

Depression in patients after coronary artery bypass grafting

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Summary

Surgical revascularization is a recognized method of treatment of ischaemic heart disease. The number of patients undergoing coronary artery bypass grafting (CABG) is constantly increasing, both in a population of young patients with coronary heart disease and in elderly patients. It is estimated that even one out of three patients undergoing CABG in the perioperative period can develop symptoms of depression. Numerous individual factors as well as factors related to the surgery have an impact on the occurrence of depression. The most common factors are: age, sex, socio-economic status, co-existing diseases, and the occurrence of preoperative depression. Researchers are currently looking for biochemical markers concentration of which before surgery could serve as a predictor for the occurrence of post-CABG depression. It is suggested that inflammatory response, particularly intense in the perioperative period, is linked to the occurrence of depression after surgical revascularization. Recognizing these factors is of utmost importance since it will help develop a stratification aiming at the identification of patients who are particularly prone to the occurrence of postoperative depression. Due to the fact that depression not only lowers the quality of life but also affects the short-term and long-term prognosis, identifying patients at risk is significantly important.

Key words: depression, coronary artery bypass grafting

Introduction

Ischaemic heart disease is the leading cause of death throughout the world. The death rate due to cardiovascular disease per year amounts to 0.6-1.4 %, whereas the annual incidence of nonfatal MI totals 0.6-2.7 % [1, 2]. Coronary artery bypass grafting (CABG) is a recognized method of coronary revascularization, whose effec-

tiveness in the improvement of prognosis among patients with ischaemic heart disease has been demonstrated in numerous clinical studies [3, 4]. The number of patients with ischaemic heart disease undergoing surgical coronary revascularization increases systematically; on the one hand operations are performed on younger and younger patients, on the other hand, due to increasing lifespan, it is becoming more common for patients aged over 80 years to undergo operations. Depression following CABG is a major problem which has an impact on both the postoperative period and long-term prognosis [5, 6].

The incidence of post-CABG depression

The incidence of affective disorders in general population ranges from a few to several percent. It is estimated that every sixth person from the study group at a certain point in their lives shows depressive symptoms [7]. Depression occurs more frequently in patients with somatic diseases than in those who are physically healthy.

According to estimates, 16-23 % of patients with ischaemic heart disease suffer from major depression, while 31-60 % of patients with diagnosed ischaemic heart disease demonstrate symptoms of depression [5]. In a random sample of Polish patients (6392 men and 7153 women), BDI score ≥ 10 was assigned to 46.3 % of men with ischaemic heart disease and 21.2 % without ischaemic heart disease ($p < 0.0001$). In female population, the incidence of depression was also statistically significantly higher in women with ischaemic heart disease than in those without it (60.2 % vs. 30.7 %, $p < 0.0001$) [8].

The incidence of depression in CABG patients depends on the extent of cardiac surgery (isolated CABG or CABG in combination with heart valve reconstructive surgery), as well as on miscellaneous individual factors. The data on the epidemiology of depression in patients after CABG and valve repair surgeries is scarce in the literature. Oxlad et al. [9] demonstrated that in a group of 119 patients who underwent CABG and valve repair surgeries, depression was diagnosed in 15.7 % subjects 5-7 days after the surgery. Table 1 shows the incidence of depression in patients after isolated CABG, taking into account the questionnaire used as well as the elapsed time since the surgery in which the patients were examined [10-19].

Table 1. **The incidence of depression in patients after isolated CABG in clinical studies.**

| Author | Study group | Research tool | Incidence of depression | Elapsed time since surgery in which the occurrence of depression was evaluated |
|-----------------------|-------------|---------------|-------------------------|--|
| Kendel [10] | 833 | PHQ | 8.5 % | 2 months |
| Mitchell [11] | 137 | BDI | 16.4 % | 6-12 weeks |
| Krannich [12] | 142 | HADS | 17.5 % | 10 days |
| Young [13] | 232 | PHQ | 18.1 % | 6 months |
| Connerney et al. [14] | 309 | BDI | 28 % | 4-10 days |

