

Postoperative depression in patients after coronary artery bypass grafting (CABG) – a review of the literature

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ABSTRACT:

Introduction: Ischemic heart disease is the most common cause of death in the world. The lives of patients with vascular defects can be saved by coronary artery bypass grafting (CABG). However, it is associated with an increased risk of developing depression after surgery.

Material and Methods: The aim of the study is to present the results of the latest research on postoperative depression after CABG, including studies describing the course of the disease, its consequences for the patient's prognosis and treatment. The publications available on the PubMed platform published after 2011 were reviewed.

Results: Depression before and after CABG affects 30–40% of patients, mostly women. Established after surgery and untreated, it persists for many years. The level of anxiety in patients decreases systematically after surgery. Indicators that may correlate with the patient's postoperative depression, including cortisol, high sensitivity C-reactive protein (hsCRP) and oxidative stress biomarkers, are being investigated. The occurrence of depression in patients after CABG has a number of negative consequences. Those include: weaker response to treatment, greater chance of relapse, and increased readmission frequency and mortality. Treatment of patients with this disorder involves the use of antidepressants (most often SSRIs – selective serotonin reuptake inhibitor) and/or various types of psychotherapy with cognitive behavioral therapy (CBT) at the forefront.

Conclusions: Depression following CABG decreases the quality of life and worsens patient prognosis. It is necessary to detect this condition early after surgery and to apply treatment, taking into account the cardiological disorders of the patient.

KEYWORDS:

coronary artery bypass grafting, depression

ABBREVIATIONS

BAI – Beck Anxiety Inventory
BDI – Beck Depression Inventory
CABG – coronary artery bypass graft surgery
CBT – Cognitive behavioral therapy
CR – cardiac rehabilitation
CVD – cardiovascular disease
HADS – Hospital Anxiety and Depression Scale
HRQoL – Health-related quality of life
hsCRP – high-sensitivity C-reactive protein
LOT-R – Life Orientation Test-Revised
NRD – National Readmission Database
PHQ-2 – Patient Health Questionnaire-2
PHQ-9 – Patient Health Questionnaire-9
RCBT – Religiously-integrated CBT
RFA – reactive nitrogen species
RFT – reactive oxygen species
SNRI – Serotonin and norepinephrine reuptake inhibitors
SSRI – selective serotonin reuptake inhibitor
STAI – Spielberger State-Trait Anxiety Inventory
TCA – tricyclic antidepressants

INTRODUCTION

Ischemic heart disease is defined by the World Health Organization, or WHO as the most frequent cause of death in the world. Together with stroke, in 2016 it has caused more than 15 million deaths out of 56.9 million [1]. The salvation for patients with stenosis of the arteries that supply blood to the heart muscle is coronary artery bypass grafting. While this procedure is characterized by high efficiency [2, 3], it carries the risk of psychological complications. Beside surgical interventions, such as: spine surgery, hysterectomy or cholecystectomy, CABG (coronary artery bypass grafting) is among the procedures most often associated with postoperative depression [4].

PURPOSE OF PAPER

The paper aims to demonstrate the result of the latest research on postoperative depression. This article describes the prevalence and outlines the specificity of its course. We also touch on the matter of factors correlating with the frequent occurrence of depression following CABG, whose study can help predict the occurrence of this disorder in patients. The consequences of postoperative depression in patients and their impact on prognosis are described. The article covers the possible treatment of depression after CABG and indications for cardiologists regarding the management of people particularly at risk.

DESCRIPTION OF STATE OF KNOWLEDGE

Prevalence of depression after CABG

Depression is a common mental disorder affecting over 264 million people worldwide [5]. The disease concerns approx. 6% of the population, whereby almost every fifth person will experience at least one episode of depression in their lifetime [6]. This percentage is much higher among people before or after CABG and amounts to 30–40% [7]. On top of that, the occurrence of depression is about twice as frequent in people with cardiovascular diseases than in the corresponding group without such conditions [8], and depressive symptoms are prevalent in women than in men [6, 8, 9].

Wilson et al. have looked at data of over a million patients hospitalized over the years 2000–2010 for occurrence of depression within 5 years of admission (patients with depression diagnosed before surgery were excluded). Among those people, over 39,000 have undergone coronary bypass surgery. In this group, 1,062 patients developed depression within five years, which represents 2.7%. For comparison: the percentage of depression cases was 5.1% after spine surgery, 2.6% after hysterectomy and 3.2% after cholecystectomy [4].

