Treating low perceived social support and depression after myocardial infarction does not increase event-free survival

Q **Does treating depression and low perceived social support (LPSS) with cognitive behaviour therapy and, where indicated, a selective serotonin reuptake inhibitor (SSRI) within 28 days of myocardial infarction (MI) reduce risk of subsequent MI and death?**

METHODS

Design: Randomised controlled trial.

Allocation: Concealed.

Blinding: Open for clinicians and patients; outcome assessors and data analysts blinded.

Follow up period: 29 months (mean).

Setting: 73 hospitals associated with 8 clinical centres in the USA; recruitment October 1996 to October 1999, study completed April 2001.

Patients: 2481 people (1084 female, 1397 male) with MI in the previous 28 days, diagnosed with major or minor depression or dysthymia (ENRICHD modified DSM-IV criteria: symptoms present ≥14 days or ≥7 days provided at least 1 prior episode of major depression) or LPSS (ENRICHD Social Support Instrument (ESSI)), or both. Exclusions: MI following a coronary intervention; receiving psychotherapy for depression; major comorbidity; participation in another research protocol. Ongoing treatment with antidepressants was a criterion for exclusion before April 1998 but was altered at that time to allow inclusion of people on antidepressants for >14 days whose depression had not improved.

Intervention: The treatment group received CBT for depression. For participants with LPSS, CBT was supplemented with techniques adapted from social learning theory and other psychotherapeutic support trials. Group sessions were initiated after at least 3 individual sessions. Treatment group participants who, after 5 weeks, showed a poor response (reduction of <50% in Beck Depression Inventory (BDI) scores; Hamilton Rating Scale for Depression scores >24) were considered for pharmacotherapy. Participants were initiated on sertraline (50 mg/d to 200 mg/d) and if necessary changed to another SSRI or nortriptyline. Behavioural intervention continued for ≤6 months, group therapy for an additional 12 weeks, and pharmacotherapy for 12 months. The control group received usual care.

Outcomes: Non-fatal recurrent MI and all-cause death. Change in BDI and ESSI scores at 6 months were secondary outcomes.

Patient follow up: 93%.

MAIN RESULTS

At 29 months, there was no significant difference between the treatment and usual care groups for the primary outcome (recurrent MI or death: 24% v 24%; hazard ratio 1.01; 95% CI 0.86 to 1.18). At 6 months, (see table) the treatment intervention improved psychosocial outcomes compared with usual care (p<0.001). These differences were not maintained at 30 months for BDI or at 42 months for ESSI scores.

CONCLUSION

Although the intervention may improve depression and LPSS after MI in the short term, it does not decrease the risk of recurrent MI and death.

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Commentary

The rationale for the ENRICHD trial was clear and convincing. Coronary heart disease (CHD) is a major cause of morbidity and mortality; depression and low perceived social support are clearly associated with worse outcome in patients with CHD; and there are treatments of proven effectiveness for depression. An intervention that can reduce depression and improve perceived social support should, therefore, reduce cardiac mortality following myocardial infarction (MI).

The ENRICHD investigators carefully developed an intensive, multi-faceted, individually tailored intervention. They then sought to demonstrate that it would significantly reduce mortality in the largest trial of psychological therapy ever conducted. Disappointingly, the intervention did not affect their primary outcome of death or non-fatal infarction.

Debate is underway on the explanation for this negative result, and is focusing on the power of the trial.[1] The smallest of the four ISIS trials had over 16000 participants,[2] and cardiology has led the way in the design and implementation of large RCTs. Despite randomising 2500 patients, it is possible that the ENRICHD trial was underpowered. The estimate of effect size was probably optimistic, due to significant improvements in the ''usual care'' management of depression in the years since the trial was designed. The results may therefore not represent evidence of no effect, and this is supported by significant improvements in depression and perceived social support at six months in the intervention group.

So how should cardiology and primary care services manage post-MI patients who might be depressed? There is increasing interest in the development of effective systems of care for depression. This trend has mirrored that in cardiac rehabilitation, and in both settings there is now good evidence for the provision of systematic and structured care.[3][4] Integrating management of depression with cardiac rehabilitation makes good clinical sense. Despite the ENRICHD trial, the effective identification and treatment of depression remains an important part of rehabilitation following MI.

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1 Frasure-Smith N, Lesperance F. Depression—a cardiac risk factor in search of a treatment. *JAMA* 2003;**289**:3171–3.
2 ISIS-1 Collaborative Group. Randomised trial of intravenous atenolol among 16 027 cases of suspected acute myocardial infarction: ISIS-1. *Lancet* 1986;**ii**:57–66.
3 Gilbody S, Whitty P, Grimshaw J, *et al.* Educational and organizational interventions to improve the management of depression in primary care: a systematic review. *JAMA* 2003;**289**:3145–51.
4 Giannuzzi P, Saner H, Bjornstad H, *et al.* Secondary prevention through cardiac rehabilitation: position paper of the Working Group on Cardiac Rehabilitation and Exercise Physiology of the European Society of Cardiology. *Eur Heart J* 2003;**24**:1273–8.

Table Mean BDI and ESSI scores at baseline and 6 months

	Mean BDI score				Mean ESSI score			
	Baseline	6 months	Change	Mean treatment difference (95% CI)	Baseline	6 months	Change	Mean treatment difference (95% CI)
Treatment	15.7	8.2	−7.6	−2.8 (−3.7 to −2.0)	23.1	26.3	3.2	1.5 (1.0 to 2.0)
Usual care	15.7	11.0	−4.7		23.3	25.0	1.7	