Relationship between left ventricular ejection fraction and depression following myocardial infarction: an original article

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Original Article

Abstract

BACKGROUND: The aim of this study was to examine the association between left ventricular ejection fraction (LVEF) and incidence of depression following the myocardial infarction (MI).

METHODS: In a prospective study, 176 patients aged 32-84 years with the mean age of 56 years (SD = 10.05) with a definitive diagnosis of myocardial infarction and admitted to one of the coronary care units (CCU) of Isfahan during April to August 2006 were selected through consecutive sampling method. The demographic and medical characteristics were collected by their medical record and also the results of the LVEF assessment of the patients were obtained through echocardiography or angiography following the myocardial infarction. Thereafter, the patients were given Beck Depression Inventory for the primary care (BDI-PC) in three months after myocardial infarction. The collected data were analyzed during the hospitalization and follow-up periods using logistic regression method.

RESULTS: The findings indicated that left ventricular dysfunction identified by the Left ventricular ejection fraction index was significantly correlated with depression three months after the myocardial infarction (P < 0.01). In addition, the exploratory model (which only includes LVEF variable) had the predictive validity of 64.8% with 55.7% sensitivity and 72.1% specificity.

CONCLUSION: Left ventricular dysfunction is associated with increased risk of depression following the myocardial infarction.

Keywords: Depression, Myocardial Infarction (MI), Left Ventricular Ejection Fraction (LVEF)

Introduction

Incidence of depression symptoms following myocardial infarction (MI) is a very common psychological problem among patients with MI. This psychological problem has negative impacts on the prognosis of cardiac disease.[1] Many researchers believe that regardless of cardiac disease intensity, depression is associated with its negative prognosis. In addition, the question of whether or not characteristics of MI intensity such as left ventricular ejection fraction (LVEF) are associated with the incidence of depression has been raised by some researchers.[1]

Although the number of conducted articles regarding the effects of depression following MI and its etiology is increasing, many studies have not given attention to indicators such as LVEF as MI intensity.

Lesperance et al. in a study regarding major depression before and after MI as well as risk factors of depression after MI including LVEF and history of MI, found no relationship between the required variable and depression.[2] Moreover, while Frasure-Smith et al.[3] showed a significant correlation between LVEF (which has been defined as a two-level variable higher than 35% and lower than 35%) and depression scores in Beck Depression Inventory (BDI), Carney et al showed no significant correlation between LVEF and depression.[4] It seems that Carney et al. had created some limitations in their analysis by controlling the

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social isolation; because social isolation and depression are often manifested together in cardiac patients.[5]

van Melle et al. confirmed lower age, low LVEF and high depression level during admission as variables predicting depression following the MI.[1] van Melle et al. in a separate analysis of the data of their study reviewed the relationship of LVEF and incidence of depression in MI patients and found that the LVEF level has a significant inverse correlation with the depression score of patients in BDI three months after MI.[6] These researchers demonstrated that by controlling the demographic variables, risk factors of cardiovascular diseases, comorbidities and depression score during hospitalization, there is still a significant correlation between LVEF level and depression intensity.

Spijkerman et al. also reported a high risk of depression following MI in Netherland. They also evaluated a wide range of psychological, cardiovascular, physical and demographical risk factors as predictors of depression variables following MI and concluded that history of depressive disorder, being female, low LVEF and hospitalization duration can be considered as independent predictive variables for depression symptoms following MI.[7] Certain studies did not report any significant relationship between LVEF and depression; however, they showed a higher tendency toward depression in patients with lower LVEF.[1] Carney et al.[5] analyzed LVEF as a continuous variable and found no correlation between LVEF in depressed and non-depressed patients.

The present study was also conducted in line with this objective aiming to determine the potential correlation between left ventricular dysfunction and incidence of depression following MI.

Materials and Methods

This was a prospective study. The study subjects were 176 MI patients aged 32 to 84 years (Mean age = 56 ± 10.05 years) with a definitive diagnosis of MI who had been admitted to one of the hospitals of Isfahan equipped with a Cardiac Care Unit (CCU) during April to August 2006. The majority of the subjects were males (84%), married (89%) and of low-moderate socioeconomic class (87%). 123 of them had no previous history of MI. 48.3% of the patients have been admitted with diagnosis of anterior MI and 51.7% with non-anterior MI.

