Casscells et al. have shown ex vivo significant heterogeneity within the plaques. Secondly, the atheromatous plaque is considered as solid rather than a biologic material with completely different properties being difficult to be interpreted by the Newton’s Law which is valid for inorganic solids and liquids. Physics suggest that any dynamic change of the measurement conditions, most important of all being the blood flow, reduces the heat transferred to the sensing element (thermistor) leading to underestimation of plaque temperature. Therefore, by blood flow obstruction this limitation is eliminated and in addition the influence of friction locally is avoided.

In the clinical setting, we need to know whether an increase of temperature is indicative of a hot plaque with inflammatory involvement. The current data from experimental and clinical studies showed that there is correlation between thermal heterogeneity and macrophage content. A discrepancy however between ex vivo and in vivo plaque temperature measurements is observed. The ‘cooling effect’ of blood flow leading to underestimation of the temperature measurements is a potential interpretation for this discrepancy. In our study there is a criticism from the authors regarding the complete attachment of the thermistor to the atherosclerotic plaque and the possible effect of normal saline at 37 °C used for balloon inflation that may have affected the measurements. However, in a study from our institution with a balloon-thermography catheter, which ensures the full attachment of the thermistor to the plaque by inflation of the balloon by carbon dioxide, similar results were found without the mentioned possible limitations. Additionally, from our experience temperature is not increased in all lesions, in which complete interruption of flow is accomplished. Thus by flow interruption more reliable temperature measurements are obtained. Diamantopoulos et al. recently presented their experience in an atheromatous porcine model and they observed that plaques with an increase of temperature during blood flow interruption had higher macrophage concentration. This study documented that by complete interruption of flow the real temperature of atheromatous plaque is approximated and the inflammatory substrate is identified. Interestingly, these results do not support the hypothesis that flow reduction threatens the accuracy of intravascular thermography, but instead that by flow obstruction we approximate the real plaque temperature. Finally, we have to recognize that temperature measurements are influenced by several biological and mechanical factors and we need more studies in our search for the pathophysiology insights of plaque heat generation.

References

Konstantinos Toutouzas
Eleftherios Tsiamis
Manolis Vavuranakis
Christodoulos Stefanadis
Department of Cardiology
Athens Medical School
Hippokration Hospital
9 Tepeleniou str., 15454
Paleo Psychico
Athens, Greece
Tel.: +30-1-671-8694
Fax: +30-210-6457230/7585039
E-mail address: cstefan@cc.uoa.gr
(Christodoulos Stefanadis)

Probable need for psychiatric treatment is not the same as depression

The title of the article by Stewart et al., in the November 2003 issue, implies that depression was assessed. However, the authors used the 30-item General Health Questionnaire with a cut-point ≥5 to identify those with “depressive symptoms,” who are elsewhere in the manuscript referred to as the "depressed." The GHQ is intended to screen primary care patients for probable need for psychiatric treatment. It is non-specific indicator of a variety of anxiety and mood disorders. It is not a measure of depressive symptoms or depression. Second, previous publications by the authors used a cut-point of 10 on this same measure to identify "GHQ cases of depression". This mixing of terminology and shifting of cut-points is troubling. There are similar problems with the literature review. Table 5 represents "cohorts studies published before March 2003 that reported at least 30 fatal events." While the number of events is important for covariate control, the measures used and the timing of their administration are as important. Four of the studies listed did not use recognized measures of depression (Stewart et al.1 and Jenkinson et al., 1993, Carinci et al., 1997 and Denollet et al., 1996). One assessed patients up to three years before an MI (Berkman et al., 1992), one assessed cardiac rehabilitation patients (Denollet et al., 1996), and one assessed patients taking amiodarone (Irvin et al., 1991). Three studies adjusted for covariates that are highly related to depression (Type-D personality (Denollet et al., 1996), social support and fatigue (Irvin et al., 1999), and perceived global health (Stewart et al.)) and thus not true confounders. By doing so these studies explained away depression’s impact on outcomes. In this context, the statement that “in eight of the 10 studies listed, there was no statistically significant association between depression and mortality after adjustment for potential confounders” is misleading.

