DEPRESSION AND MYOCARDIAL INFARCTION

The association of depressive symptoms in patients with acute myocardial infarction in a regional hospital in Durban, South Africa

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INTRODUCTION

Although depression develops in almost 20% of patients after myocardial infarction (MI) and is suspected as a risk factor for MI,⁽¹⁾ the mechanisms linking depression and MI still remain unclear.⁽²⁾ Recent observations suggest that the relationship between depression and MI is both complex and bi-directional.^(2,3) Depression is suspected as a risk factor for MI whilst MI can contribute to depression, both in acute disease onset and prognosis after a MI.^(1,4)

Data from several studies have described one, or more, possible triggers for MI, the most common of which is emotional distress.^(5,6) The INTERHEART study, a world-wide study of cardiac risk factors in patients with MI, found that stressful life events occurred more frequently within the prior year among patients with MI.⁽⁷⁾ These factors included: marital separation or divorce, loss of job, loss of crop or business failure, retirement, violence, major intra-family conflict, death of a family member and major personal injury. An increase in cardiovascular events has also been associated with natural disasters.^(8,9)

ABSTRACT

Objective: To examine the association of depressive symptoms and contributing psychosocial factors during hospitalisation and I-month post discharge in patients with acute myocardial infarction (MI).

Methods and results: The study population comprised consecutive patients from a multi-ethnic background, admitted June 2015 - November 2015 to the Coronary Care Unit at R. K. Khan Hospital, Durban, South Africa, with a diagnosis of MI. Demographic and clinical data stored in a specialised electronic cardiac database were extracted for all patients. Patients were screened for depressive symptoms using the Cardiac Depression Scale (CDS). Levels of perceived stress were evaluated using the 4-item Perceived Stress Scale (4-PSS).

The study cohort consisted of 117 patients with a mean age of 58.16 ± 11.12 years, the majority of whom were males (70%, mean age 56.54 ± 1.23 years) and 30% females (mean age 61.97 ± 1.75 years). Forty-nine percent of the participants were diagnosed with depressive symptoms with a significantly greater number of females experiencing depressive symptoms compared to males (p <0.01). Patients with depressive symptoms were more likely to have a previous history of depression (p=0.02), positive family history of depression (p=0.04), greater non-adherence to their medication (p <0.01) and lower levels of physical activity (p <0.01). Depressed patients also reported higher levels of stress on voluntary (p <0.01) and subjective rating (p <0.01), experienced greater financial stress (p <0.01), major life events (p <0.01) and had higher 4-PSS scores (p <0.01). Thirteen percent of patients experienced major adverse cardiac events (MACE) with a significantly greater number of events found in those with depressive symptoms (p <0.01).

Conclusion: Depressive symptoms are a common finding in a South African population presenting with MI. They are linked to higher rates of MACE, a previous history and/or family history of depression, greater stress levels and major life events. Females with MI are significantly more likely to present with depressive symptoms. These findings suggest that patients with MI should be screened for depressive symptoms and psychosocial factors as this may serve as an important arena for research and therapeutic intervention. SAHeart 2018;15:108-115

Even though there is an increasing body of evidence supporting a relationship between depressive symptoms and MI, such information is scarce or non-existent in South Africa. A local study that examined the association between traditional risk factors and acute MI in 4 418 patients, listed the absence of psychosocial data as one of the limitations in their analysis.⁽¹⁰⁾ Therefore, the present study examines the association of depressive symptoms and contributing psychosocial factors with MI in a South African setting during hospitalisation and I-month post discharge.

METHODOLOGY

This prospective study was conducted at R. K. Khan Hospital, a large referral hospital in Durban, KwaZulu-Natal, South Africa. The hospital services a large geographical area, including the township of Chatsworth, which is historically home to a predominantly Asian Indian population. All English speaking patients who were admitted to the hospital's Coronary Care Unit (CCU) from June 2015 - November 2015, with a confirmed diagnosis of acute MI as defined by the Joint European Society of Cardiology/American College of Cardiology Committee(11) were included in the study. Ethical approval was obtained from the Biomedical Research Ethics Committee (BREC) of the University of KwaZulu-Natal. Participation was voluntary and written informed consent was obtained from all patients prior to any study related procedures. Patients were excluded if they suffered from cognitive impairment, including delirium or intellectual disability, malignancies, chronic renal failure, hypothyroidism, or other life-threatening diseases.