Another study involving 65 people undergoing coronary artery bypass graft examined the change in the occurrence of depressive symptoms in patients before and after CABG. Symptoms were assessed using Beck Depression Inventory, or BDI and Beck Anxiety Inventory, or BAI. BDI median before surgery was 8 and 13 on the third day after surgery. For BAI, the results were 9 and 17. The respondents had reduced symptoms of depression within 30 days, which were noticeable due to the reduction of the median BDI to 10, and BAI to 14 [10].

Course of depression after CABG

Research confirms that the occurrence of depression in patients shortly after revascularization is an unfavorable prognostic factor. However, there are no exact descriptions of the course of this disorder after coronary bypass surgery.

The study by Kustrzycki et al. examined the severity and change in time of anxiety and depression symptoms in patients after CABG over 8 years [11]. Depressive symptoms were measured using BDI, and patients were classified into subgroups with and without diagnosed depression based on the results of this questionnaire. There was a decrease in depressive symptoms in both groups immediately after surgery and within 3 months (a decrease in the median BDI). In the group with low BDI indices, it was possible to observe a considerable ($p = 0.04$) increase in depression symptoms in the period from 3 months to 8 years after the procedure (median BDI increase).

After 8 years, the mean BDI was $11.5 (\pm 9.5)$, of which more than 37% of patients had the index not lower than 13, which is synonymous with the occurrence of symptoms of depression [12]. In this study, the level of anxiety in patients undergoing CABG treatment using the Spielberger State-Trait Anxiety Inventory, or STAI was studied. The researchers noted a significant decrease in anxiety symptoms both after 3 months ($p = 0.02$) and 8 years after surgery ($p = 0.01$).

Similar conclusions were reached by Korbmacher et al. [13], who examined a group of 135 patients undergoing CABG. They found elevated levels of anxiety tested with the Hospital Anxiety and Depression Scale, or HADS, in over 39%. This percentage fell to 28.9% in the six months following operation. On the other hand, depressive symptoms observed in 20.7% of people before surgery (with the use of HADS) became noticeable in 28% after 6 months.

Tindle et al. investigated the relationship of optimism in patients (confirmed using the Life Orientation Test-Revised, or LOT-R) with their response to treatment of depression and the frequency of rehospitalization in patients after coronary artery bypass grafting. The study covered 430 people after CABG, 284 of whom were diagnosed with depression using the Patient Health Questionnaire-2/-9; PHQ-2, PHQ-9). Optimists responded positively to the treatment of depression over three times more often than pessimists ($p = 0.01$). In the course of the study, 197 patients were readmitted to hospital, of which 148 had previously been diagnosed with depression. Patients who were identified as optimists in the LOT-R test had an average 46% lower risk of being rehospitalized than pessimists (17% lower in the group of people with depression and 65% lower if PHQ-2 and PHQ-9 did not indicate depressive disorders in those patients) [14].

Factors correlating with the occurrence of depression after CABG

It is argued that the occurrence of depression in patients undergoing CABG is related to psychological factors as well as somatic changes and gender. A substantial factor influencing the presence of depression after undergoing CABG is the manifestation of affective disorders also before surgery [11, 13, 15].

The results of analyses give no evidence of a proportional relationship between the age of people undergoing CABG and the incidence of depression [15]. The results of a retrospective study by Aguayo et al. reveal that patients who developed depression after CABG are at a younger age than those rehospitalized without psychiatric disorders at the time of readmission (66.3 and 67.5 years, respectively; $p < 0, 0001$) [16]. A separate analysis indicates a threefold increase in depressive symptoms among patients in the seventh decade of life six months after CABG, and almost normalization of the mental state of patients over 80 years old after the same time after undergoing CABG [13].

Analyses of patients diagnosed with depression after CABG indicate that women are at higher risk than men [7, 13, 16, 17]. Upon rehospitalization in the range of 14 to 90 days after CABG, the percentage of patients diagnosed with depression was higher in women than in men (41.5% and 31.9%, respectively; $p < 0.0001$) [16].

