

# Depression associated with cardiac surgery and the probable risk factors- A randomised observational clinical study

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## Abstract

**Introduction:** Cardiovascular surgery can trigger depression; counselling and medications can easily beat it. The earlier we identify people who have depression, complicating their ability to get back to normal life, better is the chances of recovery. We conducted a prospective randomized observational study to assess incidence of depression in patients undergoing cardiac surgery and risk factors which can trigger depression. **Materials and Methods:** A prospective randomized double blind controlled Observational clinical study was conducted in 250 patients who underwent open heart surgery with and without assistance of cardio pulmonary bypass (CPB) from May 2013 to July 2014. All patients were screened for depression with Patient Health Questionnaire (PHQ-9) preoperatively (Q1), at hospital discharge (Q2), 3months (Q3) and 6months (Q4) postoperatively. At each interval patients were identified as "not depressed" (PHQ-9 score 0), minimally depressed (score 1-4), mild(score5-9), moderate (10-14), moderately severe(15-19), severe depression(20-27). Multiple regression analysis was used to identify variables associated with depression. **Results:** On regression analysis, preoperative depression for depression at discharge (OR 88.5, p<0.0001), depression at discharge for incidence of depression at three months (OR 4004, p<0.0001) and 6 months (OR 1194, p<0.0001) had significant Odds ratio (OR) with statistical significance. Patients who had depression at discharge were older, had lower preoperative ejection fraction (EF), prolonged waiting period, ICU stay, hospital stay. Other risk factors identified were higher NYHA class, history of prior CCF, abnormal lipid profile, pre-existing hypertension, diabetes mellitus, peripheral vascular disease and patients on beta blockers. **Conclusion:** Depression is common after cardiac surgery. Among all the risk factors, preoperative depression was associated with the highest risk for postoperative depression.

**Keywords:** Depression, PHQ-9 Questionnaire, Cardiac surgery.

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## INTRODUCTION

Depression is commonly present in patients undergoing cardiac surgery and is independently associated with increased cardiovascular morbidity and mortality.<sup>1</sup> Research till date indicates that the number of cardiac surgery patients affected by depression approximates between 30% - 40% of all cases.<sup>2</sup> Numerous meta analysis and review articles in the past 40 years suggest the role of depression in increasing the morbidity and mortality after cardiac surgery worsening the natural history of the disease. Despite differences in cohort, sample size, duration of follow-up and assessment of depression and depressive symptoms, these studies have demonstrated relatively consistent results.<sup>2,6,7,8,9,10</sup>

## MATERIALS AND METHODS

Approval from the institute ethical committee was obtained. A prospective randomized double blind controlled observational clinical study was undertaken in 250 patients who underwent open heart surgery with or without cardiopulmonary bypass (CPB) from May 2013 to July 2014. Cardiac surgery requiring CPB included coronary artery bypass surgery (CABG), valve replacement/repair and congenital heart surgeries. Patients more than 18 years age were enrolled. Exclusion criteria included patients with diagnosed psychiatric disorders and patients who had a period of stay longer than 3 months, emergency surgery and death during the study period. Written informed consent was taken from all patients. Patients demographic and clinical parameters, family history of depression, previous history of depression, patients using antidepressants, living alone and recent stressful event, history of diabetes mellitus (DM), hypertension, NYHA class, renal parameters, lipid profile, ejection fraction (EF), history of cardiac failure, history of smoking and peripheral vascular disease, waiting period in the hospital before surgery were collected. Intraoperative and post operative parameters included CPB time, aortic clamp time, EF and creatinine levels.

### Statistics

Continuous variables are described as mean with deviation, categorical variables as numbers and proportions. One way annova was used to compare means and chi-square test for categorical data comparisons. Multi-variate regression analysis was performed with stepwise method with  $p < 0.1$  as significant criteria to be enrolled in the model. Two tailed  $p < 0.05$  was considered as statistically significant. Statistical analysis was performed with SPSS ver.16 and MedCalc ver.11.

