

# The Relationship Between Preoperative Depression and C-Reactive Protein Levels and Postoperative Hospitalization in Patients Having Coronary Artery Bypass Grafting

Elena Johnson \*

Editorial Office, Surgery: Current Research, Belgium

## Corresponding Author\*

Elena Johnson

Editorial Office, Surgery: Current Research, Belgium

E-mail: [surggenopen@peerjournal.org](mailto:surggenopen@peerjournal.org)

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## Abstract

In order to better understand how preoperative depressive symptoms and postoperative length of stay in patients undergoing Coronary Artery Bypass Grafting (CABG) are related, this study looked at preoperative and postoperative C-Reactive Protein (CRP) levels. The Beck Depression Inventory (BDI-II) was used to assess the preoperative depressive symptoms in 212 elective CABG patients. Prior to surgery, information about the patient's clinical and demographic characteristics was obtained from medical records. Patients were monitored during their stay in the hospital to assess the CRP response to CABG surgery early (1 day-3 days after surgery) and persistently (4-6 days after surgery). A longer postoperative hospital stay was significantly ( $p=0.001$ ) correlated with a higher persistent CRP response. The connection between persistent CRP change and extended hospital stays was verified by the binary logistic regression analysis (OR=1.017, 95% CI=1.005 to 1.029,  $p=0.009$ ). When the gender subgroups were examined separately, only the male subgroup's significance persisted (OR=1.016, 95% CI=1.004 to 1.028,  $p=0.005$ ). Higher BDI-II depression scores did not significantly correlate with a longer postoperative hospital stay. Furthermore, no discernible relationship between BDI-II scores and preoperative or postoperative CRP levels, or the other way around, was found. The degree and potential mechanisms by which depression may affect the postoperative recovery of CABG patients require further investigation.

**Keywords:** Coronary artery bypass grafting • Depression • C-reactive protein • Postoperative length of stay

## Introduction

One of the main types of heart disease and one of the main factors in morbidity and mortality worldwide is Coronary Artery Disease (CAD). On-pump or off-pump Coronary Artery Bypass Grafting (CABG) is a frequently used therapy method that bypasses atherosclerotic occlusions and increases blood supply to the heart muscle, restoring function and viability. Age, gender, unhealthy lifestyle choices including smoking and eating poorly, obesity, high blood cholesterol, diabetes, hypertension, family history, and race are some of the classic risk factors linked to the development and spread of atherosclerotic lesions in the walls of coronary arteries. Patients with CAD, particularly those with stable CAD, unstable angina, or myocardial infarction, frequently experience depression (17% to 27%). More than 20% of CAD patients have major depressive symptoms diagnosed, although many more have subsyndromal depressed symptoms

that are below the diagnostic cutoff. Depressive symptoms may exist for a long period prior to the development of the disease, but they are usually underdiagnosed in CAD patients and subsequently neglected. The comorbidity of depression and CAD is caused by complicated, multiple bidirectional pathways. The link between depressed symptoms and CAD may be influenced by a number of pathophysiological factors, such as neuroendocrine dysregulation, inflammation, enhanced platelet activation and aggregation, oxidative stress, and endothelial dysfunction. Inflammatory markers and pro-inflammatory cytokines are frequently high in people with depressive disorders, which impairs their ability to respond to traditional antidepressant medication. Numerous studies suggest that depression and inflammatory response are symbiotic. Although there is a strong correlation between depression and high inflammatory markers, it is yet unknown how these two factors affect the development of CAD. While some research imply that depression precedes an increase in inflammatory biomarkers, others suggest that depression predates an increase in inflammatory processes in clinical entities such as coronary artery disease. Another idea is that inflammation and depression are both outcomes of a different pathogenic process.

Inflammatory markers and pro-inflammatory cytokines are frequently high in people with depressive disorders, which impairs their ability to respond to traditional antidepressant medication. The most widely utilized among them as a biomarker of systemic inflammation in clinical practice is the C-Reactive Protein (CRP), a marker of acute phase response, which is regularly evaluated across medical facilities and research labs. In many areas of medicine, CRP levels are used to identify and monitor disease, and its dynamics following major surgery procedures are typically connected to an inflammatory response to infection.

