

# Pre-operative depression predicted longer hospital length of stay among patients undergoing coronary artery bypass graft surgery

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**Purpose:** Coronary artery bypass graft surgery (CABG) is a common and remarkably effective treatment for coronary heart disease, improving health status and enhancing quality of life. However, some outcomes after surgery remain unexplained, including psychological factors such as depression. The prevalence rates of pre- and post-operative depression among CABG patients are high, which is associated with negative short- and long-term outcomes. This study explores the impacts of pre-operative depressive symptoms on post-operative hospital length of stay (LOS) among patients undergoing CABG in Jordan.

**Patients and methods:** This was a non-experimental, prospective observational study among 227 CABG patients recruited from 5 hospitals in Amman, Jordan. Depression was measured within an average of two weeks prior and one month after the operation using the Hospital Anxiety and Depression Scale. Length of stay was abstracted from medical records after discharge.

**Results:** The average post-operative LOS was  $11.40 \pm 10.41$  days. The average pre-operative depression level was moderate;  $12.76 \pm 6.80$  and 42.47% complained of varying levels of depressive symptoms. The average post-operative depression level was moderate;  $11.11 \pm 6.78$  and 40.53% complained of varying levels of depressive symptoms. In stepwise regression models, depression scores and female gender were independent predictors that increased post-operative LOS. On the other hand, high income ( $\geq 1501$ \$/month) and use of statins had protective effects and decreased post-operative LOS. The model explained 22.4% of the total variance regarding LOS.

**Conclusion:** Pre-operative depressive symptoms increased post CABG LOS. Application of policies and depression assessment protocols prior to CABG by health care providers can identify high-risk groups (eg, females), so appropriate interventions can be designed and implemented to decrease morbidity and mortality.

**Keywords:** depression, length of hospital stay, coronary artery bypass graft, Jordan

## Introduction

Coronary artery bypass graft surgery (CABG) is a remarkable treatment for coronary heart disease worldwide, including in both developed and developing countries.<sup>1-4</sup> CABG is a very common performed procedure, with 371,000 operations performed in 2017 in the US alone.<sup>1</sup> In 2007, over 800,000 CABG operations were conducted worldwide.<sup>4</sup> CABG usually improves health status, functional status, prolongs life, decreases symptoms and disability, and enhances quality of life.<sup>2,3,5,6</sup> However, some outcomes after surgery are still unexplained.<sup>2,4,7,8</sup> For

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instance, approximately 35% of the patients complain of anginal pain, and 40% have activity limitation a year after surgery.<sup>7</sup> Therefore, identifying modifiable causative agents contributing to these negative outcomes might improve patients' response after CABG.

It has been shown that recovery from acute cardiac events (ie acute myocardial infarction) depends more on psychological factors and retrieval than physical function.<sup>9–12</sup> One of the most prevalent psychological factors that might affect this status is depression. The prevalence rates of pre-operative depression among CABG patients have been found to range from 14% to 60%,<sup>5,6,13–15</sup> while post-operative depression rates are near-ubiquitous at 97.9%.<sup>4,16</sup> Despite this endemic prevalence, more than 50% of the patients undergoing CABG are not screened for depressive symptoms by their health care providers.<sup>4,17</sup> Moreover, health care providers still face challenges in the early identification and management of the negative outcomes during the early phase of post-CABG treatment.<sup>4,17</sup>

Different studies have shown negative effects of depression on outcomes among CABG patients. Pre-operative depression increases anginal pain, rehospitalization rates, occurrence of delirium, postoperative length of stay (LOS), mortality,<sup>2–6,18</sup> and predicts higher levels of post-operative depression.<sup>3,19</sup> Pre-operative depression has been associated with higher levels of cholesterol, C-reactive protein and inflammatory markers, including IL-6 and IL-8.<sup>4,5</sup> These high levels of inflammatory markers are associated with greater rates of inflammation, lower immunity, and poor wound healing in the post-operative period.<sup>4,5</sup> With regard to long-term outcomes, pre-operative depression increases psychosocial morbidity up to five years after the operation, augments the development of new cardiac events, and decreases quality of life 2–5 years following surgery.<sup>6,20</sup>

Similarly, post-operative depression has its own negative consequences after CABG. Usually, patients with high post-operative depression suffer from impaired quality of life, lack of adherence to medication, and lifestyle changes.<sup>2,4</sup> Additionally, post-operative depression increases hospital readmissions and LOS, while reducing ability to walk and wound healing.<sup>2,3,15,21</sup>

