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The Hospital Anxiety and Depression Scale depression subscale, but not the Beck Depression Inventory-Fast Scale, identifies patients with acute coronary syndrome at elevated risk of 1-year mortality.

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The hospital anxiety and depression scale depression subscale, but not the Beck depression inventory – fast scale, identifies acute coronary syndrome patients at elevated risk of one-year mortality

Brief depression scale predicts mortality in ACS

Objective: To investigate the use of short-form depression scales in assessing one-year mortality risk in a national sample of acute coronary syndrome (ACS) patients.
Methods: ACS patients (N=598) completed either a Hospital Anxiety and Depression Scale depression subscale (HADS-D) or the Beck Depression Inventory - Fast Scale (BDI-FS). Mortality status was assessed at one-year.
Results: Cox proportional hazards modelling showed that patients depressed at baseline (combining HADS-D and BDI-FS depressed cases) were more likely to die within one year (HR 2.8, 95% CI 1.4 to 5.7, p=0.005), even when controlling for major medical and demographic variables (HR 4.1, 95% CI 1.6 to 10.3, p=0.003). Scoring above threshold on the HADS-D predicted mortality (HR 4.2, 95% CI 1.8 to 10.0, p=0.001), but scoring above threshold on the BDI-FS did not (HR 1.8, 95% CI 0.6 to 5.6, p=0.291).
Conclusion: The HADS-D predicted increased risk of one-year mortality in ACS patients.

Introduction

Acute coronary syndromes (ACS) are an important mode of cardiovascular diseases, and include unstable angina and acute myocardial infarction (AMI) [1]. Morbidity and mortality post-AMI are determined by a number of independent risk factors, including extent of coronary artery disease, infarct size, severity of left ventricular dysfunction, and depression [2-6]. Depression following ACS has been found to be an important risk factor for further coronary events, with even low levels of depression having a significant effect on mortality risk [7-9]. A recent meta-analysis has concluded that post-AMI depression is associated with a 2- to 2.5-fold increased risk of impaired cardiovascular outcome [10]. Similar findings have been found for patients with all types of coronary artery disease [11,12].

The identification of depression in ACS patients is therefore a concern for clinicians. Early diagnosis and active management of depression may improve cardiac morbidity and mortality [13]. A recent review found that between 8 to 45% of patients who have suffered an AMI exhibit symptoms of major depression [5]. The mechanisms by which depression increases risk of post-AMI mortality are not fully understood. It is feasible that some of the negative association between depression and outcome reflects poorer cardiac function post-event. Alternatively, depression may have a causal association with worse outcomes. Physiological explanations have been proposed, including increased sympathetic activity, arterial atherosclerosis, and heart rate variability [14]. One important psychosocial factor is that depressed patients are less likely to adhere to recommendations for secondary prevention [15,16]. A recent meta-analysis across a range of medical conditions showed that non-adherence to medical treatment is three times more likely to occur with depressed than non-depressed patients [17].

Assessment methods for depression have traditionally involved either clinical interviews conducted by experienced mental health professionals or lengthy self-completion questionnaires [3,18]. These preclude routine assessment of depression in most cardiac settings. If evidence showing the effects of depression on mortality is to translate into information useful for the care of individual patients, depression assessment needs to become a routine aspect of coronary care. Brief screening instruments for depression exist but have not been tested for their sensitivity and predictive validity in the cardiac setting. The present study assessed the feasibility of using short-form depression scales in an acute setting to ascertain the impact of self-assessed depression on one-year mortality post-ACS. Two short-form scales were assessed: the Hospital Anxiety and Depression Scales depression subscale (HADS-D) [19] and the Beck Depression Inventory - Fast Scale (BDI-FS) [20].

Method

Sample/Participants

Hospitals

The methodology has been described in detail elsewhere [21]. Briefly, all Irish centres admitting patients with suspected ACS to intensive/coronary care units were invited and agreed to participate in a general ACS survey. Hospitals were randomly assigned to distribute the either HADS-D (n=19) or the BDI-FS (n=19) instruments (one hospital did not participate in the depression assessment aspect of the survey). Ethics committee approval was obtained from individual centres/areas as appropriate [22].