## RESULTS

Two hundred and fifty patients undergoing various cardiac surgeries were enrolled for analysis. Of these, 33

patients were excluded in view of inadequate data for analysis (lost for follow up, unable to comprehend the questionnaire). Among the remaining 217 patients, preoperatively (Q1) 13.8% of the study group had minimum depression and 12.4% had mild depression, whereas postoperatively (Q2) at the time of discharge 15.2% had minimal depression, 37.8% had mild depression, 4.1% had moderate depression. At third month (Q3) patients suffering from minimal depression were 8.8%, 40.6% had mild depression, 5.1% had moderate depression and 0.5% had moderately severe depression. At six months, the overall incidence of depression decreased with 18% having minimal depression, 28.6% patients having mild depression, 1.8% having moderate depression and 0.9% having moderately severe depression (Table 1).

Patients who had depression were older than those without depression, lower mean preoperative EF, prolonged preoperative waiting period, prolonged ICU stay, prolonged hospital stay. Patients also had higher mean postoperative creatinine and lower mean post operative EF (Table 2).

Other risk factors identified were higher NYHA class ( $\geq$  II), history of prior CCF, abnormal lipid profile, pre-existing hypertension, diabetes mellitus, peripheral vascular disease, surgeries conducted on cardiopulmonary bypass and patients on beta blockers. Those patients who had depression preoperatively continued to have depression at discharge and at third and sixth months. Patients who had prolonged ICU stay and low preoperative ejection fraction had depression only at the time of discharge. Patients who had prolonged waiting period and underwent surgery on cardiopulmonary bypass had higher incidence of depression at three and six months but not at the time of discharge. Patients with dyslipidemia had higher incidence of depression at six months, but the incidence was same as patients with normal lipid profile at discharge and at three months (Table 3).

**Table 1:** Incidence of depression

Grades of depression	Duration ( Frequency, percent)			
	Preoperative (Q1)	At discharge (Q2)	3 months (Q3)	6 months(Q4)
Minimal (1-4)	30 (13.8%)	33 (15.2%)	19 (8.8%)	39 (18%)
Mild (5-9)	27 (12.4%)	82 (37.8%)	88 (40.6%)	62 (28.6%)
Moderate (10-14)	-	9 (4.1%)	11 (5.1%)	4 (1.8%)
Moderately severe(15-19)	-	-	1 (0.5%)	2 (0.9%)
Severe (20-27)	-	-	-	-

**Table 2:** Risk factors for Depression at Discharge

Risk Factors	Mean	Standard Deviation	p Value
Age	53.20 (years)	13.05	0.0001
Preoperative EF	52.74(%)	8.51	0.0001
Waiting period	6.17 (days)	5.34	0.0006
ICU Stay	3.65 (days)	1.33	0.0001
Hospital Stay	8.55 (days)	3.71	0.0001
Post operative creatinine	1.09 (mg/dl)	0.49	0.0002
Post operative EF			0.0001

EF – ejection fraction

**Table 3:** Multiple Regression Analysis Results

Timing	Variable	Odds ratio	p value
DEPRESSION @ DISCHARGE	PREOPERATIVE DEPRESSION	88.5	<0.0001
	ICU STAY	1.7	0.0135
	PRE OP EF	0.9	0.0001
DEPRESSION @ 3 MONTHS	DISCHARGE DEPRESSION	4004	<0.001
	WAITING PERIOD	1.4	0.0053
	CPB	0.11	0.047
DEPRESSION @ 6 MONTHS	DISCHARGE DEPRESSION	1194	<0.001
	DYSLIPIDEMIA	5.4	0.071
	WAITING PERIOD	1.4	0.0005
	CPB	0.27	0.02

## DISCUSSION

Analysis of pre- and postoperative data indicates that there is increase in the incidence of depression after cardiac surgery and presence of preoperative depression was the single most important determinant. In our study all patients who had preoperative depression continued to have depression at discharge and at 3 and 6 months. This finding is comparable with that of David Horne *et al*<sup>3</sup> who concluded that depression at discharge was not associated with operative or postoperative risk factors, with the exception of prolonged hospital stay >7 days and presence of preoperative depression. There is lot of evidence in the literature which suggest age, functional status of the patient, ejection fraction, duration of hospital stay and many other factors, to increase psychological morbidity after cardiac surgery leading to increased risk of infectious complications, impaired wound healing and depressed immune pathways in-turn resulting in increased cardiac morbidity and mortality. Significant risk factors for depression in our study at discharge were older age, lower preoperative EF, prolonged preoperative waiting period, prolonged ICU stay, prolonged hospital stay, higher mean postoperative creatinine and lower mean post operative ejection fraction. A study by Jens-Holger A Krannich *et al*<sup>11</sup> on relationship between age, anxiety and depression in patients undergoing CABG surgeries concluded that younger patients were more anxious than older patients before surgery and show a decline in