A newly investigated indicator of outcomes between depression and CABG is the LOS, which is considered as an important marker of surgical recovery,<sup>5,6</sup> a proxy measure of acute physical recovery, and a vital indicator of long-term recovery.<sup>5,6</sup> Post-operative LOS has been connected with postoperative depression,<sup>4</sup> re-admissions,<sup>22</sup>

and recurrent cardiac events.<sup>23</sup> Patients who developed complications and have poor recovery after CABG are expected to stay longer in hospital. Recently, post-CABG LOS has decreased significantly due to efforts seeking to reduce the burden placed on health systems by hospital-based post-operative care.<sup>5,6</sup> For instance, one day of post-CABG care in the ICU costs approximately \$1300.<sup>5,6</sup> For these reasons, most health care institutions implement policies to discharge patients as soon as possible, usually within 5–7 days.<sup>5,6</sup>

A few studies have checked the effect of pre-operative depression on the LOS among patients undergoing CABG.<sup>5,6,13</sup> Poole et al<sup>5</sup> showed that patients with high depressive symptoms prior to CABG had 3.51 times greater risk to stay in hospital more than seven days, and this relationship was mediated by high levels of C-reactive protein. In another study by the same authors,<sup>6</sup> high levels of pre-operative depressive symptoms were associated with longer LOS, even after controlling of covariates. There was an interaction effect between high depression levels with economically disadvantaged levels, whereby patients with high levels of depression and low socioeconomic status had the longest post-operative LOS. Oxald et al<sup>13</sup> showed that high pre-operative depression and low PTSD were responsible for 4.4% of the variance with regard to longer post-operative LOS.

To our knowledge, only one study was conducted in Jordan to check the prevalence of depression and its associated factors post CABG, in which the authors used a cross-sectional design with a convenience sample of 143 participants (76 men and 67 women).<sup>4</sup> Their mean age was 64 years, and approximately 40% were employed. Depression was measured one time during the early recovery period (1–2 weeks post-operatively) using the self-rating depression scale. The results indicated that: the total level of post-operative depression was moderate (62.7±5.6) on a 0–100 scale; 2.1% of the sample were depression-free; 31.2% had mild depression; 60.1% had moderate depression; and 5.6% had severe depression. In terms of demographic variables, higher levels of depression were reported among female, unemployed, low-income, and older patients, while in clinical terms it was more prevalent among patients who did not receive education from nurses, and who stayed longer in the cardiac intensive care unit. The model explained 54.7% of the depression variance. The authors concluded that the incidence of depression post CABG is high, especially for females, the unemployed, and who did not receive education from nurses. However, this study<sup>4</sup> used a cross-sectional design with a relatively small

convenience sample. Moreover, depression was measured one time only during the post-operative period. This design did not assess depression levels over time (ie, longitudinally) and was particularly lacking in consideration of the pre-operative period.

Therefore, the general purpose of the current study was to check the effect of pre-operative depressive symptoms on post-operative hospital LOS among patients undergoing CABG in Jordan. *Research hypotheses:* (1) Patients with moderate to severe pre-operative depression levels will have longer post-operative LOS compared to other patients (2) Pre- and post-operative depression will be high ( $\geq 8$ ) among patients undergoing CABG (3) Pre-operative depression will be higher than post-operative depression among patients undergoing CABG (4) Pre- and post-operative depression for female patients will be higher than for male patients; and (5) Female patients will have longer post-operative LOS compared to male patients.