Participants/procedure

Hospitals recruited consecutive suspected ACS patients, until 25 suspected cases of AMI were admitted. Where considered appropriate by staff, patients were invited to participate in the depression assessment and in a one-year follow-up survey (results to be reported elsewhere). Patients thus completed the depression scales 2-5 days after admission. To participate, patients provided written informed consent, and completed either a HADS-D (n=316) or BDI-FS (n=282). This paper analyses data from patients discharged with confirmed ACS, who completed a depression scale, and whose mortality was assessed at one-year (Fig 1). Demographic and clinical data were collected. Primary care physicians were contacted one year later to ascertain patients' vital status, and date of death was obtained from a national births, marriages and deaths registry.

Fig 1 about here

Depression measures

The 14-item HADS consists of two 7-item scales for depression (HADS-D) and anxiety (HADS-A) [19]. Each item has a four-answer option format. Scores range from 3 for most severe to 0 for absence of problem in that area. The HADS was developed to identify psychological disturbances in general medical and non-psychiatric samples. Using the optimal cut-off score of >7, the HADS-D can indicate probable cases of depression with an average sensitivity and specificity of approximately 0.80 [23]. This threshold (>7) was used in the current study for the HADS-D.

The 7-item BDI-FS is a shortened version of the BDI [24], and the two versions are highly correlated with high internal reliability [25]. The BDI-FS is a screening instrument that minimises the possibility of yielding spuriously high estimates of depression for patients with medical problems by focusing on cognitive (as distinct from physical/somatic) symptoms of depression. Each item has a four-

answer option format. Scores range from 3 for most severe to 0 for absence of problem in that area. A BDI-FS cut-off score of >3 yields a sensitivity and specificity of 0.82 for detecting major depressive disorders [26]. This threshold (>3) was used in the current study.

Both scales are designed not to be contaminated by clinical factors, as they focus on cognitive aspects of depression. Both can be easily completed within five minutes.

Statistical analysis

Data were analysed using robust variance estimation methods with STATA/SE 8.2 to account for the clustering of patients within hospitals. This method was used as patients in the same hospital will be more similar than patients randomly sampled from the entire population, leading to under-estimation of standard errors and confidence intervals and a greater than 5% rate of false positive (type I) errors. Robust variance estimation adjusted standard errors (and therefore confidence intervals and significance tests) for the homogeneity introduced by cluster sampling. Differences between the HADS-D and BDI-FS samples were assessed using the χ^2 test or t-tests as appropriate. Logistic regression predicted odds-ratios (OR) for event occurrence. Cox proportional hazards regression predicted hazard ratios (HR) for one-year mortality. Personal and medical variables were analysed as univariate predictors of mortality (having private health insurance was used as a proxy for socioeconomic status, length of hospital stay after admission to coronary care was used as a proxy for severity of ACS) and predictors were combined to determine the overall HR for depression. One-year mortality for the HADS-D and BDI-FS samples were calculated independently, but due to sample size, only age and sex were used as covariates when analysing the HADS-D and BDI-FS samples separately. To combine data for the overall sample, patients scoring above threshold on either the HADS or BDI-FS were defined as depressed. In order to compare depression scales, dummy variables were created for the total sample (i.e. scoring above cut-off for BDI-FS or not – all participants who completed a HADS-D were given a score of zero in this variable; and vice versa). Both dummy variables were incorporated into a model predicting mortality. A post-hoc (Wald) test determined whether one scale was superior to the other for mortality prediction.

Results

Baseline characteristics

There were no differences between the groups on baseline characteristics other than cholesterol (Table 1). Patients who completed the HADS-D had a lower total cholesterol level than those who completed the BDI-FS (t=2.47, p= 0.014).