Furthermore, according to the results of studies by Korbmacher et al., gender is important in the prediction of postoperative depression. When assessing the condition of patients using the HADS scale, it was shown that one week after the surgery, 42.2% of women and 19.5% of men in the study achieved a score that allowed to diagnose depression. Reexamination six months after CABG confirmed depressive symptoms in 40.7% of women and in 21.8% of men. Women also had an even more significant increase in the trend of developing anxiety symptoms throughout the study [13].

Because cortisol is believed to be involved in the pathological process leading to depression, it is treated as a potential predictor also in the case of mood disorders occurring after CABG [15, 18]. In a prospective study by Poole et al. conducted on a group of 171 patients, a relationship was found between the level of cortisol and the likelihood of developing depressive symptoms. No correlation was revealed between the output level of this hormone, measured approximately one month before surgery, and the appearance of affective disorders after twelve months of observation ($p = 0.352$). However, it has been shown that a steeper course of the daily cortisol secretion curve 2 months after surgery correlates with a lower probability of developing depressive disorders within a year of undergoing CABG ($p = 0.049$) [18].

The latest research evidence indicates similarities in the course of inflammatory processes in the metabolic syndrome and mood disorders, including major depressive disorder. The study of metabolic biomarkers related to the activation pathways of reactive oxygen species (ROS) and reactive nitrogen species (RFA) may be helpful in assessing the risk of depression in patients with concomitant cardiovascular disease (CVD) [19]. The immune system and the modulation of inflammatory processes, in particular by T lymphocytes, play a considerable role in the multifactorial pathogenesis of developing depressive disorders. It is postulated that the elevated amount of proinflammatory cytokines and increase in the population of T cells already during fetal life predispose patients to the occurrence of depression symptoms in adulthood [20]. Also, Maes et al. indicate a relationship between the processes in which proinflammatory cytokines are involved and the development of depressive disorders [21].

A study by Yang et al. conducted on 232 patients showed that the level of hsCRP is a significant predictor of the occurrence of symptoms of depression within six months of CABG. It has also been observed that patients with higher hsCRP levels have more severe depressive symptoms. The best predictive value of hsCRP is seen when its level is greater than 2.5 mg/L [17]. According to the results of studies by Poole et al., an increase in hsCRP in patients undergoing CABG by one unit within three days of surgery implied an increase in the chance of a longer hospital stay by 1% [22].

Also, patients with postoperative complications show a greater tendency to develop depressive symptoms six months after the procedure, compared to individuals who did not experience complications ($p < 0.0001$) [13]. The relationship between the presence of postoperative complications, worse mental state and a less favorable prognosis is also visible in the eight-year perspective [11].

Health implications of depression after CABG

A correctly performed CABG procedure and the inclusion of patients in cardiac rehabilitation, or CR should lead to an increase in capacity for exercise, minimization of the scale of depression and anxiety symptoms and a general improvement in the quality of life [23]. The metaanalysis by Rauch et al. showed an association between participation in CR in patients undergoing CABG and reduced mortality also among people with depression following surgery (HR 0.62, 95% CI 0.54–0.70) [24].

In a study involving a group of 50 people after coronary artery bypass grafting, Szczepańska-Gieracha et al. demonstrated

a correlation between the occurrence of severe depressive symptoms and the effectiveness of CR. The study included 11 women and 39 men over 50 with an average age of 63.3 (± 7.2) years. None of the respondents had been previously diagnosed with disorders such as psychosis, depression or anxiety, and had not been treated psychiatrically. Using the Beck Depression Inventory, the threshold for dividing the study population into a subgroup without depression symptoms and a subgroup manifesting such symptoms was determined. During the three-week duration of CR, the patients subjectively rated the degree of exercise intensity twice using a 20-point Borg scale. The intensity of depressive disorders correlated with the level of perceived effort in the final stage of CR ($p = 0.007$). Despite the lack of significant differences in age and pulse frequency during CR, no subjective improvement was observed in the assessment of exercise intensity between the first and last rehabilitation in the depressed subgroup, in contrast to the subgroup without mood disorders [23].