## Materials and methods

### Design, sample, and setting

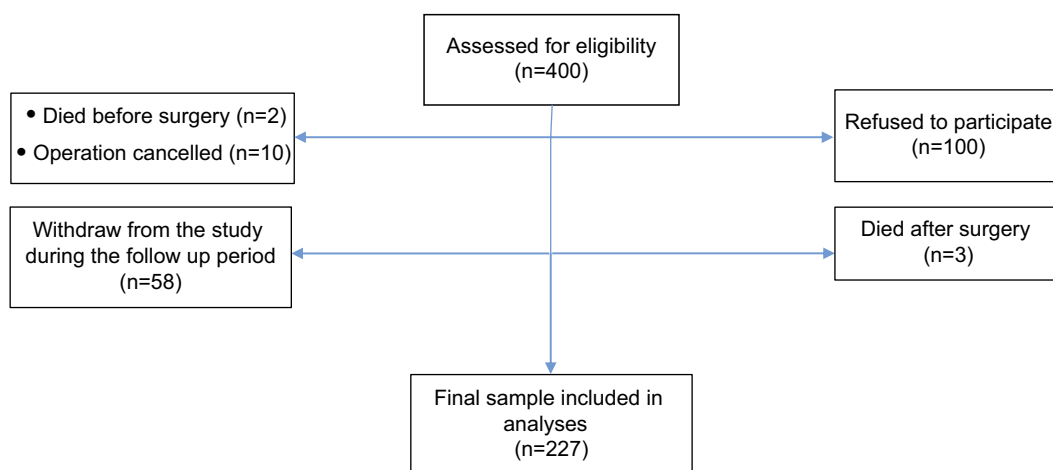
This was a non-experimental, prospective observational study. Research assistants used a consecutive recruitment method at the cardiology clinics of five hospitals (1 governmental, 1 teaching, and 3 private), in Amman, Jordan. The inclusion criteria were: (a) aged 18 years or older, (b) not having an emergency operation, (c) not diagnosed with any psychiatric disease, (d) not on anti-depressant medications, (e) able to read and write Arabic, and (f) capable and willing to sign informed consent. A total of 227 participants were included in the final analyses (Figure 1).

## Ethical considerations

The principal investigator presented the study to the Institutional Review Board (IRB) Committee at the Applied Science Private University, Amman, Jordan. The Committee approved the study and issued the IRB approval letter, which is officially accepted by institutions at Jordan. The medical directors of the selected hospitals acknowledged this IRB and delivered their permission to start data collection. The research team explained the study in full to all potential participants when inviting them to voluntarily participate in this study and those who agreed signed an informed consent form prior to data collection. They were fully informed of their right to withdraw from the study at any time without this affecting the care they received or their statutory rights. They were also given an opportunity to ask any questions if they wished. All data were kept in locked cabinet with access only by the principal investigator, and aggregate data were used for publication purposes.

## Procedure

Five trained research assistants approached all participants at the cardiology clinic and explained the study in details, including its benefits and risks, as explained earlier. Participants answered the Arabic version of the Hospital Anxiety and Depression (HADS) within an average of 16 days before surgery, along with socio-demographic questions about age, gender, marital status, working status, and monthly income. One month after surgery, participants were asked to answer HADS another time. All other required information was collected from medical records after discharge, including post-operative hospital LOS, history of hypertension, diabetes mellitus (DM), previous angina, previous myocardial



**Figure 1** Flow diagram of participants.

infarction, Body Mass Index (BMI) ( $\text{kg}/\text{m}^2$ ), and statins use (yes/no). Data collection was conducted during the period from August 2017 to March 2018.

## Measurement of variables

### Depression

The Arabic version of the HADS was used to measure depression at both time points. This version is valid and reliable, with a Cronbach's  $\alpha$  of 0.87.<sup>9,24</sup> It is a self-reported questionnaire commonly used in clinical settings.<sup>9,24</sup> Only the 7-items depression sub-scale was used. Each item has scores from 0 to 3, with higher scores indicating higher symptoms frequency and severity. The total score ranges from 0 to 21, with scores of 0 to 7 indicating normal; 8 to 10 mild; 11 to 14 moderate; and 15 to 21 severe depression.<sup>9,24</sup>

### Post-operative LOS

This was abstracted from the medical records after discharge, reported in days.

### Data analysis

SPSS version 21 was used to analyze the data. All test results were considered statistically significant at  $P < 0.05$ . To test the associations between pre-operative depression and the covariates, Pearson correlation was used for continuous variables, and Spearman rho for categorical variables. For this test *only*, the statistical significance was set at  $P < 0.1$  (to be more conservative when we used the covariates later in the regression analysis). The general purpose of this study was checked by stepwise multiple regression to control for the effects of covariates. The independent variables entered in the models were age, gender, marital status, and monthly income in block one; history of hypertension, DM, previous myocardial infarction, previous angina, BMI, and use of statins in block two; and pre-operative depression scores in block three. Hypothesis one was checked by ANOVA with post hoc test. Depression scores were transformed into levels as the following: 0–7 normal, 8–10 mild, 11–21 moderate to severe. Hypothesis two was tested by descriptive statistics (mean  $\pm$  SD). Hypothesis three was tested by paired *t*-test. Hypotheses four and five were tested using independent *t*-test.