Response rates

Staff did not offer (according to institutional assignment) the HADS-D to 2 (0.5%) patients, and the BDI-FS was not offered to 7 (1.6%) patients (OR 0.3, 95% CI 0.1 to 1.6, p=0.152). Overall, 598 (73%) completed a scale. The response rate between scales did not differ, with 316 (78%) completing the HADS-D and 282 (67%) completing the BDI-FS (OR 1.6, 95% CI 0.9 to 2.9, p=0.118). Non-responders were older (OR 1.02, 95% CI 1.0 to 1.03, p=0.017) and more likely to have diabetes (OR 1.6, 95% CI 1.0 to 2.3, p=0.035), when controlling for sex and private health insurance.

Baseline depression

Fewer patients who completed the HADS-D were found to be depressed, with 47 (15%) patients shown to be depressed, whereas 62 (22%) of those who completed the BDI-FS were depressed (OR 0.6, 95% CI 0.4-1.0, p=0.035). Overall 109 (18%) patients were depressed.

Mortality

Mortality rates for the two groups did not differ (OR 0.9, 95% CI 0.4 to 1.9, p=0.758), with 12 (4%) of those who completed either scale confirmed as deceased after one-year (Fig 1). Patients who did not complete either scale had a higher one-year mortality rate, with 30 (13%) patients deceased (OR 3.5, 95% CI 2.0-6.2, p<0.001).

Significant univariate predictors of mortality (Table 2) were age, sex, private health insurance, prior diabetes, prior unstable angina, total cholesterol level, length of hospital stay (after intensive/coronary care admission) and depression. Prior ACS (overall), hypertension, reperfusion during admission and having smoked (ever smoker) were not significant predictors of mortality. The Kaplan-Meier survival curve for depressed and non-depressed patients is shown in figure 2 (a).

Depression predicted mortality in multiple Cox regression when controlling for age and sex (HR 3.0, 95% CI 1.5 to 6.1, p=0.002), and when including other univariate predictors with a p-value <0.15 (see Table 2) (HR 4.1, 95% CI 1.6 to 10.3, p=0.003).

Fig 2 about here

Scale comparison

Scoring above threshold on the HADS-D predicted mortality (HR 4.2, 95% CI 1.8 to 10.0, p=0.001), even when controlling for age and sex (HR 4.0, 95% CI 1.7 to 9.1, p=0.001). Raw scores also predicted mortality, with a 19% increase in risk per unit increase on HADS-D score (HR=1.2, 95% CI 1.1 to 1.4, p=0.008).

Scoring above threshold on the BDI-FS did not significantly predict mortality (HR 1.8, 95% CI 0.6 to 5.6, p=0.291), even when controlling for age and sex (HR 2.3, 95% CI 0.7 to 7.4, p=0.156). BDI-FS raw scores did not predict mortality (HR 1.1, 95% CI 0.9 to 1.4, p=0.38). Figure 2 shows survival curves for patients who completed (b) the HADS-D, and (c) the BDI-FS.

The data were then analysed for the total sample, using dummy variables and incorporating the data for the HADS-D and BDI-FS samples separately. A Wald post-hoc test revealed no significant difference between the HADS-D and the BDI-FS for risk prediction (χ^2=0.82, p=0.365).

Discussion

The present study evaluated the use of short-form depression questionnaires in an acute cardiac setting, comparing the HADS-D with the BDI-FS. Factors which increase risk post-event were similar in the two groups, with two exceptions. Serum total cholesterol was lower in the HADS-D group, and the HADS-D found a lower prevalence of baseline depression.

The response rates showed that the scales were generally acceptable to patients in acute settings, with older patients and those with diabetes less likely to complete the scales. There was therefore an expected higher mortality rate in those patients who did not complete a depression scale. Also, staff distributed the questionnaires to virtually all (99%) of patients in the current sample, indicating high staff acceptance. The findings of this study show a substantial level of depression (18%) in post-ACS patients, in line with previous research with cardiac patients [3,15].