According to Culler et al., 44.4% of CABG beneficiaries in 2012 belonged to the age group from 70 to 79 years [25]. Among the patients studied by Szczepańska-Gierach et al., who achieved ≥ 10 points in the BDI scale after undergoing CABG, 83% maintained the result confirming the persistence of depressive disorders four weeks after surgery [23]. It has been indicated that depression in the elderly poses a therapeutic challenge due to the unsatisfactory response to antidepressants and implies a higher risk of developing severe neurocognitive disorders [26]. On the other hand, cognitive disorders are treated by Gustavson et al. as a considerable predictor of suicide risk among older patients [27]. It is also worth noting that male caregivers who took care of patients after CABG described cooperation with them as more demanding due to the challenges stemming from depressive symptoms and the unsatisfactory improvement of patients' mental state within three months of surgery [28, 29].

The results of conducted analyses clarify the importance of depression as a prognostic factor of increased mortality, readmission and cardiac events after CABG [7, 26, 30, 31]. Postoperative depression is associated with an increased risk of arrhythmia and remanifestation of angina symptoms within five years of operation [7]. The correlation between the presence of depression and the occurrence of neuropsychological disorders, such as delirium after CABG, is also considered [7, 32].

In a prospective study by Geulayov et al., 850 patients were assessed using HADS one year after CABG. Considering the component of the scale measuring the level of depression, it was documented that achieving a HADS-D score of ≥ 8 by respondents was associated with a 1.8-fold increase in mortality after 11 years compared to those who obtained a score < 8 (aHR = 1.78, 95% CI 1.29–2.45; $p < 0.0001$). Gender differentiation showed a correlation between the patients' gender and mortality. Obtaining a result of ≥ 8 points on the HADS-D scale correlated with a 1.6-fold increase in mortality among men ($p = 0.039$) and a two-fold increase in mortality in the group of women ($p = 0.007$). It was also found that a high level of anxiety in women in the postoperative period was associated with a higher 11-year mortality ($p = 0.049$); no such relationship was demonstrated in the group of male patients ($p = 0.65$) [31]; it increased with a 1.6-fold increase in mortality among men ($p = 0.039$) and a two-fold increase in mortality in the group of women studied ($p = 0.007$).

In a retrospective cohort study by Aguayo et al. using the National Readmissions Database (NRD), a group of patients undergoing CABG in the years 2010–2014 from January to September, who required rehospitalization of 14 to 90 days after surgery, was analyzed. Readmission was required by 11.7% of subjects. Of these, 5.1% of respondents had new cases of depression. Using multivariate regression, no significant correlations were found between the development of depression after undergoing CABG and the increased costs of rehospitalization and extended stay compared to the group rehospitalized without symptoms of depression. From among the patients diagnosed with postoperative depression during a repeat hospital stay, the mortality rate was 1.2%, while in all patients who were readmitted it was 2.3% ($p = 0.014$) [16].

Increased morbidity of both general and cardiovascular disease entities in patients who have experienced emotional disturbances and depressive symptoms after undergoing surgery as a result of coronary artery disease may have various causes. Depression correlates with the occurrence of: hypercholesterolaemia, arterial hypertension, obesity, nicotine addiction and endocrine dysfunction such as diabetes [7, 9]. The increased concentration of cortisol, high levels of β -thromboglobulin and proinflammatory cytokines also have a significant influence on the elevated number of diseases accompanying patients with depression [15, 18]. It is also postulated that atherosclerotic processes are more intense in patients with depression compared to people who do not suffer from this disease [9, 15]. Individuals who develop depressive symptoms after CABG are also more at risk of experiencing postoperative infections [33].

Research also indicates the existence of a relationship between inflammatory processes in depression and the development of neurodegenerative diseases. In patients with depression, there is a clear polymorphism of genes related to the production of ROS and RFA, which are responsible for the degenerative processes of the nervous tissue characteristic, for example Alzheimer's disease and Parkinson's [34].

Regardless of the number of indications for pharmacotherapy, patients with emotional disorders show a lower propensity to use the prescribed drugs, despite numerous risk factors [7, 35]. A different stance is taken by Stenman et al., who suggest that there is no significant difference in the use of drugs prescribed to prevent cardiovascular events after CABG between patients with depression and those who have not been diagnosed with this condition [36].