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|-----------------------|-----|------|--------|--------------|
| Connerney et al. [14] | 309 | DIS | 20.4 % | 4-10 days |
| Tully [15] | 226 | DASS | 23.5 % | 4 days |
| Korbmache [16] | 135 | HADS | 24 % | 1 week |
| Korbmache [16] | 135 | HADS | 25 % | 6 months |
| Rymaszewska [17] | 53 | BDI | 28 % | Several days |
| Rymaszewska [17] | 53 | BDI | 26 % | 3 months |
| Kustrzycki [18] | 37 | BDI | 37.8 % | 8 years |
| Pawlak [19] | 100 | BDI | 50 % | 7 days |

BDI – Beck Depression Inventory, DASS – Depression Anxiety Stress Scales, DIS – diagnostic interview schedule HADS – Hospital Anxiety and Depression Scale, PHQ – Patient Health Questionnaire Factors conducive to the occurrence of post-CABG depression

The occurrence of post-CABG depression is determined by psychological factors, socioeconomic conditions and somatic disorders. It has been demonstrated that depression after CABG occurs more often in patients who had showed symptoms of depression before the surgery [17, 20]. Pirraglia et al. [21] identified significant factors which promote depression after CABG: low social support, low level of education, the occurrence of at least one stressful situation (of those included in the Stressful Life Events Scale) within a year before the surgery, limited access to medical care, and prolonged intensive care after the surgery. Little support provided by family members during perioperative period and living in one-person household also increases the incidence of depression after surgical revascularization [22].

The incidence of post-CABG depression was evaluated in a study carried out on 142 patients from different age groups who underwent CABG [12]. HADS score ≥ 8 was reported in 9.7 % of patients aged 36-60 years, 20.7 % of patients aged 61-66 years, 14.3 % of patients at the age of 67-72 years, and 25 % of the oldest patients aged 73-78 years 10 days after the surgery. No evidence on the incidence of depression growing proportionally with age has been found but the number of patients suffering from post-CABG depression was the highest among patients aged ≥ 73 years.

The identification of factors conducive to postoperative depression in young professionally active people is of utmost importance because its occurrence in this particular population of patients has not only health effects but also social consequences. Krzych et al. [23] conducted a study on 50 professionally active men at the age of 64 or less. BDI was used to evaluate depression intensification before and after surgery. The level of depression after the surgery was correlated to the output Beck scores ($r = 0.7$, $p < 0.01$). In both pre- and postoperative evaluation, men after MI suffered from more intense depression gained higher scores for depressive symptoms than patients with no MI history. The level of depression before the surgery depended on the left ventricular ejection fraction (LVEF) and operational risk, whereas depression levels after the surgery was also determined by operational risk and the number of past CABGs. The impact of medical history of hypertension, diabetes, stroke or nicotine use

on the occurrence of depression after CABG has not been demonstrated [23]. However, the analysis of the population of patients participating in the LIPID study has revealed that patients suffering from dyspnoea, intermittent claudication or diagnosed somatic disorders such as hypertension, diabetes and ischaemic heart disease demonstrated more often symptoms of post-CABG depression [24].

The researchers are currently looking for biochemical markers whose levels would serve as a predicative factor for the occurrence of depression after CABG. It is suggested that inflammatory response, significantly intense during perioperative period, is linked to the occurrence of post-CABG depression. The meta-analysis performed by Howren et al. [25] revealed a link between CRP, IL-1, and IL-6 levels and the depression occurrence. Few studies evaluated the effect of inflammatory markers on the occurrence of depression in patients undergoing cardiac revascularization. A study carried out on 232 CABG patients has provided evidence that the increased CRP concentration was an independent predicative factor for the occurrence of depression during 6 months of post-operative care [13]. Poole et al. [26] conducted a study on a sample of 142 patients in which they compared the mean CRP levels in the first 72 hours after CABG with that measured during the subsequent five days after the surgery. Patients with BDI score of less than 10 points and those with BDI score of 10 or more points had the same CRP levels in the first 72 hours after the surgery. The mean CRP concentration during the subsequent days (from the fourth to the eighth day) was significantly statistically higher in patients whose BDI score was at least 10 points than in those whose score was less than 10 points.

