REFERENCES


APPENDIX

For a table outlining the comparison between DTB time assessment in HQA and NCDR data based on: 1) patient selection; 2) definitions for determining specific time points; and 3) data abstraction, quality checks, and standards in 2005, please see the online version of this article.

Letters to the Editor

Throw the Window Out the Door

Recently, Dickens et al. (1) reported that neither depression before myocardial infarction (MI), assessed retrospectively, nor depression 12 months post-MI is associated with cardiac mortality up to 8 years after MI. They hypothesized that the association between depression and post-MI mortality may be limited to a defined window of time post-MI and concluded that “defining the window when intervention for depression might benefit survival is crucial.” However, neither current evidence nor their results support a search for a “window” of this nature.

To demonstrate the existence of a “window,” it would be necessary to show that studies measuring depression during some window period find an association with mortality, whereas studies measuring depression outside of that period do not. In fact, many, but not all, studies that assess depression soon after an MI report an association with mortality (2,3). Studies that have assessed depression both pre-MI and soon after an MI disagree whether recurrent depression (4) or incident depression (5,6) predicts mortality. Similarly, it is unclear whether depression measured 6 months or longer post-MI is associated with mortality (4,7), although there is evidence that the longitudinal trajectory of post-MI depressive symptoms may be related to mortality (7) or to cardiovascular events (8).

The results reported by Dickens et al. (1) do not clarify this issue. Surprisingly, among their results, they found that patients who had depression both pre-MI and 12 months post-MI had a significantly lower mortality risk (p = 0.03; 0 deaths in 53 depressed patients vs. 32 in 387 nondepressed patients). The authors did not, however, report baseline data for patients with and without depression that might have helped explain this result. The finding was no longer significant in the multivariate model (p = 0.97), but this may be because of the modeling strategy used in their study. Dickens et al. (1) used discharge medications as one of the measures of MI severity, although the rationale for this is unclear. Since discharge medication is associated with survival after an MI and may itself be influenced by depression (9), this unjustified modeling approach is problematic. The authors preselected variables for their regression model based on associations with cardiac death and overfit the model by including far too many predictors per outcome event (78 cardiac deaths, 25 predictors, ratio = 3.1 to 1). Both practices are known to produce spurious results that are not likely to generalize to other samples (10). Indeed, such a low ratio of outcomes to predictors produces coefficient estimates that are either less than one-half or more than 2 times actual values more than 50% of the time (11).

In summary, it is not clear how existing evidence or the results of the study by Dickens et al. (1) supports searching for a “window” when intervention for depression might affect survival. Instead, more work is needed to develop a better understanding of the longitudinal trajectory and natural history of depression in patients with MI.

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REFERENCES


We are grateful for the comments of Dr. Thombs and colleagues. In our recent study we set out to examine the effects of the timing of assessment of depression on mortality after myocardial infarction (MI) (1). We showed that depression before MI, whether chronic or not, does not increase cardiac mortality. This was a surprise to us because we anticipated that pre–MI depression, which was associated with chronic social difficulties (2) and likely to be persistent (3), would be related to increased mortality after MI. We have published this paper to make it clear that this is not the case. Furthermore, we found that depression present 12 months after MI did not predict subsequent mortality. We acknowledge that our study alone does not provide direct evidence for a window of effect for depression predicting increased mortality. However, if we contrast our findings with those studies showing an association of depression in the days or weeks after MI with post–MI mortality, it seems likely that it is those people who develop depression in the period immediately after MI that are at increased risk of cardiac mortality. Patients developing depression after an acute cardiac event have been shown to be at increased risk of dying in previous studies (4,5), and we are now looking at this particular question in our own data. Our negative findings for depression cannot be dismissed as resulting from our statistical methods. We accept the point that the number of independent variables included was large, but our finding was the same in the uncontrolled (univariate) comparison. Furthermore, our findings remained stable if we used backward elimination of variables, so that the number of independent variables in the final model was few (hazard ratio [HR] for depression = 0.86, p = 0.60) or if we performed our analyses using fewer variables (e.g., age, gender, educational level, degree of cardiac dysfunction, and revascularization procedures (4), HR for depression = 1.02, p = 0.94). Our findings also remained negative when we did not control for medications at discharge (HR for depression = 0.87, p = 0.62). Our finding that subjects with depression at both baseline and 12 months had an apparent survival advantage is confusing and counterintuitive. We can clarify here that, compared with the remainder, this group was more likely to be female gender (49% vs. 28%) and younger (mean age 45.3 vs. 60.8 years). Controlling for age and gender alone eliminated the association between persistent depression and subsequent mortality (p = 0.97).

The fact that depression that predates the MI and persists through the post–MI period does not predict mortality is extremely important. It supports the suggestion that it is not depression alone that is having the adverse impact on survival but that some additional factor interacts with depression to create this effect (6,7). Rather than ignoring the heterogeneity in previous findings, future research should continue to examine possible reasons for this heterogeneity as it may identify vulnerable subgroups and explain how and why depression has this effect on survival.

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REFERENCES

Eliminating Plaque Angiogenesis

We have read with great interest the article by Kolodgie et al. (1) focusing on elimination of intraplaque angiogenesis. It seems that neovascularization within the vessel wall plays an important role in plaque destabilization, and it is a determinant of vulnerability. The beneficial effect of statins in patients with atherosclerotic disease is well established. This effect goes beyond lipid lowering, because statins also have other effects, which is why statins are considered pleiotropic. One of these is its effect on angiogenesis. We recently presented that patients on statin treatment have reduced intraplaque angiogenesis in their carotid endarterectomy specimens when compared with patients not receiving this kind of drug (2). This finding provides a new insight to the statins’ pathophysiologic mechanism of action. The fact that it was a