Treatment of postoperative depression

The aim of treatment is to achieve remission of depressive symptoms, which can be obtained through psychotherapy, pharmacotherapy or a combination of those. Essential drugs in the treatment of depression are: selective serotonin reuptake inhibitors and selective serotonin norepinephrine reuptake inhibitors (SNRIs). Tricyclic antidepressants, or TCA are also used, as well as monoamine oxidase inhibitors. Among the psychological therapies we can mention: cognitive-behavioral therapy (CBT), interpersonal therapy and acceptance and commitment therapy [6].

SSRIs and SNRIs are considered firstline drugs. Once implemented, their effectiveness should be assessed. Depending on the response to therapy, the drug is maintained, the dose is increased or another substance is introduced for treatment. If therapy with at least two

antidepressants is ineffective, depression is classified as refractory to treatment. Diagnosis of treatment-resistant depression requires the implementation of appropriate therapeutic measures, such as optimizing the dose of the drug or simultaneous introduction of another substance with antidepressant effect. Psychotherapy can be implemented at any stage of pharmacological treatment [37].

The studies emphasize the interaction of antidepressants and cardiac medications and the side effects of antidepressants, which may have particular negative consequences in patients with CVD. For example, TCAs may contribute to cardiac arrhythmias in patients, which is why it is recommended to use SSRIs in the first place; SSRIs allow for remission of depressive symptoms without causing side effects from the cardiovascular system [6, 9, 38]. Studies have shown an increased risk of developing renal dysfunction ($p = 0.03$) in patients receiving SSRIs or SNRIs and an increased number of cases in which the patient required artificial ventilation ($p = 0.04$) after such medication. Nevertheless, the relationship of medicinal drugs with bleeding episodes or increased mortality has not been demonstrated ($p = 0.36$) [35].

Psychotherapy can be used as an alternative to pharmacological treatment or in parallel with it. Numerous studies have confirmed the effectiveness of cognitive behavioral therapy in the treatment of depression in patients with CVD, including those after coronary bypass surgery [39]. In a study comparing the effectiveness of CBT with other forms of care for patients with depression after CABG, a higher percentage of remission of depression symptoms was found in the group of people undergoing cognitive behavioral therapy (71%) than in those who were helped to cope with stress (57%), and patients in the control group who were not treated (33%). The differences discovered by examining patients 3 months after the surgery were smaller after 6 months of surgery, but they deepened again during the 9 months after the start of the study and amounted to: 73% of remissions in CBT, 41% in the group learning how to cope with stress and 23% in those receiving standard care [9]. There are studies comparing the effectiveness of CBT with the religious variant (RCBT) of this therapy [40].

Alongside CBT, collaborative care is also helpful in treating depression in patients after coronary artery bypass surgery. Enhancing cooperation between units responsible for the patient's mental health and those treating his somatic ailments has a positive impact on his general condition [41]. A study by Mayer et al. showed a positive effect on health-related quality of life (HRQoL), regardless of the pharmacological treatment used [42].

A study conducted on a group of 326 patients treated with CABG by Højskov et al. revealed the effectiveness of early postoperative rehabilitation in reducing the incidence of depressive symptoms in patients. Individuals who performed rehabilitation exercises for 4 weeks after admission and underwent four nursing consultations showed an improvement in mood, measured using HADS, compared to patients in the control group who did not participate in rehabilitation [43].

CONCLUSION

Depression is a frequent condition, both before and after coronary bypass surgery. It can persist for a very long time after

surgery, and the procedure itself is not a factor that will mitigate depressive symptoms in people who have manifested them before CABG. The results of analyses show that, taking into account the patient's mental state, gender, age, and metabolic changes, it is possible to define a population that is particularly prone to depression after CABG. Individual factors present variable predictive values, depending on whether they are assessed before or after surgery. Adequately early awareness of the increased risk of developing affective disorders offers an opportunity to take specific measures to prevent the intensification of depressive symptoms. The consequences of post-CABG depression include: worse results of cardiac rehabilitation,

intensification of atherosclerotic processes, larger likelihood of rehospitalization and higher mortality. Taking into account nonsomatic consequences, the relationship between postoperative depression and severe cognitive and neuropsychological disorders, such as delirium, is also of significance. Treatment of postoperative depression is associated with drawing attention to interactions of antidepressants with cardiological drugs. At present, the most commonly used are SSRIs. Psychotherapy, including CBT, also proves to be effective. The results of the research indicate necessity of a more detailed screening of depression among cardiac patients, which, if left untreated, may significantly worsen their prognosis.

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