Depression and cardiovascular disease: a complex relationship

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A large literature attests to the strong relationship between depression and cardiovascular disease. A number of studies have shown an association between depression and coronary mortality raising the obvious question as to whether depression is a causative factor contributing to coronary heart disease, a consequence, or both. This area of study where cardiac and psychosocial scientists have joined only relatively recently is a very difficult one. Nevertheless, modern paradigms for coronary heart disease have certainly now been extended beyond purely biomedical concepts to include the important broader dimensions of psychosocial, and socioeconomic aspects which are of fundamental and increasing importance. Likewise, in many instances recent health strategies have acknowledged the importance of interaction amongst these different dimensions through providing a broader definition of health than formerly and emphasising the importance of intersectoral collaboration to achieve population and personal health goals.

Firm conclusions from previous psychosocial and cardiac literature have often necessarily been limited by a number of considerations including publication bias, subject selection and response rates. Studies of association, often retrospective, are inevitably highly confounded by the interaction between depression and disease severity, symptoms and functional status, comorbidities, treatment and compliance. Further confounding may result from interaction with other psychosocial factors, particularly psychosocial interactions and social support. Needless to say correction for all these factors can only be relatively crude at best. Methods of measurement are numerous and poorly standardized with questionable validity across different cultures and social support structures making data comparisons difficult.

A multidimensional complexity is now evident which cannot be reduced to any simple algorithm and within which the application of group data to individual case management requires considerable flexibility and judgement.

This edition of the journal contains two excellent studies both of which are helpful in defining more clearly the relationship between depression and coronary mortality. Both studies were prospective cohort studies although in different groups and settings with different methods of assessment. The study by Stewart et al., was an extended substudy of the well known LIPID study, a clinical trial of cholesterol-lowering with pravastatin, involving more than 9014 patients in Australia and New Zealand. From 36 LIPID study centres, 1222 patients were randomly selected and invited to participate in the substudy with 1130 (93%) completing the General Health Questionnaire. Importantly the Questionnaire was administered at least 5 months from the time of previous hospital admission with acute myocardial infarction or unstable angina. No subsequent association was found between depressive symptoms and fatal or nonfatal cardiovascular events during a median follow-up period of 8.1 years after adjustment for the effects of symptoms, socioeconomic variables and life events on mood.

In discussion of this study the authors note concordance of their findings with eight of ten previous large cohort studies in which no association between depression and mortality after myocardial infarction has been shown after adjustment for confounding factors. A broader systematic review including smaller studies and more varied patient groups has suggested an association between depressive symptoms and coronary events but with several possible sources of bias acknowledged. Also in most previous studies, assessment of depression was generally in close proximity to hospitalization, whereas most importantly in this study, assessment was more than 5 months after hospitalization in a clinically stable patient group. A minor qualification is the possibility that such a clinical trial population as this may not fully represent the general range of patients. Subjects who...
consented serially to participation (for both the main study and subsequent substudy) may have been more motivated, psychologically robust and more compliant with treatment and healthy lifestyle recommendations from within the supportive clinical trial setting than those who declined. Although participation rates for the LIPID main study and this substudy were very high, it is still possible that the small group excluded may have had particular risk characteristics which could have influenced analyses had they been included. An interesting subsidiary finding of more depressive symptoms in Australian patients than in New Zealand patients is not discussed (perhaps in the best interests of maintaining present excellent trans-Tasman relationships).

The study by Luukinen et al.4 targeted all persons aged 70 years or more in a defined area of North Finland (n=1113) of whom 915 (82%) completed the Short Zung Depression Rating Scale questionnaire. The mode of death was examined through death certificates for the following 8 years during which time 52% of the subjects died. Of all deaths 8% were classified as sudden cardiac deaths and 22% non-sudden cardiac deaths. After multivariate analysis adjusting for clinical variables, depressive symptoms remained a significant predictor of sudden cardiac death and total mortality but not of cardiac mortality, non-sudden cardiac death and non-fatal myocardial infarction. Removal of users of antidepressants did not change the main results. Interestingly, depression emerged as an equally strong predictor of sudden cardiac death as male gender, history of myocardial infarction and presence of diabetes mellitus. The widely discussed difficulty of definition and reliable classification of sudden cardiac death was obviated to a great extent by the relatively high autopsy rate with good agreement between clinical and autopsy coronary heart disease diagnoses. The limitation of the Rating Scale is acknowledged, having being validated for screening purposes in the elderly but not in the assessment of severity of depression. A plausible mechanism of association involving altered cardiovascular autonomic regulation with increased vulnerability to arrhythmias is suggested.

Together these studies are valuable additions to the literature which provide clearer guidance and reassurance for the rehabilitation of cardiac patients on one hand and further rationale for detection and treatment of depression in the elderly together with ongoing research on the other.

References