Relevent clinical information, laboratory results and sociodemographic data stored in an electronic database were extracted for all eligible patients. The following cardiovascular risk factors were assessed: self-reported diagnosis of hypertension, diabetes mellitus, history of smoking (never, previous, or current), visceral obesity based on ethnic specific waist circumference cut-offs, and a family history of vascular disorders. Additional clinical data included a detailed description of major adverse cardiac events (MACE) encountered during hospital admission and at 1-month follow-up such as arrhythmias, heart failure, cardiogenic shock, death, complete heart block and recurrence of angina and MI.

THE CARDIAC DEPRESSION SCALE

Patients were screened for depressive symptoms 48 hours after admission to hospital and at 30-days post discharge to exclude an adjustment reaction to the MI or the hospitalisaion. The Cardiac Depression Scale (CDS), a 26-item self-report instrument, was used to screen for depressive symptoms.⁽¹²⁾ It is the only validated instrument designed to measure depression in cardiac patients and is capable of detecting symptoms ranging from subclinical to severe depression. It has been established to be a reliable and sensitive measure in English speaking populations.^(13,14) The scale is made up of 2 dimensions and 7 subscales including: sleep, anhedonia, uncertainty, mood, cognition, hopelessness and inactivity. Each item is scored using a Likert-scale of I (strongly disagree) to 7 (strongly agree). A higher score is indicative of more severe depression (range 26 - 182). Depressive scores were evaluated as 3 categorical variables: <80 was defined as not depressed, ≥80 but <100 was defined as minor depressive symptoms and \geq 100 as major depressive symptoms.^(13,14) Using these cut-off scores, the CDS has been shown to have a sensitivity of 95% and a specificity of 92% for major depressive symptoms and a sensitivity of 94% and specificity of 77% for minor depressive symptoms in cardiac inpatients and outpatients.⁽¹⁴⁾

PERCEIVED STRESS SCALE

The participants' level of perceived stress was evaluated using the 4-Item Perceived Stress Scale (4-PSS), which is a valid and reliable instrument that measures psychological distress.⁽¹⁵⁾ The 4 questions ask respondents how often they felt unable to control their lives, handle their difficulties, felt things were going their way and could not overcome their difficulties. Total PSS scores ranged from 0 - 16 with higher scores indicating more perceived stress.

Furthermore, each participant completed a questionnaire that elicited information regarding their family and psychiatric history as well as lifestyle factors including level of physical activity, alcohol use, pscyho-social stressors and adherance to their chronic medication.

STATISTICAL ANALYSES

Data was processed and analysed using Stata 13.0. (StataCorp. 2013 Statiscal Software Release 13, College Station, TX: StataCorp LP). Categorical factors associated with depression were assessed using the standard Pearson's chi-square (χ 2) test. If an expected cell count in the cross tabulation was less than 5 (sparse numbers) then the Fisher's exact test was preferred. Comparison of predictors by binary depressed classification was assessed using the standard t-test. If the normality assumption was not upheld, then the non-parametric equivalent Wilcoxon rank-sum test was used instead. Strength of association between explanatory factors and depressed status was assessed using a bivariate logistic regression. Coefficients were exponentiated to present odds ratios (ORs). A p-value of <0.05 was considered statisically significant.

RESULTS

One hundred and twenty nine patients were admitted with MI over the study period. Twelve patients in total were excluded from the study, 5 of whom because they were unable to complete their questionnaire due to language difficulities and the other 7 due to the study's exclusion criteria. The final study sample consisted of 117 patients with acute MI, with a mean age of 58.16 ± 11.12 years, the majority of whom were males (n=82 [70%]) as per Table I. Female patients were older than their male counterparts (mean age 61.97 ± 1.75 vs. 56.54 ± 1.23 years, respectively).

Eighty-eight percent of the patients were of Asian Indian origin, 8.6% were White, 2.6% Black African and 0.9% Coloured. Visceral obesity (71%), dyslipidaemia (71%), diabetes mellitus (59%) and hypertension (59%) were the most commonly observed risk factors among study subjects. The principal source of income for 51% of patients was from pension funds, while the majority (74%) had completed their secondary level of education and 13% obtained a tertiary level education. Sixtyfour percent (n=75) experienced a major life event in the year prior to their admission to CCU.

