

## SCIENTIFIC LETTER

# Depression, indirect clinical markers of cardiac disease severity, and mortality following myocardial infarction

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Based on observational epidemiological research, depression following acute myocardial infarction (MI) is considered an independent risk for subsequent mortality.<sup>1</sup> This is despite the fact that in the only large scale randomised control trial to date, the successful treatment of depression yielded no relative advantage in terms of survival.<sup>2</sup> Furthermore, not all prospective observational studies have found an association between depression following MI and mortality.<sup>3</sup> In such studies, depression would not appear to be related to conventional indices of disease severity. Thus, where associations between depression following MI and mortality appear, they could reflect the confounding of depression with disease severity.<sup>4</sup> We have discussed elsewhere<sup>5</sup> why depression and disease severity might be correlated in some studies but not in others; we have argued that it depends on the accuracy of patients' perceptions about the severity of their condition.

Although some, but by no means all, observational studies have attempted to control statistically for disease severity, the measures employed have been varied and all are imprecise indices of overall cardiac status. Thus, even in studies<sup>1</sup> where positive associations between depression and mortality emerge and also withstand, in terms of statistical significance, adjustment for some measures of disease severity, residual confounding remains a possibility. The present study sought to determine, from a range of possible clinical markers, the strongest predictor(s) of mortality at various time points following the index MI.

## METHODS

Clinical details of the 288 MI patients studied have previously been reported.<sup>3</sup> Depression was measured in-hospital (2-15 days post-MI) by the Beck depression inventory; scores  $\geq 10$  indicated mild to severe symptoms of depression and on this basis, 89 patients (30.9%) were classified as depressed. Disease severity was assessed using various indirect markers.<sup>3,5</sup> Killip class (dichotomised as no evidence of heart failure versus evidence of heart failure) measured the severity of cardiac dysfunction on a four point scale based on chest x ray, heart and lung sounds, and signs of cardiac shock. The

Peel index (dichotomised as scores  $< 17$  v  $\geq 17$ ) is a prognostic device encompassing age, sex, cardiac history, degree and severity of shock, presence and severity of heart failure, cardiac rhythm, and ECG abnormalities. Length of initial hospital stay (dichotomised as  $< 8$  v  $\geq 8$  days), prescription of warfarin at discharge, history of previous MI, type of MI (ST elevation MI or non-ST elevation MI), and whether or not patients were thrombolysed were also included as further proxies of disease severity. Survival status was determined at 4, 12, and 36 months. Logistic regression analyses were undertaken for cardiac and all cause mortality. Only those variables that consistently predicted mortality in bivariate analyses were included in subsequent multivariate analyses.

## RESULTS

In bivariate analyses, Killip class, Peel index, length of hospital stay, and prescription of warfarin at discharge predicted both cardiac and all cause mortality at 4, 12, and 36 months. Depression predicted neither cardiac nor all cause mortality at any time point, nor was it correlated with any of the disease severity markers. Table 1 presents the outcome of multivariate analyses of the four disease severity markers emerging from prior bivariate analyses. Although Killip class emerged as a significant predictor of cardiac and all cause mortality at 12 and 36 months from multivariate analyses, prescription of warfarin at discharge proved to be a significant predictor throughout, and the strongest single predictor of outcome, with the exception of all cause mortality at 12 months. A composite disease severity variable was also constructed from the four markers: possession of  $\geq 3$  constituted a substantial risk for mortality at all three time points for both cardiac and all cause mortality (table 1). This composite measure conferred a sevenfold increased risk of both cardiac and all cause mortality at all three time points.