When compared to the non-depressed control group, a subset of individuals with depression had higher concentrations of CRP, which were frequently present before the onset of illness. The lower variability of CRP, one of the heightened inflammatory markers in depression, supports better homogeneity of the associated inflammatory phenotype. Numerous studies have also demonstrated a link between elevated peripheral CRP levels and a higher risk of developing CAD. Additionally revealed was the link between preoperative sadness and longer hospital stays following CABG surgeries. However, less than half of CABG patients have their depression symptoms regularly evaluated and treated. Furthermore, only a small number of research have examined the connection between depression and CRP proteins in CABG patients. Furthermore, little is known regarding the causal connection between these two factors and CABG recovery prediction. Additionally, only one study has to date demonstrated that post-surgery inflammation and high CRP levels may act as mediators between preoperative depressive symptoms and postoperative hospital stays in CABG patients. Particularly, a larger change in CRP from baseline preoperative levels to 4days-8 days after CABG surgery served as a partial mediator of this connection.

Based on these reports, the present study aimed to assess the relationship between preoperative depressive symptoms with postoperative hospital Length of Stay (LOS) of patients undergoing elective CABG surgery and to examine the extent to which this association could be influenced by preoperative and postoperative CRP values. Specifically, we hypothesized that the presence of preoperative depression symptoms measured using the Beck Depression Inventory (BDI-II) would be associated with the length of postoperative hospital stay and that the effect of preoperative depression score on the length of stay would be mediated by the higher values of preoperative and postoperative CRP levels.

## Discussion

The purpose of the current investigation was to determine how preoperative and

postoperative C-Reactive Protein (CRP) levels affected the relationship between preoperative depressive symptoms and postoperative hospital stay in patients having Coronary Artery Bypass Grafting (CABG). There was no discernible link between higher BDI-II depression symptom scores (>13) and longer (>7 days) postoperative inpatient LOS. Greater BDI-II scores had no discernible impact on early (1 day-3 days post-surgery) or persistent (4 days-6 days post-surgery) CRP response, or vice versa, even though the higher persistent CRP response was substantially related with a longer postoperative hospital stay. 12.3% of the patients in our cohort had medium to severe depressive symptoms, as determined by the BDI-II depression inventory before surgery. The obtained frequencies fall between 0.6% and 60% of the previously reported data on the prevalence of depressive symptoms prior to CABG surgery. This variation in reported estimates across the relevant literature may be due to one or more of the following factors: clinical and demographic differences between patient cohorts, a variety of inclusion and exclusion criteria, variations in the questionnaires or clinical interviews used for measurement, a variety of timing factors, and a variety of cut-off values used to identify high or low levels of depression.

When compared to patients without depressive symptoms, CABG patients with high preoperative Beck Depression Inventory (BDI) scores had considerably higher risks of spending more than a week in the hospital. But in their research, neither Bonferroni nor any other multiple comparisons correction was used. For the non-depressed and depressive CABG patient groups, the cut-off value for the BDI-II depression score was set at 10 and 10, respectively. Notably, when the same cut-off values were applied to our cohort of CABG patients, no statistically significant correlation between binary BDI-II levels and hospital LOS was found. Several other studies also indicated that longer hospital stays and poorer CABG patient outcomes were related to higher depression symptom scores. Accordingly, every one-unit increase in preoperative depressive symptoms in their patient group led to a 0.37-day increase in hospital stay. Additionally, in their population, female patients had a 0.18 day longer hospital stay than male patients, and they experienced greater levels of depression symptoms. In the patient population, female CABG patients were also more likely than male patients to experience preoperative depression and a lengthier hospital stay. However, after using the Bonferroni correction for multiple comparisons, the gender disparity was no longer statistically significant. Separate analyses of male and female patient subgroups within our cohort of CABG patients also highlighted the non-significant gender-related association of prolonged hospital stay with higher depression score, with females having more than a four times higher odds ratio for prolonged hospital stay than the male subgroup that exhibited a negative association. This supports the idea of the gender gap in depression aetiology and is consistent with the disparities in depression prevalence between men and women. Preoperative depression increased the likelihood of several unfavorable outcomes for CABG patients, including a higher frequency of postoperative inflammation, slower wound healing, and diminished patient resistance, all of which had an adverse effect on their postoperative hospital LOS. The amount of CRP and other inflammatory indicators strongly correlates with these negative outcomes. As was already mentioned, the primary regulator of CRP synthesis, inflammation, plays a significant part in the pathogenesis of atherosclerotic cardiovascular illnesses, including CAD. Rising early and persistent CRP response was found to be a partial mediator of the relationship between a higher BDI score and greater odds of a protracted hospital stay. The likelihood of a longer hospital stay increased by 1% for every rise in early CRP response in their patient population. On the other hand, probabilities were 1.3% higher when persistent CRP response increased by the same amount. On the other hand, in our CABG cohort, only persistent CRP levels were linked to a longer hospital stay, with a one-unit increase in persistent CRP translating into a 1.7% increase in the odds of an extended hospital stay. It's interesting to note that a separate analysis of the gender subgroups within our cohort of CABG patients revealed a significant association of persistent CRP change only among the male subgroup, whereas none of the CRP measures were associated with a prolonged hospital stay in the female patient subgroup.

