Failure to improve during first 6 months of treatment and depression severity predict increased mortality in people with ACS and MDD

QUESTION

Question: In people with acute coronary syndrome (ACS) and major depressive disorder (MDD), what features of MDD are associated with long-term mortality?

Population: 369 adults with ACS meeting criteria for MDD who participated in the SADHART randomized controlled trial comparing safety and efficacy of sertraline versus placebo.

Setting: SADHART study was conducted in 44 outpatient centres in 7 countries; study participants were recruited between April 1997 and December 1999

Prognostic factors: Baseline depression severity: Hamilton Depression Rating Scale (HAM-D) score of less than 18 *vs* 18 or higher, onset of MDD before or after index ACS event, previous episodes of MDD; 8 months of sertraline treatment, mood improvement during 6-month placebo or setraline treatment (Clinical Global Impression-Improvement subscale, CGI-I) and left ventricular ejection fraction (LVEF <0.30 vs ≥0.30). Remission was defined as a CGI-I score of 1 (very much improved), which is similar to a Ham-D score of 7 or less. Cox proportional hazards regression models were used to analyse effects of risk factors at time of death and were controlled for age and sex.

Outcomes: Vital status. Mortalities were collected 5 years after the final participant completed the trial. Evidence of the last date on which participants were known to be alive or date of death (office visits, laboratory testing or documented telephone calls) was provided by site personnel from the SADHART study. For US participants, if evidence that the patient was alive in the previous 18 months was unavailable, names were submitted to the National Death Index, at the US Department of Health and Social Services.

METHODS

Design: Randomized controlled trial.
Follow up period: 6.7 years (median).

MAIN RESULTS

Vital status information was recorded for 361 of the 369 SADHART participants (978%); a total of 75 (20.9%) of participants died during follow-up. Severity of depression during hospitalization for ACS was significantly associated with mortality (HAM-D ≥18 *v* HAM-D < 18; HR 2.71, 95% CI 1.51 to 4.85, p < 0.001). Baseline MDD severity of HAM-D ≥ 18 was associated with increased long-term mortality (HR 2.30, 95% CI 1.28 to 4.14, p < 0.006). Increased mortality was not associated with previous episodes of MDD, regardless of whether the first episode of MDD occurred before or after hospitalization. Participants with substantial mood improvement (CGI-I score 1–2 at 6 months) regardless of treatment had significantly lower mortality at follow-up, compared with participants with little or no improvement in depression (15.6% died v 28.4%; HR 2.39, 95% CI 1.50 to 3.81, p < 0.001). When controlling for both hypertension and LVEF (participants whose depression did not improve had a lower LVEF and were more likely to have a history of hypertension), participants with substantial mood improvement still had significantly lower mortality at follow-up compared with participants with little or no improvement in depression (HR 1.76, 95% CI 1.04 to 2.97, p = 0.04). Cox regression models revealed that greater improvements in mood (lower CGI-I scores) were associated with decreased mortality (p < 0.001).

CONCLUSIONS

Mortality more than doubled in participants whose MDD had failed to improve during the 6 months following ACS, and in those with severe MDD measured shortly after hospitalization.

ABSTRACTED FROM

Glassman AH, Bigger JT Jr, Gaffney M. Psychiatric characteristics associated with long-term mortality among 361 patients having an acute coronary syndrome and major depression: seven-year follow-up of SADHART participants. *Arch Gen Psychiatry* 2009;**66**:1022–9.

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COMMENTARY

The depression and heart disease story is still revealing itself. Despite a threefold increased mortality in those who are depressed after a myocardial infarction, compared to those who are not depressed, we still do not know why this occurs or what can be done about. Treating people who are depressed after a heart attack does not seem to alter this risk.

What the authors did in this paper was a cohort study of patients enrolled in the SADHART trial of sertraline versus placebo. They were able to follow up 361 of the original 369 patients for nearly 7 years to see what factors were associated with mortality. Of the original cohort, 1 in 5 had died at follow-up. What they found was that, contrary to expectations, a previous history of depression did not affect the risk but that baseline severity of depression and lack of improvement in the condition were both associated with increased mortality. The increased risks are clinically important, especially in those patients who did not improve in the 6 months after their myocardial infarction; 28% of these patients died after 7 years, compared to 16% of those who improved. These increased risks applied to both the antidepressant and placebo arm.

The explanation for the decreased mortality associated with improvement possibly lies with increased adherence to treatment in those who recover quickly from their depression. In this study those patients whose depression improved after 6 months were slightly but significantly more likely to be adherent to their antidepressant or placebo medication, and their adherence to medication started to improve simultaneously with a decline in depression.

The finding that a failure of depression to improve after a myocardial infarction is associated with increased mortality is important, as this is a risk factor that health professionals can modify. In patients who have had a heart attack, whose depression is failing to respond to treatment after a few weeks, health professionals need to treat the depression more intensely. This may mean combined drug and psychological therapies; advice about lifestyle factors, especially involving behavioural activation; and more frequent appointments and referral to mental health specialist services. Not doing this substantially increases patients' risk of dying.

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Competing interests None.

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