the MI is a definite merit of this study. However, death of a loved one is a rare precipitant of MI (<1%). More knowledge about the biobehavioral effect of bereavement on cardiovascular risk is needed. Evidence indicates that grief is associated with a proinflammatory state,5 which is relevant to atherosclerotic plaque instability and subsequent MI. The upcoming trial by Tofler and colleagues investigating the effects of aspirin or β-blockade on hemodynamic and thrombotic changes related to early bereavement will be of substantial interest.

Disclosures

None.

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