Demographic and clinical characteristics of patients with (49%) and without (51%) depressive symptoms are presented in Table II. A significantly greater number of females experienced in-hospital depressive symptoms compared to males (OR 3.24 [95% Cl 1.4 - 7.5]; p<0.01). Patients who suffered from depressive symptoms during hospitalisation were more likely to have a previous history of depression (OR 8.07 [95% Cl 1.19 - 54.95]; p=0.02), a positive family history of depression (OR 4.04 [95% CI 1.05 - 15.54]; p=0.04), a greater nonadherence to their medication (OR 1.53 [95% CI 1.07 - 2.19]; p<0.01) and lower levels of physical activity (OR 2.39 [95% Cl 1.14 - 5.01]; p<0.01). These patients also reported higher levels of stress on voluntary (OR 7.9 [95% CI 3.45 - 18.1]; p<0.01) and subjective rating (OR 5.63 [95% CI 2.63 - 12.02]; p<0.01), experienced greater financial stress (OR 2.64 [95% CI 1.44 - 4.84]; p<0.01), and major life events (OR 4.47 [95% CI 1.95 - 10.25]; p<0.01) and had higher 4-PSS scores (medium vs. low OR 24.73 [95% CI 8.14 - 75.12], high vs. low OR 100.7 [95% CI 12.07 - 840.1]; p<0.01).

Fifteen patients (13%) experienced MACE, with a greater number of events occuring in those with depressive symptoms (23%) compared to those without (3%) (OR 8.57 [95% CI 1.84 - 39.94]; p<0.01). The 15 index events were: 8 heart failures, 2 ventricular arrymthias, I cardiogenic shock, 2 atrial fibrillation and 2 deaths (both the deceased patients had depressive symptoms).

TABLE I: Baseline demographic and clinical characteristics.

Characteristics.	Summer (n = 1 7) (%)
Characteristics	Summary (n=117) (%)
Age (years), mean (SD)	58.16 ± 11.12
Male (mean age 56.54 ± 1.23 years)	82 (70)
Female (mean age 61.97 ± 1.75 years)	35 (30)
Race	
Asian Indian	103 (88)
White	10 (8.6)
Black	3 (2.6)
Coloured	I (0.9)
STEMI*	74 (63)
NSTEMI**	43 (37)
Risk Factors Visceral obesity	83 (71)
Dyslipidaemia	83 (71)
Diabetes Mellitus	69 (59)
Hypertension	69 (59)
Previous MI	28 (24)
MACE***	15[13]
Behavioural factors	19[19]
Smoking	82 (72)
Adherent to chronic medication	63 (54)
Physical activity	58 (50)
Alcohol use	47 (40)
Marital Status	17 (10)
Married/co-habiting	85 (73)
Widowed	19 (16)
Divorced/separated	9 (8)
Single	4 (3)
Educational Level	1 (5)
Secondary	87 (74)
Primary	15 (13)
Tertiary	15 (13)
Source of Income	
Pension	60 (51)
Employed	40 (34)
Other	17 (15)
Psychiatric factors	
Current history of depression	6 (5)
Past history of depression	5 (4)
Family history of depression	13 (11)
Subjective stress rating at home/work	
Never	6 (5)
Sometimes	69 (59)
Several periods	33 (28)
Permanent	9 (8)
Major life events in last I year	75 (64)
Death of family member	21 (18)
Other major stress	20 (17)
Intra-family conflict	(9)
Job loss	10 (9)
Death of spouse	6 (5)
Business failure	5 (4)
Marital separation/divorce	2 (2)

*STEMI = ST Elevation Myocardial Infarction, **NSTEMI = Non-ST Elevation Myocardial Infarction, ***MACE = Major Adverse Cardiac Events.

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TABLE II: Demographic and clinical characteristics of depression during hospitalisation.

