AETIOLOGY

Self reported depressive symptoms were associated with an increased risk of mortality from stroke


Question
What is the association between self reported depressive symptoms and death from stroke?

Design
29 year cohort study of participants in the Alameda County Study.

Setting
Alameda County, California, USA.

Participants
6676 of 6928 adults (mean age 43 y, 54% women) for whom complete data were available from the Alameda County Study which began in 1965. Participants were 17–94 years of age and did not have a history of stroke at baseline.

Assessment of risk factors
Depression was measured by the Human Population Laboratory Depression Scale. Other risk factors included years of education, alcohol consumption, body mass index (BMI), smoking, and self reported hypertension and diabetes.

Main outcome measure
Stroke mortality was verified by death certificates.

Main results
39 of 969 (4%) participants who reported ≥5 depressive symptoms and 130 of 5707 (2%) non-depressed participants died from stroke. Participants who reported depressive symptoms were older, less educated, and more likely to be hypertensive, diabetic, or smokers (on self report) than those who did not report mood symptoms. Self reported depressive symptoms were associated with increased stroke mortality in unadjusted analyses (p = 0.005) and in analyses adjusted for age, sex, and race (p = 0.006); the association remained when the results were further adjusted for education, alcohol consumption, smoking, hypertension, diabetes, and BMI (p = 0.02) (table). The association also remained when patients with cardiovascular disease or those who died within the first 3 years were excluded from the analysis. Time dependent covariate models, which incorporated changes in reported depressive symptoms and risk factor levels during follow up, reported a similar but non-significant association between self reported depressive symptoms and increased stroke mortality.

Conclusion
Self reported depressive symptoms were associated with an increased risk of mortality from stroke.

Association between self reported depressive symptoms and stroke mortality at 29 years

<table>
<thead>
<tr>
<th>Depression measure</th>
<th>Hazard ratio (95% CI)</th>
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<tr>
<td>1 point increase on Human Population Laboratory Depression Scale</td>
<td>1.09 (1.03 to 1.15)</td>
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<tr>
<td>≥5 self reported depressive symptoms</td>
<td>1.54 (1.06 to 2.24)*</td>
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*Hazard ratio adjusted for age, race, sex, education, alcohol consumption, smoking, hypertension, diabetes, and body mass index.

Source of funding: National Institute on Aging.

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Abstract also published in ACP Journal Club.

Commentary
Everson et al document an association between depressive symptoms at baseline and risk of death from stroke over the next 29 years. A similar association between depressive symptoms and later cardiovascular disease has also been shown in large epidemiological studies. After excluding people who initially reported heart disease, those reporting depressive symptoms had an increase in age adjusted risk of stroke mortality by 70%. The magnitude of the effect increased with the number of reported depressive symptoms.

Depression is known to be associated with various vascular risk factors which could confound the link with stroke related mortality. In this sample, the effect of conventional risk factors appeared to be small, and controlling for these made little difference to the observed effect. However, these risk factors were elicited by self report only, leaving the possibility of residual confounding. In addition, several potentially important clinical and biochemical risk factors were not considered. Atrial fibrillation, cholesterol, clotting markers, and apolipoprotein E have been linked with both vascular disease and mood disorder. Further studies will be required to elucidate whether these factors have any role in this relation or whether depression is an independent vascular risk factor.

If the results of Everson et al’s study are correct, and depressive symptoms influence stroke mortality independent of established risk factors, how can this be explained? Unfortunately, Everson et al did not measure stroke events, but rather stroke deaths. We cannot therefore distinguish between the effect of depression on the onset of stroke and the effect of depression on risk of mortality after stroke. This may be important because evidence suggests that depression is associated with higher rates of mortality in healthy older or bereaved people and in those with chronic illness. Considering vascular illness, evidence of a relation of depression to mortality after myocardial infarction is conflicting and after stroke is weak. Until it is clear that the effect shown here is neither because of confounding risk factors nor a function of mortality alone, it is premature to consider stroke as a specific outcome of depression.

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