

More Aggressive Treatment for Depression?

TO THE EDITOR: In the April 2009 issue of the *Journal*, Robert M. Carney, Ph.D., and Kenneth E. Freedland, Ph.D. (1) noted that depressed patients in an intervention group who did not experience treatment response had a higher risk of late mortality (which was described as incidence of death ≥ 6 months following acute myocardial infarction) compared with patients who responded to treatment. The authors pointed out that this relationship was not significant in the usual care arm of the study. They also reported that in the intervention group, there was a lack of improvement, although subjects received 6 months of aggressive treatment. However, only approximately 15% of patients in the usual care group received any form of nonstudy treatment during the first 6 months. Among patients in the usual care arm who did not experience improvement, less than 15% had received any treatment for their depression.

Drs. Carney and Freedland stated that it is not immediately evident why major depression that is not responsive to treatment is associated with a higher risk of cardiac-related mortality and morbidity and concluded that major depression may warrant more aggressive treatment.

It seems to me likely that less improvement of depression would tend to lead to more aggressive treatment. Perhaps, at least in part, the explanation for why the greater risk of cardiac-related morbidity and mortality is “not immediately apparent” is because we do not wish to think that our efforts at treatment, even aggressive treatment, might have harmed our patients. Psychotropic drugs certainly do affect other organ systems—and not always beneficially. A more apt conclusion might be that less aggressive treatment is better, at least with regard to the treatments that were used in the study, while we search for different treatments, a search that the authors rightly advocate.

Reference

1. Carney RM, Freedland KE: Treatment-resistant depression and mortality after acute coronary syndrome. *Am J Psychiatry* 2009; 166:410–417

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The Effects of Treatment-Resistant Depression and First-Ever Depression on Mortality Following Acute Coronary Syndrome: Interactive or Independent?

TO THE EDITOR: Drs. Carney and Freedland (1) presented a fascinating review on treatment-resistant depression and mortality following acute coronary syndrome. As a possible mechanism explaining the association between treatment-resistant depression and mortality in acute coronary syndrome patients, the authors suggested the presence of first-

ever depressive episodes, which are associated with both treatment resistance and increased risk of cardiac events.

We therefore explored the association between treatment-resistant depression, first-ever depression, and cardiovascular prognosis using data from the Myocardial INfarction and Depression Intervention Trial (MIND-IT), a multi-center randomized controlled trial on the treatment of post-acute coronary syndrome depression. We previously reported (2), using Cox regression analysis, that patients who did not respond to treatment had an unadjusted hazard ratio of 4.89 (95% confidence interval [CI]=1.08–22.10) for new cardiovascular events relative to patients who responded to treatment. Testing the hypothesis of Drs. Carney and Freedland, we adjusted for the presence of first episodes. However, adjusting hardly affected the association (hazard ratio=4.42; 95% CI=0.97–20.10), which is indicative of no support for the hypothesis. An explanation may be that in our sample first episodes were not associated with new cardiovascular events or treatment resistance. However, they are associated with both new cardiovascular events (hazard ratio=4.12 [95% CI=0.53–31.77]) and with treatment resistance (odds ratio=2.57 [95% CI=0.82–8.03]). The number of patients in each subgroup and their associated risk of cardiac events are shown in Table 1.

Our tentative conclusion is that first depressive episodes and treatment resistance are two independent risk factors for worse outcomes that do not interact but add up independently. Our results do not support the hypothesis that first depressive episodes would underlie the association between treatment-resistant depression and negative cardiac outcomes. Since cell numbers in our study were very low, however, we feel that caution is warranted and no firm conclusions can yet be determined.

We agree with Drs. Carney and Freedland that treatment-resistant depression is likely a marker of an underlying cardiac risk factor associated with treatment resistance in patients with coronary heart disease and that researchers should investigate this factor. One possible risk factor that is often overlooked is treatment nonadherence, which is associated with both depression and cardiac prognosis. Treatment nonadherence is one of the reasons for treatment resistance in depressed patients, and it is likely that a patient who is nonadherent to antidepressant treatment is also nonadherent to cardiac aftercare.

References

1. Carney RM, Freedland KE: Treatment-resistant depression and mortality after acute coronary syndrome. *Am J Psychiatry* 2009; 166:410–417
2. de Jonge P, Honig A, van Melle JP, Schene AH, Kuyper AM, Tulner D, Schins A, Ormel J: Nonresponse to treatment for depression following myocardial infarction: association with subsequent cardiac events. *Am J Psychiatry* 2007; 164:1371–1378

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