The brain and the heart: the twain meet

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This editorial refers to 'Relationship between left ventricular dysfunction and depression following myocardial infarction: data from the MIND-IT† by J.P. van Melle et al., on page 2650

'Oh, East is East, and West is West, and never the twain shall meet...'

Rudyard Kipling
The Ballad of East and West

A little more than a decade ago, we formed a group—comprised of both cardiologists and psychologists—to study post-myocardial infarction (MI) depression, stimulated by the paucity of information on the care of patients with this condition at the time and by the seminal work of Frasure-Smith et al.1 reporting a link between depression and increased mortality after MI. When we discussed this topic and our research with other cardiologists, most had a similar response, 'Of course a patient after an MI is depressed, he’s got a bad heart. You’d be depressed too!' Cardiologists typically noted that it seemed natural to them that a person with a sick heart would be depressed. They explained away the relationship between depression and increased post-MI mortality by saying that those with the weakest hearts were the highest risk patients and that, quite naturally, having a weak heart would make someone sad. If anything, they argued, we were foolish to be looking for other pathways linking emotional disturbance to poor outcome. To paraphrase a popular recent American campaign phrase, they told us rather bluntly 'It’s the heart, stupid.' Perhaps somewhat haughtily, we replied that they just did not get it, and that depression is a problem with neurotransmitters in the central nervous system. And, somehow, that disturbance in the brain was the problem; we just needed to figure out how. After all, the brain and the heart are separate, and never the twain shall meet.

The study by van Melle et al.2 causes us to re-think this view. The authors assessed 1989 patients in the Myocardial Infarction and Depression—Intervention Trial (MIND-IT) for symptoms of depression (using the Beck Depression Inventory), ICD-10 depressive disorder (by a standardized psychiatric interview), and left ventricular ejection fraction (LVEF) (by echocardiography). The authors report that the severity of left ventricular (LV) dysfunction is significantly related to the severity of depressive symptoms during the hospitalization. In a multivariate analysis, LV dysfunction was strongly associated with BDI scores, even after controlling for demographic factors, coronary risk factors, co-morbidities (including diabetes mellitus), and Killip class. A relationship was also observed between LVEF measured at the time of the initial hospitalization and both depressive symptoms and ICD-10 depressive disorder during the follow-up period from 3 to 12 months post-discharge.

This study adds considerably to the literature in this area and should cause us to refine our view of post-MI depression. The findings should cause us to think about the pathogenesis of post-MI depression and to re-consider the potential mechanisms that link depression and increased mortality.

The van Melle study is not the first to look at the relationship between LVEF and post-MI depression, but it is the largest and the one that considers it the most carefully. In the early report by Frasure-Smith et al.,1 depression and LVEF were not associated. In that study of 222 patients, approximately one in five (20.3%) who had an LVEF ≤35% was depressed on the basis of a modified version of the National Institute of Mental Health Diagnostic Interview Schedule (DIS) for major depressive episode. In comparison, 14.1% of patients with an LVEF >35% were depressed (P = 0.21). In the same patient cohort,3 a BDI score ≥10, consistent with symptoms of at least mild-to-moderate depression, was found in 34.9% of those whose LVEF was ≤35% and in 29.4% of those whose LVEF was >35% (P = 0.43). In another report,4 358 depressed patients from a subsample of the Enhancing Recovery in Coronary Heart Disease (ENRICHD) trial were compared with 408 patients who met ENRICHD medical inclusion criteria but were not depressed. About one in four patients from both the depressed and the non-depressed groups was found to have an LVEF <40% (23.9% in the depressed group and 22.4% among those not depressed, P = 0.90). In a similar, but not identical, cohort of patients,5 the LVEF was 45.8% among 307 depressed patients and 46.8% among 366 non-depressed patients (P = 0.39). Strik et al.6 found no relationship between LVEF and depression (assessed by the Symptom Check List-90), among 318 men post-MI. In a separate study of 206 men and women, these authors...
again found no significant relationship between LVEF and depression assessed by structured interview 1 month after an MI, although only 31% of non-depressed patients had an LVEF <50% when compared with 44% of depressed patients.7 Our group reported that in 204 post-MI patients, LVEF <35% was more common among those with a BDI score ≥10, although not significantly so, during the initial MI hospitalization when compared with those with a BDI score <10 (36.7 vs. 23.3%, P = 0.12).8 Interestingly, there was no relationship whatsoever between LV dysfunction and DSM mood disorder (i.e. major depression, dysthymia, or both); an LVEF <35% was found in about one of every four patients, whether they had a mood disorder or not.8 Our group also reported9 that among patients 65 years of age and older, 33% of those with an LVEF <35% had some form of depression (either a BDI score of 10 or more or a DSM mood disorder); although this was about twice the prevalence of depression found in those with an LVEF ≥35%, the difference was not significant (P = 0.07).

So, why the difference between the study by van Melle et al.2 and these other reports? One difference is that van Melle et al. divided LVEF into four categories, whereas most other studies1,3,4,6–10 dichotomized this variable. As a rule, statistical power is reduced as quantitative variables are less precisely categorized. Perhaps most important, however, is the size of the present report; this is the largest cohort of patients to date in which both LV function and depression were examined. As van Melle et al. note, most studies of post-MI depression did not assess—or at least did not report—LVEF. In addition, most of the others which did were small, having studied typically 200–300 patients.1,3,6–9 Interestingly, when Frasure-Smith et al. (who reported no relationship between LVEF and depression in two early studies1–4) examined a larger number of patients, they found that LVEF was significantly lower in those with depression when compared with those without.10 The reports of Carney et al.4,5 are the only studies with more than 200–300 patients that evaluated LVEF and found no relationship with depression. Although van Melle et al. speculate that this may have some relationship to the absence of low social support in the control group in the Carney study, it has to be said that the reason for the negative findings of these studies is unclear. What is clear, as pointed out by van Melle et al.,2 is that several of the smaller studies that reported no significant association of LVEF and depression reported trends and may have been underpowered to detect a difference.

Whatever the reason, the present study2 is very important, because it suggests a point that heretofore was certainly not clear, namely, that poor LV function and depression are related in patients who have sustained an MI. The finding should cause us to pause. Maybe the rather terse and somewhat dismissive response of our cardiology colleagues a decade ago was right after all. Maybe it is silly to believe that depression is a disorder of the brain, and MI a disorder of the heart, and never the twain shall meet. After all, a relationship between the brain and the heart is abundantly clear in the medical literature. Patients with subarachnoid hemorrhage, for example, may develop profound electrocardiographic changes and may even present with new LV dysfunction and biochemical evidence of myocardial injury.11 Similar findings have been observed in patients with stroke12 and, most recently, with severe emotional stress.13

The findings of van Melle et al.2 should cause all people who do research in the area of post-MI depression to think about the potential nature and direction of the relationship among poor LV function, depression, and increased post-MI mortality. Hopefully, this study will be of interest both to providers of cardiovascular healthcare and to those who focus chiefly on mental health, stimulating the two groups to work together to provide better care for patients with post-MI depression. At the very least, the findings should force us to ask why two seemingly unrelated conditions should be related, and what mediators or common biological pathways could link the two. For this study puts everyone on notice that, as far as the brain and the heart are concerned, clearly the twain have met.

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References