Combined depression scores predicted mortality, even when controlling for other risk factors (including a proxy for disease severity). Depression, as measured by the HADS-D, but not the BDI-FS, predicted one-year mortality in ACS patients. One reason for this may relate to the aspect of depression each scale measures. The HADS-D concentrates on anhedonia (the inability to experience pleasure), whereas the BDI-FS focuses on psychiatric criteria for major depressive disorder. Anhedonia may therefore be an important aspect of depression in relation to cardiac mortality. The BDI-FS found a higher prevalence of depression, and this may indicate a higher sensitivity for depression detection than the HADS-D. Using more stringent criteria for the BDI-FS depression threshold had no

significant impact on results (data not shown). Therefore we recommend the HADS-D for rapid screening of depression and mortality risk prediction in ACS patients. One caveat to note is that although the HADS-D predicted mortality, a post-hoc analysis showed that it was not significantly different to the BDI-FS. Therefore, the BDI-FS was predicting some elevated risk, but not significantly different to chance. The HADS-D predicted mortality greater than chance. Although the HADS-D performed better for risk prediction in the present survey, it cannot be concluded that the BDI-FS is of no use in risk prediction. Previous studies which used the HADS have had conflicting results. Herrmann and colleagues showed that the HADS-D was associated with higher mortality in multivariate analysis in cardiology patients referred for exercise testing [27]. Mayou et al found that AMI patients with elevated HADS scores did not show higher risk of mortality [13], however these researchers used a composite of both anxiety and depression scales, and this may explain these negative findings.

Other researchers have suggested that the predictive value of depression is simply a measurement of underlying cardiac disease that is not currently picked up by conventional risk factors – i.e. it is not depressive disorder per se [28]. Indeed, one recent systematic review showed inconclusive results due to methodological issues [29]. Further research reviewed 10 studies reporting at least 30 fatal events, and showed that in 8 out of 10 of these studies there was no statistically significant relationship between depression and mortality after adjustment for potential confounders [30]. There are other explanations for these conflicting results. It may be that the time of depression assessment post-event determines whether depression predicts outcomes. Measurement in hospital may be more predictive of mortality (and it may thus be a proxy measurement of severity of cardiac disease [31]). A further explanation may be that the instrument used determines whether outcomes are predicted by 'depression'. The present study supports this conclusion. Also supportive of this is previous research that reported an increased mortality risk for the (full version) BDI scale when compared to an interview for DSM-IIIR criteria (OR=3.64 for interview vs. OR=7.82 for BDI) [4]. These authors also noted that the diagnostic interview did not significantly improve the predictive ability of a model predicting mortality, but the BDI did. Recent research using the BDI has shown that somatic/affective symptoms of post-AMI depression are confounded by somatic health status, whereas cognitive/affective symptoms of depression were not related to cardiac prognosis, and only marginally related to health status [32]. The full-length BDI could therefore be confounded by somatic items when predicting mortality in cardiac patients. Further research should be aware of possible confounding. Studies could concentrate on different theoretical aspects of depression (e.g. reduction in pleasurable activities), and whether these impact on depression and subsequent morbidity and mortality in cardiac patients. This could determine whether it is actual 'psychological' depression that is predictive of outcomes.

Previous studies of depression in this area have typically involved assessment of patients using clinical interviews and lengthy patient-completion questionnaires

[3,8,18]. This approach is not feasible in most centres. One study which used interview assessment for depression within a comparable timeframe (i.e. 2-5 days after admission) achieved a 40.9% response rate [8]. Our 73% response rate compares favourably to this figure. Short instruments are useful for drawing attention to possible mood disturbance in an environment where this would not be routinely assessed. Although the instruments assessed here are screening rather than diagnostic tools, our results show the HADS-D is an acceptable substitute for identifying patients at high-risk for post-ACS mortality, and therefore provides clinically useful information.

The treatment of depression in ACS patients has been shown to reduce depression and increase quality of life, but it has not to date reduced subsequent mortality [33]. Aside from mortality and quality of life related issues, depressed AMI patients have been found to place a greater demand on healthcare resources [34]. Identification and treatment of this group is advisable, both for service providers and patients. The prevalence of depression argues for a strong role for liaison psychiatry in helping to optimise quality of life in coronary disease patients. The challenge to psychiatry is to optimise quality of life by developing strategies for detecting and managing those at increased risk. The initial use of short-form questionnaires, such as the HADS-D, may have a role in the initial identification of these patients.