symptoms while elderly patients show hardly any change. Similarly we noticed a higher incidence of depression in older individuals and the disparity could be explained by the ability of younger patients to cope better with acute stressful event. The patterns of depression after cardiac surgery can also vary among different patients.<sup>3</sup> Few patients had a generalized improvement in depression, whereas the rest of the patients had increase in depression symptoms. One-third of preoperatively depressed patients were found to have normal mood at discharge, highlighting another different pattern of depression in cardiac surgery patients. A logical explanation for such symptoms would be the positive or the negative thinking of each patient about the uncertainty of the outcome after surgery. A positive outcome after surgery would naturally lead to decrease in depressive symptoms. McKann and colleagues<sup>12</sup> reported that an improvement in physical functioning led to decrease in depressive symptoms at one month follow up after cardiac surgery. In contrast Sansone *et al*<sup>13</sup> reported that depressed patients who had significant post operative pain had persistence of their depression.

Beta blockers<sup>14</sup> have been used since ages to treat anxiety and panic attacks and various case reports have suggested the possibility of worsening of depressive symptoms in such patients. Similarly in our study there was a positive correlation between patients on beta

blockers having higher incidence of depression in immediate discharge period.

Post traumatic stress, anxiety, depression symptoms are higher in patients with longer ICU and hospital stay<sup>15</sup> which may persist for years. In our study, patients with prolonged ICU stay, had depression only at the time of discharge and interestingly patients who had longer waiting period preoperatively had higher incidence of depression at 3 and 6 months but not at the time of discharge. The unfamiliar environment in the ICU, varying sedation levels, inadequacy of pain control, inability to express needs may be few reasons responsible. Waiting period is a crucial time where patients are constantly exposed to negative emotions regarding the outcome of surgery. Longer the waiting period more severe will be the symptoms, and longer will be the persistence of these symptoms. The positive impact of immediate improvement after surgery, being alive after such a major surgery may be reason enough for the waiting period not to cause depression at discharge.

For reasons unexplained patients with dyslipidemia had higher incidence of depression at 6 months but the incidence was same as patients with normal lipid profile at discharge and at 3 months. The significance has to be further evaluated. Patients who underwent surgery on bypass had lower incidence of depression at 3 and 6 months compared to OFF PUMP patients. Maintenance of stable hemodynamics on bypass may be a possible explanation which needs further evaluation.

Validity of PHQ-9 questionnaire. The American Heart Association has recommended PHQ-9 as an aid for identification of depressed patients. A positive response to either of the PHQ-2 questions should be followed up with assessment of the PHQ-9. Scores of  $\geq 10$  on the PHQ-9 requires further detailed assessment by a psychiatrist or psychologist.<sup>1,4,5,16,17</sup>

## LIMITATIONS

PHQ-9 though validated by ACC/AHA for rapid screening does not imply that patient is having a major depressive disorder. This can only be diagnosed with a clinical interview using Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition criteria.

Outcome can vary between OPCAB and ON PUMP surgeries. The exact reason for decreased incidence of depression in OFFPUMP cases in our study is not known.

A total of 32 patients enrolled did not complete the questionnaires at discharge and were not available for follow-up.

Symptoms of depression can overlap with anxiety, panic attack, mania and even somatic symptoms.

Symptoms of the cardiovascular disease itself could be misinterpreted with depressive symptoms (breathlessness, palpitation, perspiration).

## CONCLUSION

For patients undergoing cardiac surgery, regaining emotional strength can be a tougher challenge than recuperating physically. Usually, majority of patients who suffer emotionally recover within few months. Unmanaged stress can increase morbidity and mortality after surgery. PHQ-9 analysis during preoperative anaesthetic evaluation may be validated in identifying high risk patients and improve the outcome by timely intervention.

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