Extended postoperative hospital LOS in CABG patients has also been linked to elevated baseline CRP. Increased baseline CRP levels were found to be a reliable indicator of preoperative depression and depression that persisted up to six months after the CABG procedure, as measured by the PHQ-9 test

score. But in the cohort of CABG patients, no such connection was seen. Additionally, no correlation between preoperative CRP levels and BDI score was noted. Smoking status was one of the key intensity variables in the early and durable CRP response in our group of CABG patients. At the same time, the statistical association between the presence of (post)operative infection and anything else was limited to the persistent CRP response.

In the current study, a postoperative hospital stay lasting more than a week was linked to smoking status and EuroSCORE-II. Numerous studies have shown a connection between depression and smoking among CABG patients. Additionally, depressed young male patients with established CAD much more frequently smoked cigarettes was found. The majority of the elements that make up the EuroSCORE-II have been connected to depression and anxiety. Therefore, risks resulting from preoperative anxiety and depressed symptoms may also be covered by EuroSCORE II operational risk values. Further research should be done to determine how baseline depression and patients' EuroSCORE risk classification are related. In addition, creating a predictive screening tool that takes into account emotional, behavioural, social, and functional variables is essential to complete the risk assessment by EuroSCORE.

Although it appears that the BDI-II scale offers a reliable method for identifying depression in CABG patients, careful cut-off point adjustment and evidence-based score interpretation are required before its application in clinical decision-making. The study has a number of advantages. We looked at patients having CABG at a particular institution and subtracted the impact of discharge policy changes between hospitals. The design of the study made it possible to examine the temporal relationships among depression, preoperative, postoperative, and duration of stay. Additionally, we were able to investigate the effect of preoperative and postoperative inflammation on the postoperative recovery of CABG patients through the repeated evaluation of CRP levels. The current study has a few significant drawbacks as well. First of all, there are not enough patients included in the study to detect the effect on patient mortality and operation risk. Furthermore, the 95% confidence intervals used to report the results of the logistic regression analyses were too large due to the relatively small cohort of CABG patients evaluated in this study in order to draw a definite conclusion. Second, although they were unable to be taken into account in our analyses, non-medical variables like social housing restrictions are likely to play a part in determining hospital LOS.

## Conclusion

In contrast to earlier studies, the current investigation found no connection between high preoperative BDI-II (>13) depressive symptom ratings and the length of postoperative hospital LOS in CABG patients. Additionally, there was no correlation between preoperative depression symptoms as assessed by the BDI-II questionnaire and the patient's preoperative CRP levels, early (1 day-3 days postoperatively), and sustained (4 days-6 days postoperatively) CRP responses after CABG surgery. However, when the male and female patient categories were evaluated separately, this association remained significant only for the male patient subgroup. Higher persistent CRP responses were substantially related with a prolonged postoperative inpatient LOS. Smoking status, postoperative atrial fibrillation, and, in the case of the persistent CRP change, concurrent (post)operative infection were all significant predictors of early and persistent CRP response in our cohort of CABG patients. To determine the extent and potential mechanisms by which depression may affect the postoperative recovery of CABG patients, additional research on a larger cohort of CABG patients is required.