## Results

Table 1 describes the characteristics of the participants. The mean age was around 66 years, and approximately three-quarters of participants were males. More than half

of the sample was married, and the majority had previous history of angina. The average post-operative LOS was 11.40 days. Pre-operative depression increased with non-working status ( $t_{(225)}=3.54$ ,  $P < 0.001$ ) and higher BMI ( $r=0.178$ ,  $P < 0.01$ ), and decreased with the use of statins ( $t_{(225)}=-2.37$ ,  $P < 0.05$ ).

## The general purpose of the study: pre-operative depression with post-operative LOS

Table 2 shows the results of stepwise regression models. Among all independent variables that were entered in the

**Table 1** Clinical and sociodemographic characteristics (N=227)

Characteristics	Mean $\pm$ SD or N (%)
Age	66.12 $\pm$ 9.35
Gender	174 (76.7)
Male	53 (23.3)
Female	
Marital status	136 (59.9)
Married	91 (40.1)
Single/divorced/widowed	
Income/month	150 (66.1)
<1500\$	77 (33.9)
$\geq$ 1501\$	
Currently not-working	180 (79.30)
History of HTN	182 (80.2)
History of DM	96 (42.3)
History of previous AMI	149 (65.6)
History of previous angina	206 (90.7)
Currently smoking	66 (29.1)
Post-operative hospital LOS	11.40 $\pm$ 10.41
BMI ( $\text{kg}/\text{m}^2$ )	26.91 (4.61)
Statin medication use	171 (75.3)
Pre-operative depression	12.76 $\pm$ 6.80
Normal	130 (57.26)
Mild	27 (11.90)
Moderate and severe	70 (30.84)
Post-operative depression	11.11 $\pm$ 6.78
Normal	135 (59.47)
Mild	31 (13.66)
Moderate and severe	61 (26.87)

**Abbreviations:** HTN, Hypertension; DM, Diabetes mellitus; AMI, Acute myocardial infarction; BMI, Body mass index; LOS, Length of stay.

**Table 2** Stepwise regression analyses for predictors of the post-operative hospital LOS (N=227)

Predictor	Standardized $\beta$	t	Durbin Watson statistics	Model statistics
Pre-operative depression scores	0.40	5.74**	2.12	$R^2 = 0.224$ ; $F_{(8,195)} = 12.28$ , $P < 0.001$
Female gender	0.26	3.23**		
Income $\geq$ \$1501\$	-0.29	3.86**		
Statin use	-0.33	4.72**		

**Notes:** \*\* $P < 0.001$ . The independent variables entered in the models were: age, gender, marital status and monthly income in block one. History of hypertension, DM, previous myocardial infarction, previous angina, BMI, and use of statins in block two. Pre-operative depression scores in block three.

three blocks, depression scores and female gender were independent predictors that increased post-operative LOS. Every unit increase in depression was associated with an increase of 0.4 days in post-operative LOS. Being female increased post-operative LOS by 0.26 days. On the other hand, high income ( $\geq$ \$1501/month) and use of statins had protective effects and decreased post-operative LOS.

### Hypotheses testing

**Hypothesis one: patients with moderate and severe pre-operative depression levels will have longer post-operative LOS compared to other patients**

ANOVA test showed that there was a significant difference in the post-operative LOS based on the depression levels ( $F_{(2,225)} = 21.77$ ,  $p < 0.001$ ). Bonferroni post hoc test showed that moderate to severe depression were responsible for the main effect. They have longer post-operative LOS ( $M \pm SD$ ;  $15.11 \pm 12.52$ ) compared to normal ( $M \pm SD$ ;  $5.59 \pm 5.12$ ) and mild depression ( $M \pm SD$ ;  $7.09 \pm 5.62$ ) (Table 3).

**Hypothesis two: pre- and post-operative depression will be high ( $\geq 8$ ) among patients undergoing CABG**

Descriptive statistics showed that pre- and post-operative depression levels were moderate ( $M \pm SD$ ;  $12.76 \pm 6.80$ ) and ( $M \pm SD$ ;  $11.11 \pm 6.78$ ) respectively.

**Hypothesis three: pre-operative depression will be higher than post-operative depression among patients undergoing CABG**

Paired  $t$ -test showed that there was a significant difference between the two depression levels (mean [SD],  $12.76 [6.80]$  vs  $11.11 [6.78]$ ,  $t = 7.21$ ,  $p < 0.001$ ).