The findings of this study are limited to patients who completed a depression questionnaire at baseline and who did not decline follow-up. Indeed, higher mortality was seen in those patients who did not complete a scale at baseline. It is possible that severely ill (and/or more depressed) patients were not included at baseline. Analysis did account for standard cardiovascular risk factors, in an effort to prevent confounding. However, some standard clinical factors (prior ACS), did not predict mortality.

Conclusions

Depression can be measured in a brief but clinically meaningful way in acute settings. A 7-item depression screening scale, the HADS-D, predicted one-year mortality in ACS patients; another scale, the BDI-FS, did not. This study adds to the evidence in support of systematic screening for depression after an acute cardiac event.

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Table 1: Baseline characteristics of sample, n (%) unless otherwise stated

	Completed HADS-D	**Completed BDI-FS**	P-value
Demographics			
Age (years) (mean) (std dev)	63 (13)	62 (12)	0.331
Men	235 (74)	221 (78)	0.343
Health insurance (private)	116 (37)	101 (37)	0.963
Previous risk factor history			
Prior diabetes	37 (12)	35 (12)	0.826
Total cholesterol (mmol/l) (mean) (std dev)	4.9 (1.2)	5.1 (1.1)	0.014*
Ever smoker	241 (77)	215 (78)	0.949
Prior ACS	112 (35)	111 (37)	0.440
Myocardial infarction	60 (19)	59 (20)	0.509
Unstable angina	57 (18)	53 (18)	0.849
Prior revascularisation	47 (15)	56 (19)	0.165
Prior hypertension	132 (41)	115 (41)	0.832
Reperfusion received	109 (34)	89 (32)	0.533
Length of hospital stay (median) (inter-quartile range)	9 (5-13)	8 (6-13)	0.159

*p<0.05

Table 2: Univariate Cox regression predictors of mortality for total sample

	HR	95%	P-value
Age	1.08	1.04 to 1.1	<0.001‡
Sex	0.4	0.1 to 0.9	0.029*
Health insurance (private)	0.2	0.08 to 0.7	0.007†
Previous risk factor history			
Prior diabetes	4.9	2.1 to 11.2	<0.001‡
Total cholesterol (mmol/l) (mean)	0.5	0.3 to 0.8	0.003†
Ever smoker	0.5	0.2 to 1.1	0.1
Prior ACS	1.7	0.7 to 4.0	0.234
Myocardial infarction	1.1	0.4 to 2.5	0.909
Unstable angina	2.7	1.1 to 6.8	0.035*
Prior revascularisation	0.2	0.03 to 1.6	0.125
Prior hypertension	1.7	0.7 to 4.2	0.263
Reperfusion received	0.7	0.3 to 1.4	0.302
Length of hospital stay (median)	1.1	1.03 to 1.1	<0.001‡
Depressed	2.8	1.4 to 5.7	0.005†