Variable	Major and Minor Depressive symptoms n=57 (49%)	No Depressive symptoms n=60 (51%)	OR (95%CI)	p-value
Demographic Factors				
Age (years), mean (SD)	58.07 ± 9.86	58.25 ± 12.29	1.0 (0.97 - 1.03)	0.93
Female	24 (42)	(8)	3.24 (1.40 - 7.50)	<0.01
Male	33 (58)	49 (82)	5.2т (1.то - 7.50)	~0.01
Clinical Factors				
STEMI	37 (65)	37 (62)	1.15 (0.51 - 2.62)	0.72
Ejection Fraction (mean \pm SD)	50.88 ± 9.32	54.53 ± 8.41	0.95 (0.91 - 1.0)	0.04
MACE	13(23)	2(3)	8.57 (1.84 - 39.94)	< 0.0
Risk Factors				
Visceral obesity*	39 (71)	36 (69)	1.08 (0.47 - 2.48)	0.85
Dyslipidaemia	46 (81)	37 (62)	2.6 (1.12 - 6.01)	0.02
Diabetes Mellitus	37 (65)	32 (53)	1.62 (0.77 - 3.41)	0.20
Hypertension	37 (65)	32 (53)	1.62 (0.77 - 3.41)	0.20
Previous MI	(9)	17 (28)	0.6 (0.25 - 1.44)	0.25
Unemployed	41 (72)	36 (60)	1.71 (0.79 - 3.71)	0.17
Marital status, married	38 (67)	46 (77)	0.61 (0.25 - 1.48)	0.23
Marital status, not married	19 (33)	14 (23)	0.01 (0.25 - 1.40)	0.25
High school education (secondary & tertiary)	48 (84)	54 (90)	0.59 (0.2 - 1.79)	0.35
Psychiatric factors				
Previously diagnosed depression	5 (9)	0 (0)	8.07 (1.19 - 54.95)	0.02
Family history of depression	10 (18)	3 (5)	4.04 (1.05 - 15.54)	0.04
Family history of other mental illness	5 (9)	0 (0)	CBC	0.03
Other psychiatric disorder	I (2)	0 (0)	CBC	0.49
Behavioural factors				
Alcohol use	20 (35)	27 (45)	0.66 (0.31 - 1.39)	0.27
Smoker	38 (68)	46 (77)	0.61 (0.27 - 1.37)	0.23
Medication non-adherence (≤75%)	35 (61)	19 (32)	1.53 (1.07 - 2.19)	< 0.0
Physically Active	14 (25)	29 (48)		-0.01
Physically Not active	43 (75)	31 (52)	2.39 (1.14 - 5.01)	<0.01
Psycho-social factors				
Level of stress, high	44 (77)	18 (30)	7.9 (3.45 - 18.1)	< 0.0
Subjective stress rating				
Never	0 (0)	6 (10)		
Some periods	24 (42)	45 (75)	5.63 (2.63 - 12.02)	<0.01
Several periods	25 (44)	8 (13)	5.05 (2.05 - 12.02)	
Permanent stress	8 (14)	I (2)		
Financial stress				
Yes	29 (51)	13 (22)	2.64 (1.44 - 4.84)	<0.01
No	28 (49)	47 (78)	2.07 (1.44 - 4.84)	<0.01
Major life events in preceding year	46 (81)	29 (48)	4.47 (1.95 - 10.25)	<0.01
4-PSS score	6 (5)			
Low	10 (18)	53 (88)	2472 (014 75 12)**	
Medium	28 (49)	6 (10)	24.73 (8.14 - 75.12)**	< 0.0
High	19 (33)	I (2)	100.7 (12.07 - 840.1)***	
Locus of control	75 (64)			
Internal	26 (46)	54 (90)	10.72 (2.00 - 20.02)	20.01
External	31 (54)	6 (10)	10.73 (3.98 - 28.92)	<0.01

OR = Odds Ration, CI = Confidence Interval, MACE = Major Adverse Cardiovascular Event, CBC = Cannot be calculated. *10 subjects with missing waist circumference, **Medium vs. Low, ***High vs. Low.

Figure I shows the comparison between the prevalence of depressive symptoms in patients during hospitalistion and at I-month follow-up. In hospital, 60 (51%) of the study subjects with MI did not suffer from any depressive symptoms, 27 (23%) had minor symptoms and 30 (26%) major depressive symptoms. At follow-up a greater number of patients (n=33; 29%) experienced minor depressive symptoms, while, in contrast, fewer patients were classified with major depression (n=16; 14%).