**Table 3** Post hoc Bonferroni test for differences of post-operative hospital LOS based on depression levels (N=227)

Depression level	Compared with	Mean difference	Significance
Moderate to severe	Normal	9.53	<0.001
	Mild	8.03	<0.001

**Hypothesis four: pre- and post-operative depression for female patients will be higher than for male patients**

Independent  $t$  tests showed that there were statistically significant differences between females and males in regard to pre- and post-operative depression levels: (mean [SD],  $16.57 [6.26]$  vs  $11.60 [6.54]$ ,  $t = 4.89$ ,  $p < 0.001$ ) and (mean [SD],  $13.15 [7.22]$  vs  $10.49 [6.53]$ ,  $t = 2.53$ ,  $p < 0.05$ ), respectively.

**Hypothesis five: female patients will have longer post-operative LOS compared to male patients**

Independent  $t$ -tests showed that there were statistically significant differences between females and males in regard to post-operative LOS (mean [SD],  $17.34 [12.62]$  vs  $8.81 [7.23]$ ,  $t = 5.01$ ,  $p < 0.001$ ).

### Discussion

This was the first study specifically designed to check the effect of pre-operative depressive symptoms on post-operative hospital LOS among patients undergoing CABG in Jordan. The results showed that higher depressive symptoms independently increased the post-operative hospital LOS. Furthermore, there was a dose-response relationship between depression levels and post-operative hospital LOS, as evidenced by patients with moderate to severe depression levels exhibiting the longest post-operative hospital LOS. These results are consistent with previous studies.<sup>5,6,13</sup>

The results of this study showed pre-operative depressive symptoms among 42.74% of the patients, in line with previous studies reporting rates between 14% and 60%.<sup>5,6,13-15</sup> Different explanations have been proffered to explain the divergence in reported prevalence, including (a) the use of diverse methods to assess depressive symptoms among researchers; (b) different published norms and cut-off points for these instruments; (c) timing of depression measurement during the study period; (d) differences in the inclusion and exclusion criteria of the study participants; and (e) the lack of control for the use of anti-depressant medications in some



studies. Furthermore, the increasing use of lipid-lowering agents (ie, statins) in cardiology since the 1980s has been demonstrated by longitudinal studies to have protective effects against depression.<sup>6,25,26</sup> Consistent with these results, our study showed that the use of statins decreased post-operative LOS.

There is no formal policy for discharging patients following CABG surgery in Jordan.<sup>4</sup> However, due to the economic burden of health expenditure, all hospitals seek to discharge patients as soon as possible. In this study, the average post-operative LOS was (11.40±10.41) days. This rate is within the range of post-operative LOS among 10 European countries with 66,587 patients, from 9 days in Finland and Sweden to 17 in Ireland and Spain.<sup>27</sup> Moreover, the rate in the study is similar to that of post-operative LOS among 19,522 CABG patients in the UK (12.48±10.94).<sup>27</sup> On the other hand, our patients stayed longer in the hospital postoperatively compared to the 310 patients studied by Poole et al study.<sup>6</sup> The reason behind these results is that our sample had higher percentages of moderately and severely depressed patients. As shown by the results of this study, depressive symptoms are associated with increased post-operative LOS.

The results of this study also showed that patients had high levels of depressive symptoms pre-operatively, which subsequently declined after surgery; during the recovery period (first month duration), but did not get to a remission. This conclusion is similar to the conclusion drawn by Ravven et al<sup>3</sup> from a systematic synthesis and meta-analysis on depression and depressive symptoms from 39 prospective studies, which found that pre-operative depression is associated with a reduction of symptoms relief and faster return of these symptoms. Moreover, it is associated with higher rates of re-hospitalization and mortality immediately post-operatively.<sup>3,28,29</sup> Post-operative depression is also associated with delayed wound healing, and higher levels of pain, infection rates, and acute myocardial infarction.<sup>14,18</sup> The presence of such type of persistent depression might decrease compliance with cardiac rehabilitation and life modification programs. It is noteworthy that 52.9% of the participants in this study reported persistent depression.

In this study, post-operative depression was moderate, which is in line with the Jordanian study done by Hiweidi et al.<sup>4</sup> This level of depression is attributed to the nature of the CABG surgery being a stressful and life-threatening event. However, the percentage of participants who had moderate to severe depression in the current study was

lower. A possible explanation for this difference is the timing of depression measurement, which was done one month after surgery in the current study, while it was done in the telemetry unit one week after surgery in the previous study.<sup>4</sup> Post-CABG patients usually start to improve more rapidly when they are discharged and return home, which might decrease their depression levels.