*p<0.05, †p<0.01, ‡p<0.001

Figure 1: Flowchart of patient participation

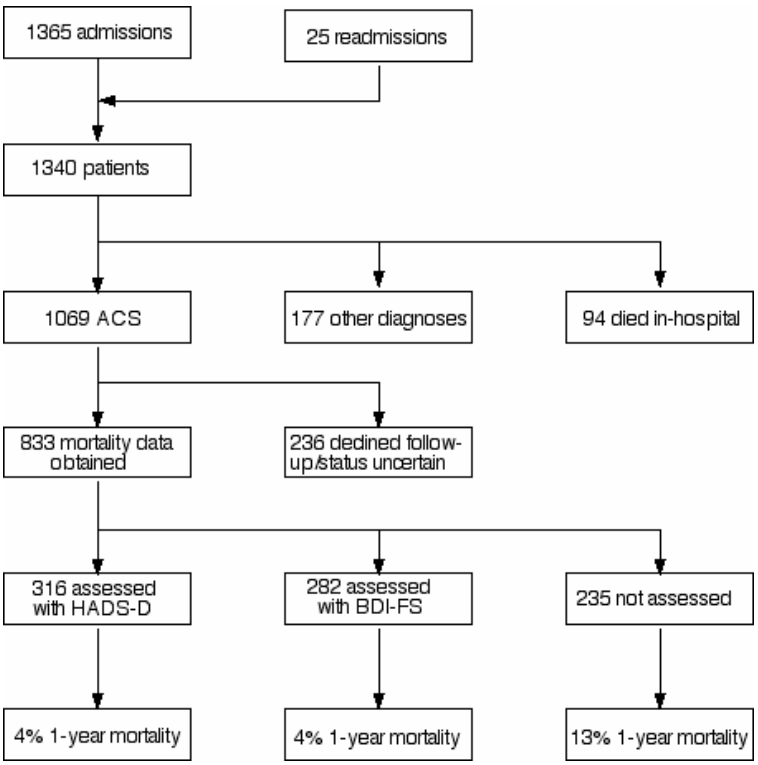
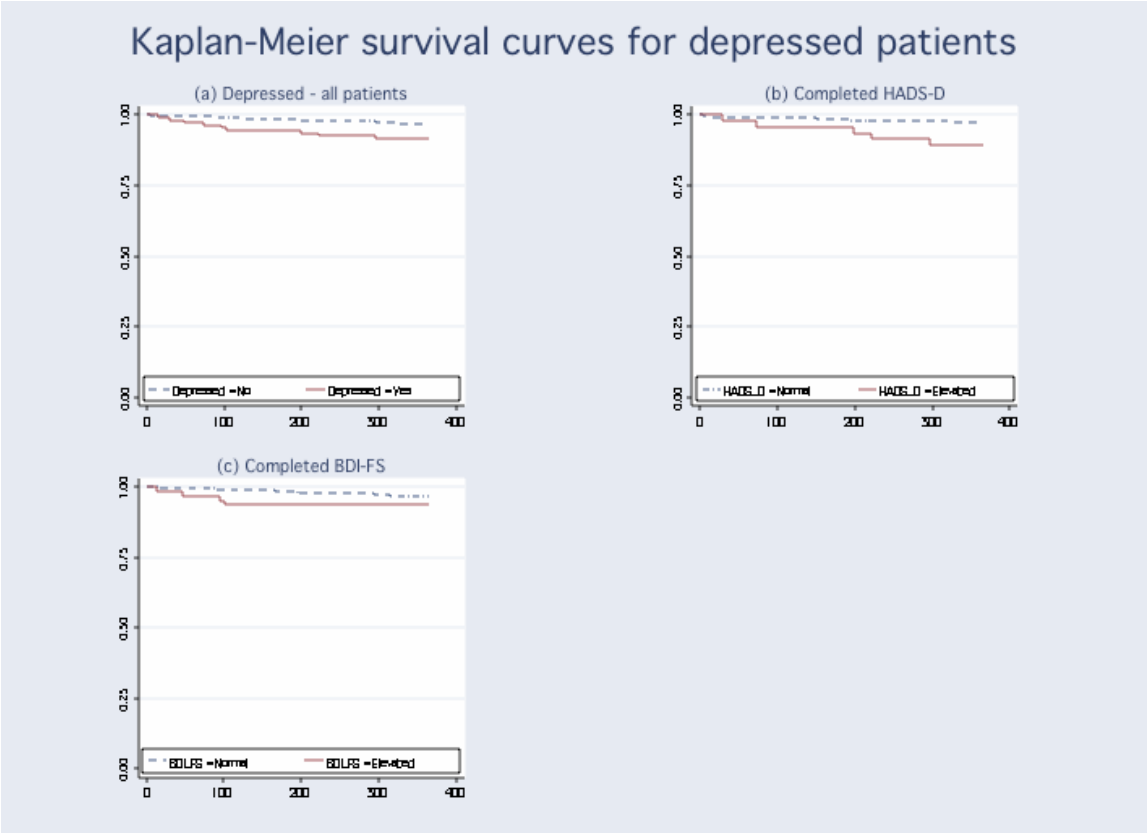
Figure 2: Survival (Kaplan-Meier) curves showing probability of survival by days for (a) depressed and non-depressed patients, (b) patients who completed the HADS-D, (c) patients who completed the BDI-FS