Journal of the American College of Cardiology
Vol. 49, No. 17, 2007

ISSN 0735-1097/07/$32.00

CORRESPONDENCE

Letters to the Editor

The Brain and the Heart: Independent or Interactive?

Recently, de Jonge et al. (1) reported that patients in the DepreMI (Depression after Myocardial Infarction) study with incident postmyocardial infarction (MI) depression, but not recurrent depression, have an increased risk of cardiovascular events compared to nondepressed patients. In their excellent and provocative study, they noted that their findings are similar to those reported by Grace et al. (2) in patients from Ontario, Canada, with an acute coronary syndrome, about half of whom had an MI. A previous report from the DepreMI study showed that post-MI patients with significant and increasing depressive symptoms as measured by the Beck Depression Inventory (BDI) are at greatest risk (3).

Studies on the prognostic significance of depression after MI have viewed measures of MI severity like Killip class as confounders. Indeed, de Jonge et al. (1) noted that incident post-MI depression "may be confounded by the severity and consequences of the MI." However, considering a variable only as a confounder may produce misleading results if there is an interaction present (4). In the study by de Jonge et al. (1), patients with incident depression were somewhat more likely to have Killip class >1 than patients without depression. In the previous study from this group (3), patients with significant and increasing symptoms of depression were significantly more likely to have a high Killip class (odds ratio [OR] 4.57).

We re-examined data from the MI patients in the study by Grace et al. (2) to assess whether an interaction between Killip class and BDI scores predicts mortality. Of 443 patients, 58 (13.1%) had only a Killip class >1, and 96 (21.7%) had only a BDI score ≥10; 29 patients (6.5%) had both. The 1-year all-cause mortality of all patients was 5.6% and was similar for patients with neither (4.6%), with only a Killip class >1 (5.2%), or with only a BDI score ≥10 (5.2%). The mortality rate of patients with both was significantly higher (5 of 29, 17.2%, odds ratio 4.31, 95% confidence interval 1.40 to 13.25, $p = 0.01$), even after controlling for age and gender (odds ratio 3.79, 95% confidence interval 1.16 to 12.41, $p = 0.03$).

Higher Killip class is associated with left ventricular diastolic dysfunction (5) that may make patients particularly intolerant of the effects of even mild ischemia or arrhythmia on left ventricular compliance. The increased platelet reactivity and increased sympathetic and diminished parasympathetic neural activity in patients with depression (6) may make them more likely to develop ischemia or arrhythmia after an MI, resulting in the interaction effects observed here. Higher Killip class is also significantly related to the persistence of depression at 1 year (7). It would be interesting to explore whether such an interaction, particularly one between Killip class and incident depression, might explain some of the findings reported by de Jonge et al. (1).

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doi:10.1016/j.jacc.2007.02.022

Please note: The authors gratefully acknowledge the Heart and Stroke Foundation of Ontario and the Samuel Lunenfeld Foundation of Toronto, Ontario, for funding this research. Dr. Grace is supported by the Ontario Ministry of Health and Long-Term Care. Dr. Ziegelstein is supported by NIH grant R21NS048593.

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Reply

In reply to the letter by Dr. Ziegelstein and colleagues, we found that incident but not nonincident postmyocardial infarction (MI) depression was associated with new cardiovascular events and that these effects were not confounded by MI severity (1). Dr. Ziegelstein and colleagues suggested that perhaps an interaction between depression and MI severity might explain our findings. This is an intriguing question that we are happy to consider.