Exploring mechanisms linking depression to poor outcomes suggests three major pathways: biological, social, and behavioral. Biologically, depression acts on hypothalamic pituitary adrenal axis, modulating immune functions and affecting immune cells that dysregulate the secretion of pro-inflammatory cytokines.<sup>5,14</sup> Moreover, it has been shown that CRP mediated the relationship between depression and post-operative hospital LOS, suggesting a link between depression and inflammation.<sup>5,6,30</sup> This inflammation is responsible for the negative outcomes after surgery. Socially and behaviorally, socioeconomically disadvantaged patients and those who lack sufficient sleep have poorer post-operative outcomes.<sup>4,6,31</sup> Moreover, depressed patients demonstrate adverse behavioral changes as poor hygiene, altered nutrition, and lack of adherence to medication, all of which exacerbate negative outcomes.<sup>6,14</sup> Therefore, appropriate management of pre- and post-operative depression is necessary.

Diverse strategies can be implemented for this purpose. The AHA recommends the use of Selective Serotonin Reuptake Inhibitors (SSRIs) prior to the use of any antidepressant.<sup>32,33</sup> Tricyclic antidepressants are not recommended for this population due to their potential cardiac toxicity.<sup>34-36</sup> Other strategies might include behavioral and psychological interventions, such as yoga and enhancing perceived control, which have been found to have positive effects on left ventricular ejection fraction, BMI, depression, and blood pressure.<sup>18,28,37</sup> Other studies showed that cognitive behavioral therapy and supportive stress management are effective in treating depression among CABG patients.<sup>17</sup> It is highly recommended that such holistic interventions be implemented for patients planning to undergo CABG surgery, especially high-risk groups.

Depression is sometimes considered a particularly feminine illness, which causes stigmatization and numerous barriers to effective care, but women do indeed have higher rates compared to males.<sup>9</sup> Women also have higher depression rates in different cardiac populations, including heart failure, acute myocardial infarction, and post-CABG.<sup>9,38-43</sup> This study reaffirmed that female patients had higher levels of pre- and post-operative depression

compared to male patients. This result is in line with the Jordanian study by Hiweidi et al.<sup>4</sup> On the other hand, some studies<sup>16,44,45</sup> did not find this, which might be due to the same reasons of the difference in depression rates among this population of patients, and the small numbers of females involved in these studies.

After CABG surgery, women have a more difficult recovery compared to men, which cannot be explained by illness severity, pre-surgery health status, or other patient characteristics.<sup>39</sup> These results suggesting that an important role may be exerted by the psychological status of patients on their outcomes, with the association being related to different gender roles and expectations.<sup>39</sup> In most cultures, including in Jordan, women usually have a greater role in the home and family life (particularly child-rearing), thus they may feel more disruption in their lives and consequently feel more depressed when they cannot resume their former role in full after surgery. This is particularly acute during the recovery period following surgery.<sup>39</sup>

Rates of depression were associated with women having longer post-operative LOS in this study, and the impact of their socioeconomic status. It has been shown that income interacts with depression and increased post-operative LOS.<sup>6</sup> Hweidi et al.<sup>4</sup> also showed that depression was higher among unemployed and low-income patients. Employment can ensure more monthly income, which is inversely related to depression levels. Higher income permits patients to be safer and less worried after CABG.<sup>4</sup> The number of women who had lower income in this study was greater than that of men. Furthermore, in Jordan, women are usually paid less compared to men, even when performing the same job.

## Conclusion

Pre- and post-operative depression rates among Jordanian patients undergoing CABG are high. Pre-operative depression increases post-operative LOS. Therefore, the application of policies and depression assessment protocols prior to CABG by health care providers can identify high-risk groups (eg, females) so appropriate interventions can be implemented to decrease morbidity and mortality.

## Study limitations

The major limitation of this study was the use of chart review in order to collect some of the data, as we depended on others for such information. Moreover, depression was measured by the HADS, which is a self-

reported questionnaire. Albeit this instrument is valid, reliable, and widely used in clinical settings, and it does not contain somatic symptoms, it is recommended that future studies undertake clinical evaluation of depression among patients with the assistance of a psychiatrist, in addition to the HADS, for further confirmation of depressive symptoms.

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## Disclosure

The author reports no conflicts of interest in this work.

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