Seven factors labelled sleep, anhedonia, uncertainty, mood, cognition, hopelessness, and inactivity were extracted from the CDS. These factors, together with their respective factor loadings and internal consistency estimates, are presented in Table III. Factor loadings ranged from 0.24 - 0.87. All factors demonstrated acceptible internal consistencies (Cronbachs α >0.70) ranging from 0.70 (anhedonia) - 0.90 (sleep).

DISCUSSION

In this single-centre prospective study, we examined the association of depressive symptoms and contributing psychosocial factors with MI in 117 patients. Patients were characterised by the presence of multiple conventional risk factors for MI.

International studies have found that depression is 3 times more common in patients post acute MI when compared to the general population, $^{(1,16)}$ with at least 45% of individuals

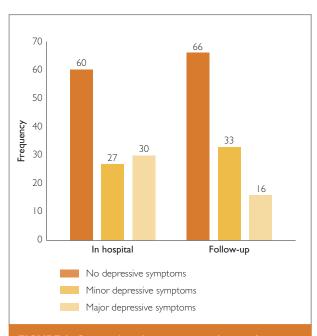


FIGURE 1: Comparison between prevalence of depressive symptoms during hospitalisation and follow-up.

experiencing depressive symptoms.^(17,18) The presence of depressive symptoms in 49% of our patients with MI compares favourably with these reports. It has been shown that depressive symptoms are associated not only with new onset cardio-vascular disease, but also with recurrent events and poor outcomes in those with established disease, and supports the need to screen for depressive symptoms in our patients with MI. Several potential mechanisms have been proposed supporting depression as a risk factor for cardiovascular disease, although their relative contribution requires further elucidation.⁽¹⁾ These mechanisms include: hypothalamic-pituitary-adrenal axis dysfunction, inflammatory and prothrombotic changes, dietary factors, reduced heart rate variability and life-style factors such as smoking and physical inactivity.

Numerous previous data have shown that depressive symptoms increase all cause mortality as well as cardiovascular morbidity and mortality.⁽¹⁹⁻²¹⁾ Depressive symptoms also increase the risk of sudden cardiac death (SCD), particularly in older patients similar to other common risk variables for coronary heart disease.⁽²²⁾ Altered cardiovascular regulation is one of the potential mechanisms explaining the association between depression and SCD. Furthermore, it has been noted that individuals with the highest depression scores have a significantly greater risk of developing MACE compared to those with the lowest scores.⁽¹⁹⁾ Although the duration of our study follow-up was relatively short, 13% of patients experienced one or more MACE.

A significantly greater number of events was found in patients with depressive symptoms compared to those without (p<0.01), with the 2 reported deaths occurring in subjects with depressive symptoms.

Patients with MI who experienced depressive symptoms were significantly more likely to present with a history of previous depression (p<0.01) and a family history of depression (p=0.04) or other mental illness (p=0.03). These results suggest that depression is a chronic and recurrent disease with approximately 40% - 60% of people reporting at least one previous episode of depression, with successive episodes increasing the likelihood of recurrence.⁽²³⁾ In these patients it has been demonstrated that lower levels of stress are equally capable of causing depressive symptoms, as suggested by the kindling or stress sensitisation theory.⁽²⁴⁾ It is postulated that both cardiovascular disease and depression have substantial genetic heritability.⁽²⁵⁾ An individual has a 2.8 - 10 times greater probability of developing depression if a first degree relative has depression. In addition, it is hypothesised that patients with depression and cardiovascular disease may represent a distinct

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TABLE III: Factors extracted from the CDS b	v Principal Components Analy	vsis with Varimax rotation (n=117)
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23 I feel independent and in control of my life 0.5
10 I feel like I am living on borrowed time 0.67
Hopelessness II Dying is the best solution for me 0.70 0.51
14There is only misery in the future for me0.7
I l have dropped many of my interests and activities 0.64
Inactivity 3 I cannot be bothered doing anything much 0.76 0.72
16 I hardly get anything done 0.68

*Factor analysis using varimax rotation.

group with similar genetic burden, and that identifying this specific genomic vulnerability, could prevent the development of both diseases.

It is important to note that in hospital, 49% of patients with MI suffered from depressive symptoms, 23% had minor symptoms and 26% major depressive symptoms. At follow-up, 42% still experienced depressive symptoms with a greater number of patients having minor depressive symptoms (29%), while, in contrast, fewer patients had major depressive symptoms (14%). This change in pattern of symptom severity may be a transient adjustment reaction to the acute myocardial event. It is worth

noting that the overall prevalence of depressive smptoms during admission and at follow-up did not significantly change, suggesting that a large number of our patients suffered from undiagnosed depressive symptoms.