The patients were selected through consecutive sampling method and by considering the inclusion and exclusion criteria. The inclusion criteria were the following:

A) Two out of three diagnostic criteria were taken into account: 1. Chest pain caused by low blood supply to heart muscle (typical ischemia) which takes at least 20 minutes, 2. Presence of pathologic changes indicative of ischemia/infarction in ECG waves, 3. Increase in cardiac enzymes; B) Patient's consent for participation in the study.

The exclusion criteria were the following:

A) Secondary MI for bypass surgery or angioplasty, B) Presence of another serious physical disease that reduces life expectancy, C) Presence of major psychiatric disorders in the patient, D) Treated with antidepressants and E) Impossibility of follow-up with the patient after their discharge.

The following tools were used to collect data:

Echocardiography: LVEF is an appropriate clinical indicator of the functionality or dysfunctionality of the left ventricular systolic which can be determined by echocardiography and its result will absolutely be identified. This indicator is shown by the following formula:

$$LVEF = \frac{End\ diastolic\ volume\ -\ End\ systolic\ volume}{End\ diastolic\ volume} \times 100$$

In most conducted studies in this regard, this index is used as a categorical variable (e.g. for the two low and normal levels).[1,8]

Demographic and medical information Questionnaire: Demographic and medical data of the patients were collected through a questionnaire designed to do so. Their medical information was gathered from their records.

Beck Depression Inventory for Primary Care (BDI-PC): It has been designed by Beck et al by removing the physical symptoms from the original questionnaire for application in medical centers as a screening tool aiming to decrease the likelihood of reaching false estimates of depression among physical patients.[9] Previous studies indicated a preference for this tool compared with anxiety and depression index in hospitals.[10,11] This is a 7-item inventory, in which each item indicated a depression symptom. The items of this inventory are in accordance with the Diagnostic and Statistical Manual of Mental Disorder 4th edition (DSM-IV) for the diagnosis of clinical depression.[12] Intensity of each symptom in each item has been stated in four phrases. Phrases of each item scored from zero to three. Zero in each item indicates lack of that symptom and 1 to 3 indicate the existence and amount of that symptom. The highest score in this

inventory is 21.

Beck et al.[9] and Steer et al.[13] reported this inventory for screening depression in physical patients with high sensitivity and efficiency. Cronbach's alpha obtained an internal consistency of 0.88 for this inventory in an Iranian population (n = 176) in the present study. Furthermore, reliability of this inventory showed correlation coefficient of 0.74 through test re-test method with a three-week interval (n = 62) in cardiac patients. Construct validity of this inventory, in comparison with the depression subscale of the Iranian version of hospital depression and anxiety scale, in 140 patients obtained 0.87.[14] Moreover, through an organized clinical interview based on DSM-IV in the mentioned sample, the cut-off point is five which was obtained with sensitivity of 0.84, and specificity of 0.97 and the maximum clinical efficiency for screening clinical depression obtained 0.91 (including major depressive disorder and minor depression).

The present study was designed using logistic regression in order to determine the medical risk factors i.e. depression following MI. First, during the hospitalization time, the required data were collected from the study subjects enrolled in the study and LVEF was assessed as an appropriate clinical indicator from left ventricular function using echocardiography or angiography by a cardiologist in a short time after myocardial infarction. The depression of the patients was evaluated three months after the MI through Beck Depression Inventory for Primary Care. In order to complete this scale, the patients were asked to read the choices of every item carefully and choose the correct one by considering their status during the past two weeks.

In follow-up stage (3 months after discharge), by the help of patients' score in BDI-PC and based on cut-off point five, depressed patients were separated from non-depressed patients. Thereafter, the collected data were analyzed during hospitalization and follow-up stages in both depressed and non-depressed groups using stepwise logistic regression test.

Results

Out of 176 MI patients, 79 patients (44.9%) suffered from depression three months after discharge. Table 1 shows depressed and non-depressed patients three months after discharge in terms of demographic and medical variables during hospitalization (base line) using univariate analysi.

