Stress

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'Perceived Stress and Risk of Ischemic Heart Disease *Causation or Bias?'*

There were no significant prospective links between stress and objective evidence of heart disease, and, weak prospective links between stress and subjective heart disease. In theory, both the objective and subjective heart diseases observed in this study are caused by the same disease mechanisms. Either they are in fact caused by different mechanisms or, there is no causal relationship between stress and the disease mechanism.

This was a large prospective study with 18 years follow-up. Participants (n=19,698) were selected at random from the general population and given a physical examination. Risk factors were assessed by questionnaire. A second examination took place 6 years later. On this occasion participants (n = 11,839) were asked to report their experience of stress (degree and frequency). Eighteen years later the medical records were checked for first ischaemic heart disease event between first examination and close of research period for all (actually 99.9%) of those who undertook the second examination.

Baseline risk factors included in the analysis were gender, age, education level, income, cohabitation status, physical activity, alcohol consumption, BMI, tobacco smoking and parental history of myocardial infarction. Blood pressure cholesterol and glucose were recorded but not included in the analysis as they could be intermediaries [mediators] between stress and heart disease [if so, to correct for them would be eliminate the effect of stress on heart disease risk].

Mean age at second examination was 56. 44% of the population reported medium stress levels, 8% reported high stress levels. The high stress group were more likely to be female of low income, living alone and to be physically inactive.

During 18 years follow-up there were 1,795 hospital discharges and 521 diagnosed deaths due to first ischaemic heart disease (IHD) event. Age at first IHD event was 74 for women and 70 for men, on average. There were 1,001 cases of myocardial infarction, 407 cases of angina pectoris and 908 due to other ischaemic heart disease.

High stress compared with low stress was associated with a hazard ratio of 1.23 (1.01–1.51) for IHD in women and 1.25 (1.00 –1.56) in men when based on total first IHD event.

When analysing sub categories of IHD there was no association between high stress and myocardial infarction (MI) but a clear association between high stress and angina in both women and men:

- women (HR = 1.83; 1.15–2.91) and
- men (2.14; 1.32–3.47).

results for MI did not vary with time from baseline [results were consistently statistically insignificant], results for angina were statistically insignificant within two years of baseline, becoming significant at 12 years and remaining so [but weaker] at 19 years.

Stress levels were not reassessed during the follow-up period.

Comment
In our view a difference in the rate of diagnosis of angina pectoris is likely, to a large extent, to be subjective. People who attach a dramatic meaning to chest pain are more likely to seek medical care and to have their fears supported, at least initially, by medical practitioners. This would in part explain why the results for MI and angina are so clearly different when both, according to the usual theories, have very similar pathogenetic bases. Alternatively, the pathogenesis of angina and MI might actually be different, one responding to stress and the other not.

There is very weak evidence of reverse causation in these findings. In our view, after 10 years, the case for reverse causation would be extremely weak.

Studies of stress over long periods find that reported stress levels do not vary much for the majority. This would encourage the use of one-off measurements and, given that atherosclerosis is a slow

process, this approach would seem to be justified. However, it could be that those with highly variable experiences of stress are at a different degree of risk of atherosclerosis to everyone else.
Self reported chest pain, and diagnoses based principally upon it, should not be used as outcome measures in research which is supposed to assess the proposal that stress causes ischaemic heart disease. Objective evidence of heart disease is required. The lack of association between stress and MI counts very heavily against there being a risk.