Patients who present with depressive symptoms are less likely to adhere to their treatment regimen and lifestyle recommendations such as diet and exercise.⁽²⁾ Similarly, in our study, patients with depressive symptoms reported lower levels of physical activity (p<0.01) and poor adherence to prescribed medication (p<0.01). Regular physical activity has been shown to improve the quality of life in people with depression⁽²⁶⁾ and

could serve as an important cost effective intervention in countries like South Africa which has limited resources.

A significant finding in our study was the gender differences in the prevalence of depressive symptoms. Although our study cohort consisted of more males, a greater number of females were at risk of developing depressive symptoms (p<0.01). These findings concur with previous studies.⁽²⁷⁾ It should be noted that gender embraces much more than the biological and genetic differences between men and women and is a multifaceted construct that includes psychological and social differences. In patients with MI, the higher prevalence of depressive symptoms in females may be explained by several biopsychosocial factors including: physiological changes related to menopause, lower functional capacity, as well as stressors related to social gender roles, for which women are more vulnerable than men.^(27,28)

These stressors include: role conflict, role overload, lack of power, sexual abuse, and lower socioeconomic status. In addition, associated psychological traits such as emotion-focused coping styles and lower self-esteem play a role. However, conflicting data still exist in the literature, with some studies showing a poorer clinical oucome and higher mortality rates in women post MI, while others have found that in older men but not women, symptoms of depression were linked to an increased risk of cardiovascular mortality and MACE.⁽²⁹⁾

This highlights the importance of screening for depressive symptoms in patients with MI, which may improve clinical outcomes and minimise gender bias in the management of coronary artery disease patients.

Although chronic stress carries an attributable risk for cardiovascular disease^(30,31) that is on par with other recognised risk factors, such as smoking, dyslipidaemia, hypertension and diabetes,^(7,32) it is difficult to measure and little is known regarding the mechanisms that translate stress into cardiovascular disease events. Similar to the INTERHEART study,⁽⁷⁾ we observed that patients with depressive symptoms were significantly more likely to present with higher levels of subjective stress, greater financial stress, more major life events and scored higher on the objective 4-PSS scale. More recently, Tawakol, et al. showed for the first time that resting metabolic activity within the amygdalar of human beings is significantly associated with the risk of developing cardiovascular disease independently of established cardiovascular risk factors.⁽³³⁾ Amygdalar activity and cardiovascular disease events were substantially mediated by arterial inflammation which, in turn, was substantially mediated by up-regualted bone marrow activity. These findings provide unique insights into the mechanism through which emotional stress can lead to cardiovascular disease in humans. This raises the possibility that alleviation of psychosocial stress could produce benefits that extend beyond an improved sense of psychological well-being by improving the atherosclerotic milieu.

LIMITATIONS

Several potential limitations merit consideration. Firstly, because of the relatively small sample size, the lack of a comparator, control group and the short duration of follow-up, results for smaller groups should be interpreted with caution. Secondly, this was a single centre study of a predominantly Asian Indian population and selection bias might exist.

Thirdly, depression was not diagnosed clinically using Diagnostic and Statistical Manual 5 Criteria.⁽³⁴⁾ Although the current study has shown that the CDS is characterised by adequate psychometric properties and can detect a range of depressive symptomatology, future research should also examine the CDS with other screening measures for depressive disorders and anxiety such as the Hospital Anxiety and Depressive Scale (HADS). Finally, none of our patients were on anti-depressant medication at the time of study entry or during study follow-up. Therefore, we are unable to comment on the benefits of such therapy, particularly the use of selective serotonin re-uptake inhibitor drugs, which may improve depression in cardiac patients.

CONCLUSION

Our study shows that depressive symptoms are a common finding in a South African population presenting with MI, with a greater number of females experencing depressive symptoms compared to their male counterparts. Patients with depressive symptoms had significantly higher rates of MACE, previous history and family history of depression, greater stress levels and had experienced major life events. These findings support the notion that patients with MI should be screened for depressive symptoms and psychosocial factors, because it may serve as an important arena for research and therapeutic intervention.

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