Table 1. Results of univariate analysis of the relationship of each possible predicting variable in base line and incidence of depression three months after discharge

Demographic and medical variables	The group of depressed patients three months after discharge (n = 79)	The group of non-depressed patients three months after discharge (n = 79)	Odds Ratio	Confidence Interval 95%	Significant level
Mean age	54.37	57.16	0.97	(0.42-1.00)	N.S.
Sex					
Male	35.20%	48.90%	2.14	(0.94-4.95)	N.S.
Female	9.70%	6.30%			
Marital status					
Married	38.10%	50.60%	1.99	(0.77-5.15)	N.S.
Single	6.80%	4.50%			
Socioeconomic class					
Low	27.30%	24.40%			0.05
Average	14.80%	20.50%	0.55	(0.35-0.86)	0.05
High	2.80%	10.20%			N.S.
History of MI					
Yes	17.00%	13.10%	1.97	(1.03-3.81)	0.05
No	27.80%	42.00%			
LVEF 40%	25.00%	15.30%	3.26	(1.74-6.11)	0.001
Family history of cardiac disease	22.16%	30.68%	0.78	(0.43-1.41)	N.S.
Hypertension	13.00%	17.61%	0.87	(0.46-1.67)	N.S.
Smoking	25.00%	25.56%	1.45	(0.80-2.64)	N.S.
Diabetes	14.00%	14.00%	1.33	(0.69-2.58)	N.S.
Hyperlipidemia	18.20%	25.00%	0.82	(0.45-1.50)	N.S.
Logarithm of maximum creatine phosphokinase	0.05	0.05	1.06	(0.59-1.90)	N.S.

As indicated in table 1, in univariate analysis most of the depressed patients were in low-moderate socioeconomic class (P < 0.05) and had a history of MI (17% vs. 13%; P < 0.05). In addition, the results of univariate analysis showed that most of the patients who have been depressed during the three months after discharge had lower LVEF 40% (25% vs. 15.3%; P < 0.001).

Hypothetical predictive variables including demographic and medical variables listed in table 1 had been assessed shortly after myocardial infarction. Data analysis related to these variables in logistic regression showed that left ventricular function lower than 40% could predict depression following MI (P < 0.01; β = 1.18; OR = 3.259; CI 95% = 1.739-6.106). These findings showed that among the variables assumed to predict depression following MI, LVEF had a significant contribution.

This study showed that exploratory model (which only includes LVEF variable) had a predictive validity 64.77% with 55.7% sensitivity and 72.2% specificity. This model correctly predicted 55.7% of depressed and 72.2% non-depressed patients. Given that this model had a degree of freedom of less than one, it was impossible to use Hosmer-Lemeshow test in determining its goodness of fit.

Discussion

In this study, demographic and medical variables were taken into account during hospitalization in predicting depression following required MI. The results showed that left ventricular dysfunction represented by LVEF had a significant contribution to analyzing the model including the mentioned variables in predicting depression three months after myocardial infarction. Nevertheless, it is generally accepted that depression by itself is associated with poor prognosis in cardiac disease; however, some researchers believe this relationship as a reflection of cardiac disease intensity.[15,16] The results of the present study showed that low LVEF is correlated with incidence of depression in patients following the myocardial infarction. Although, it seems that the number of studies conducted on depression following MI is increasing;[1] LVEF has not been evaluated in most of these studies and in most cases, the degree of depression was assessed immediately after MI.

The results of the present study were not in accordance with the study of Carney et al.[5] which found no correlation between LVEF and depression but they were in accordance with the

results of Frasure-Smith et al. who found a significant correlation between LVEF and depression scores in BDI.[3] Lesperance et al. also found no correlation between LVEF and depression.[2] However, it seems that there were two major issues in the study of Lesperance et al; first, in their study, the cut-off point 35% was considered as low LVEF; while it seems that a cutoff point of 40% is an appropriate and logical point for dividing the LVEF data.[2] The second issue was a small study sample. It is obvious that by considering a low cut-off point, many patients with really low LVEF will be excluded from the range of low LVEF and this issue in a small sample size results in the effect of low LVEF is not provided with the opportunity of emerging in the predictive model.