This article presents a secondary analysis of a randomized trial of an agent that had a significant long-term impact on cardiovascular morbidity and mortality. However, no mention is made of treatment group. Because of potential interactions between pravastatin and baseline factors in predicting cardiovascular outcomes, it is inappropriate to analyze these data without considering the role of
treatment group. More specifically, we recently observed a significant interaction between statin use and major depression in C-reactive protein (CRP) levels. While depression was linked to increased CRP in stable cardiac patients not taking statins, the relationship did not exist in the presence of statins. This suggests that links between psychological factors and cardiovascular outcomes may be moderated by lipid lowering medications. If this is the case, the current overall results, showing no significant link between GHQ scores and cardiac events, may mask an important relationship in the patients on placebo.

In summary, improved understanding of the relationship between depression and outcomes in cardiac patients depends on objective and accurate reporting of both positive and negative studies. Unfortunately, the article by Stewart et al., failed to present a balanced view of the literature and did not provide informative findings.

References


Nancy Frasure-Smith
Department of Psychiatry
McGill University
Montreal, Que., Canada
Present address: Montreal Heart Institute, Research Centre
5000 Belanger
Montreal, Que. H1T 1C8, Canada
Tel.: +1-514-376-3330x3024
Fax: +1-514-376-0979
E-mail address: nancy.frasure-smith@mcgill.ca

François Lépérance
Department of Psychiatry
University of Montreal
Montreal, Que., Canada

Robert M. Carney
Director
Behavioral Medicine Center
Washington University School of Medicine
St. Louis, MI, USA

Kenneth E. Freedland
Department of Psychiatry
Washington University School of Medicine
St. Louis, MI, USA


Bias in the evaluation of evidence linking depression to cardiovascular mortality: reply

We wish to respond to questions raised by Frasure-Smith and colleagues regarding our study, and to document differences in our interpretation of the evidence linking depression to increased mortality after myocardial infarction. In Table 5, we summarised previous studies selecting an objective criterion (<30 fatal events). For all established cardiovascular risk factors, an association with adverse outcomes has been observed across diverse populations. We therefore did not exclude studies because their subjects were participants in a clinical trial or cardiac rehabilitation programme, or because of usage of various medical treatments. We acknowledge that individual studies have limitations, but we are concerned that exclusion of studies from review on subjective grounds would bias evaluation of the evidence. The emphasis given to small positive studies, multiple reports from a single patient population, and studies reporting data only from selected subgroups, has also been misleading.

In our study we used the General Health Questionnaire (GHQ), which was originally designed to detect general psychiatric morbidity in the community. There is, however, a close correlation between scores on the GHQ and scores on questionnaires designed to detect depression alone. In a systematic review of case-finding instruments for depression, the GHQ’s sensitivity and specificity were similar to those of other self-administered “depression” questionnaires including the Beck Depression Inventory. In a previous analysis we assessed changes in mood over time among patients randomised to pravastatin versus placebo. The “Likert” method was used to score the GHQ for this purpose because it has a more normal distribution of responses. In the current study we wished to identify “cases” of depression at baseline, and therefore used the standard method to score the GHQ and prespecified the widely used “case” threshold of 5. Our results and conclusions were, however, similar irrespective of the method used to score the GHQ.

With respect to timing, mood assessed during hospitalisation may be strongly influenced by the severity and consequences of the cardiac event. On the other hand, “usual mood” (even when assessed before the myocardial infarction) might be important if “depressive symptoms” predict an increase in mortality months or years later.

Our previous study of patients in a randomised clinical trial provided evidence that psychological symptoms are not influenced by treatment with pravastatin or by cholesterol reduction. Furthermore, there was no evidence of a treatment interaction in the association between depression and outcomes. In the current study, therefore, we presented our findings for all participants combined rather than by subgroup. We are sceptical about the use of subgroup analysis to evaluate possible complex interactions, particularly when such analysis is not prespecified and when the biological mechanism is unclear.

To assess whether an association between depression and increased cardiovascular mortality is causal, it is important to adjust for confounding. Depressive symptoms are more likely with poor health and fatigue due to physical illness such as heart failure, but the associated increase in cardiovascular mortality may be explained by mechanisms independent of depression. Similarly, lack of social support may increase cardiovascular mortality by other mechanisms such as poor access to medical care.

Large randomised clinical trials provide more reliable evidence than observational studies. In the only such study completed to date (ENRICHD), the intervention had a modest impact on depression, but did not reduce mortality or reinfarction (300 versus 299 events). Our interpretation of current evidence concerning the hypothesis that depression increases cardiovascular mortality after myocardial infarction evidently differs from that of Frasure-Smith and colleagues.

References

3. Stewart RA, Sharples KJ, North FM et al. Long-term assessment of psychological...