EDITORIAL

Depression with CHD triples risk of death

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PATIENTS WITH DEPRESSION ARE MORE LIKELY TO DIE. THE STRONGEST EVIDENCE LINKS DEPRESSION with cardiac mortality (cardiac SMR 1.5-2.0), but there is also growing evidence of an increase in all cause mortality, particularly among elderly patients.[1]

A prospective cohort study has found further evidence that a combination of CHD and depression is potentially lethal. There appeared to be a synergistic effect: participants with both conditions were much more likely to die than those with just one of them.[2]

The Whitehall II study has followed up 10,308 civil servants since 1985. Between 2002 and 2004, the 5,936 remaining participants, mean age 61, were asked to complete the CES-D depression screening questionnaire.

CHD was identified by clinical examination and from medical records using international criteria. Depression was defined as a CES-D score ≥ 16. Data on all cause mortality was collected over an average of 5.6 years.

During the follow-up period, 170 patients died. After adjustment for sex and age, the hazard ratios for all-cause mortality were 1.67 for participants with only CHD (95% CI: 1.05-2.66, p<0.05), 2.10 for those with only depression (95% CI: 1.47-3.13, p<0.001) and 4.99 for those with both conditions (95% CI: 2.89-8.62, p<0.001).

'CHD plus depression is a dangerous combination'

After full adjustment for socioeconomic, biological, behavioural and iatrogenic factors, participants with CHD alone were no longer at increased risk of death. However, participants with depression alone remained at increased risk (HR 1.78), and participants with both conditions were three times more likely to die from all causes and four times more likely to die from CVD.

Although the CES-D is a sensitive screening tool, it has a low positive predictive value at the standard cut-off point of 16, so most of the participants with a score ≥ 16 would not have had major depression. Nevertheless, there is some evidence that patients with subthreshold depression may also be at increased risk of death.[1]

The wide confidence interval reflects the small number of participants with both CHD and depression (108). There were only 15 all cause and five cardiovascular deaths within this group, so the study was underpowered to give a precise estimate of the increased risk.

The increased cardiac mortality in depressed patients could be mediated directly e.g. through activation of the HPA axis, or indirectly, through the effects of poor health behaviour. The Whitehall data suggest a direct effect but this is not consistent with the findings of a larger study which implicated physical inactivity.[3] In any case, only 28% of the deaths were due to CVD. There are several possible explanations for the link between depression and noncardiac mortality:

- Suicide: however, if the cohort were representative of the national population,[4] only four suicides would have been expected
- Confounding: it is a pity that, apart from diabetes, the researchers did not adjust for chronic conditions
- Unrecognised physical illness e.g. occult cancer may present with depressive symptoms
- Poor health behaviour
- Direct causation e.g. reduced cancer survival due to immunosuppression[1]

It would be a mistake to regard this study as an endorsement of screening for depression among CHD patients. Investigators have so far been unable to show that treatment of depression can reduce mortality among CHD patients.[5] Moreover, we need to elucidate the pathway from depression to death if we are to offer effective treatment: it is possible that exercise therapy is more effective than antidepressants for this group.[3]

A randomised controlled trial of managed care for older patients with major depression did achieve a significant 45% reduction in the hazard of death. Intriguingly, the benefit was almost entirely due to a reduction in cancer deaths.[6]

CHD plus depression is a dangerous combination. We should be alert to the possibility of depression in CHD patients and we must treat it effectively. Structured group physical activity may be the treatment of choice, and case management may improve outcomes.

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