The results of the present study were in accordance with the studies of van Melle et al.[1], van Melle et al.[6] and Spijkerman et al.[7] Perhaps, these three studies were more psychologically reliable studies in this regard. In the first study, the cut-off point of low LVEF was considered as 30% and in the second study, it was considered as 40%. Nevertheless, given to the appropriate sample size in both studies, the difference in cutoff point did not prevent the emergence of the LVEF effect in predicting depression following MI. van Melle et al.[1] in a separate analysis on data of their own study reviewed the correlation of LVEF with depression in MI patients. Results of this study also confirmed the obtained findings from the above mentioned analyses. The mentioned researchers in their study showed that the LVEF level had a significant correlation with the depression score in BDI three months after MI and the lower the LVEF level was, the higher the depression score after three months.

In other studies,[17-19] there was also no significant correlation between LVEF and depression; however, most of these studies showed a tendency toward a higher degree of depression in patients with low LVEF. Therefore, perhaps lack of a significant relationship has resulted from type II error i.e. low sample size.

In most of the conducted studies, LVEF index is used as a categorical variable (e.g. low level and normal level).[1,7] van Melle et al.[6] who reviewed the correlation between LVEF and the incidence of depression following MI more than others emphasized that they prefer to use this variable as a categorical variable due to some reasons. First, it is impossible to use a similar method in all medical centers for evaluating LVEF as a continuous variable; hence, LVEF is assessed by various

methods such as echocardiography and angiography. Therefore, the difference in the assessment method can cause difference in continuous sizes. Second, although the mentioned tools are used to determine this index, clinical judgment based on individual's observation can also determine the percentage of LVEF. Hence, it seems that its classification has less error.[6]

Generally, given to the findings of the present study and previous studies it can be said that there is a correlation between LVEF and depression following MI. It is worth mentioning that the circumstance of the relationship between poor left ventricular function and incidence of depression in MI patients is important. In terms of possible mechanisms among left ventricular dysfunction and depression there are two considered ways; 1. Psychological way: in revising the conducted studies about heart failure, this correlation can be due to low quality of life resulting from overall poor physical conditions,[18] increased rate of hospitalizations and inappropriate social functioning[20] and increased unemployment.[21] All these factors can lead to depression due to stress. 2. Biological way: on the other hand, the correlation between left ventricular dysfunction and depression can be due to biological adaptability, which merges with left ventricular dysfunction.[22] The correlation between brain and heart has been reported very much in medicine; e.g. patients with subarachnoid haemorrhage may show severe changes of echocardiography and even refer with new (recurrent) left ventricular dysfunction and some symptoms from myocardial injury.[23] There were some similar findings in MI patients[24] and in those with severe emotional stress.[25]

Perhaps, it can be said that an increased level of cytokines in heart failure such as interleukin 1 (IL-1), IL-6 and tumor necrosis factor-alpha have a mediating role in the incidence of depression.[6] However, it is also possible for depression to lead to LVEF.

In reviewing the conducted studies regarding the objective of this study, the finding that left ventricular dysfunction is correlated with an increased risk of depression following MI is a new achievement and has only been obtained in two other recently implemented studies. This finding can illustrate the necessity of reviewing the role of nervous-hormonal system function or increased inflammatory cytokines associated with left ventricular dysfunction. Perhaps these processes have a major role in incidence of depression

following MI. Moreover, the achievement that low LVEF can predict depression is a reasonable logic for further more accurate studies about the effect of LVEF in the prognostic role of depression.

Due to time limitation in selection criteria of the study subjects, the sample size was small. Therefore, generalization of the results should be done with caution. Lack of accurate information about consumed drugs and their dosage during the three months after incidence of myocardial infarction confined the definite conclusion of the results in the present study. In order to generalize the findings, it is suggested that the sample size be increased in further studies, similar method of assessment of LVEF be used, the role of cardiac medications in exacerbation and incidence of depression symptoms in MI patients be evaluated and also the role of cardiac diseases risk factor such as diabetes mellitus, hypertension and hyperlipidemia in incidence of depression following MI be considered.

Conflict of Interests

Authors have no conflict of interests.

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