## DISCUSSION

It would be wrong to interpret the results for warfarin as signalling that warfarin treatment represents a major health

**Table 1** Dichotomised indices of disease severity (Killip class, Peel index, length of initial hospital stay, prescription of warfarin at discharge, and composite disease severity index) as predictors in multiple logistic regression analyses of cardiac and all cause mortality following acute MI

Variable	4 months		12 months		36 months	
	Cardiac (n=22)	All cause (n=25)	Cardiac (n=27)	All cause (n=31)	Cardiac (n=33)	All cause (n=38)
Killip class	2.90 (0.75 to 11.14)	3.24 (0.86 to 12.19)	4.32 (1.18 to 15.80)	4.96 (1.38 to 17.85)	4.43 (1.41 to 13.88)	3.95 (1.40 to 11.16)
Peel index	1.02 (0.26 to 4.05)	1.82 (0.56 to 5.93)	1.98 (0.64 to 6.07)	2.53 (0.91 to 7.03)	1.24 (0.41 to 3.79)	1.63 (0.60 to 4.42)
Length of hospital stay	4.10 (0.50 to 33.44)	4.64 (0.58 to 37.26)	2.56 (0.54 to 12.00)	3.04 (0.66 to 14.03)	2.16 (0.59 to 7.91)	2.72 (0.76 to 9.71)
Warfarin at discharge	6.63 (1.87 to 22.46)	4.54 (1.36 to 15.16)	4.75 (1.49 to 15.18)	3.57 (1.15 to 11.08)	6.80 (2.26 to 20.48)	4.95 (1.71 to 14.30)
Composite severity index	7.16 (2.41 to 21.23)	9.20 (3.29 to 25.77)	7.08 (2.68 to 18.68)	7.93 (3.18 to 19.77)	7.24 (2.96 to 17.71)	7.48 (3.22 to 17.40)

Data are represented as odds ratios and 95% confidence intervals.

risk in this context. Rather, warfarin prescription and, accordingly, our findings reflect the astute judgements being made by cardiologists about how ill their patients are—for example, by the presence of concomitant atrial fibrillation, intracardiac/systemic/venous thromboembolism, severe cardiac dysfunction, and other symptoms. Very few studies of depression and mortality following MI have adjusted for prescription of warfarin at discharge and none, to our knowledge, have adjusted for a composite measure of disease severity of the sort developed here. Since no single precise measure of cardiac disease severity exists, including the individual measures employed in this study, composite indices may be the best way to capture how ill patients are. Our findings suggest that greater credence could be given to inferences that depression is an independent risk factor for mortality in MI patients if analyses were adjusted for various drug treatments, such as warfarin, and preferably for the sort of composite index of disease severity developed here, given its consistently large association with mortality.

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## IMAGES IN CARDIOLOGY

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### Endophthalmitis, pneumonia, and a heart murmur

A 50 year old woman was admitted to the emergency room because of loss of vision in her right eye. She was a healthy woman until three weeks earlier when she developed fever and cough. A seven day course of amoxicillin was prescribed, but she continued with the symptoms. The day before admission, she developed a red eye.

On physical examination, her temperature was 38°C. The conjunctiva of her right eye was injected. She presented peripheral stigmata as petechiae, splinter haemorrhages, and Janeway lesions. A systolic murmur was heard along the left sternal border and apex. Crackles were present in the left lung. There was notable peripheral oedema.

She had anaemia and thrombopenia, and a long prothrombin time. Chest x rays showed a consolidation in the upper left lobe. A transthoracic echocardiogram was performed showing a vegetation attached to the posterior leaflet of the mitral valve and severe

mitral regurgitation. The ophthalmologic evaluation disclosed bilateral endophthalmitis.

Blood cultures were negative, but diplococcus was found in the vitreous sample, and the urine was positive for *Streptococcus pneumoniae*. After diagnosing pneumococcal pneumonia with endocarditis and endophthalmitis, antibiotic treatment was started; however the patient's condition deteriorated so mitral valve replacement was undertaken. The patient died 10 days later from septic shock.

*S pneumoniae* is a rare cause of endocarditis, accounting for only 1–3% of cases. Its prognosis is worse than *S viridans* endocarditis. Endocarditis is the most common source of endogenous bacterial endophthalmitis, and streptococcus is the most common organism.



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