Outcomes of post-CABG depression

The occurrence of depression in the early postoperative period is an adverse prognostic factor, usually prognosticating a bad psychological condition of a patient during subsequent post-operative care and increased likelihood of cardiovascular complications. The available data showing the outcomes of postoperative depression, especially during the first days after surgery, is scarce. The studies conducted by Doering et al. [27] demonstrated that the symptoms of depression are the most intense in the first 48 hours following the patient's extubation. Factors such as: pain, sleep deprivation, isolation and loss of control might additionally elevate the depressive mood in patients. However, the studies carried out by McCrone's team [28] indicated that younger patients and women are more prone to depression occurring within the first several days and weeks after CABG. The first group scored significantly higher for depressive symptoms than the other patients in the first 48 and 72 hours after surgery, as well as in the second and fourth week after hospital dismissal. By comparison, women had elevated depression levels for up to 12 weeks after CABG. Studzińska et al. [29] also pointed out to the more frequent occurrence of depression after myocardial revascularization among women than among men. Foss-Nieradko et al. [30] conducted a study on 170 patients whose purpose was to evaluate the dynamics of symptoms of depression in patients undergoing isolated CABG during two-year follow-up. The participants

were divided into two groups on the basis of the obtained BDI scores: patients with symptoms of depression and those who did not demonstrate any. The evaluation was made using the previously mentioned questionnaire after 3 and 24 months since CABG. In a group of 88 patients without the output symptoms of depression no symptoms were observed in 76 % of subjects in the third and 24 month of follow-up, whereas in the remaining 24 % of patients incidental depression was observed. In a group with output symptoms of depression (82 subjects), the majority of patients (62 %) was diagnosed with incidental depression and only 38 % suffered from chronic depression. The studies of other researchers also indicated the occurrence of chronic depression in patients having postoperative depression. Timberlake et al. [31] demonstrated that among 37 % of CABG patients with depressive symptoms at the initial stage of the medical follow-up, symptoms of depression were observed in 44 % of subjects after 2 months following CABG and 42 % after a year since the surgery was performed. The other study revealed symptoms of depression after a month and a year after CABG in 50 % of patients who had showed the symptoms during perioperative period [20]. Contrary results were presented by the authors of a 6-month study in which the highest percentage of patients with depression (72 %) was observed only in the postoperative period [32]. The evaluation of the occurrence of depressive symptoms is significantly important throughout the entire period of patient care, during both the short-term and long-term follow ups, the reason being that the outcome of postoperative depression cannot be predicted with any certainty. The likelihood of depressive disorders in patients in whom they had not occurred neither before CABG nor during the early postoperative period should also be taken into account. In a Polish study, 24 % of patients who showed no symptoms of depression in the perioperative period were diagnosed with incidental depression during two-year follow-up [30]. The studies of other authors revealed that the percentage of patients who did not suffer from depression immediately after CABG surgery but demonstrated the symptoms of depression at a later stage, was lower and amounted to 9-13 % [20, 31].

Quality of life among depressive CABG patients

Improving the quality of life immediately after the prognosis is a primary goal for patients undergoing cardiac revascularization. It has been indicated that lowering the quality of life is related to even a short-term depression in the postoperative period exclusively, as well as the occurrence of depressive symptoms during a long-term follow-up in patients who had not suffered from depression shortly after CABG. [33,34]. The following subjective symptoms significantly lowering the quality of life were observed more often in patients with post-CABG depression: dyspnoea, atypical chest pain or shortness of breath [35]. In the *Post-CABG Biobehavioral Study* carried out on 674 CABG patients, the improvement of the quality of life was reported in all patients after the surgery during the 12-month follow up; however, to the least extent in patients with the symptoms of depression [36]. A shorter 6-month follow-up has also revealed a link between the occurrence of depression in the perio-

perative period and the lower physical and psychological conditions evaluated by means of the Quality of Life Questionnaire (SF-36). Postoperative depression was a predicative factor for malfunction also after taking into consideration such conditions as: diabetes, past MI or reduced LVEF [34]. Contrary results were obtained by Kendel et al. [10], who demonstrated that post-CABG depression was related to the malfunction of patients, in particular those with reduced LVEF. A special group constituted patients suffering from depression in the perioperative period who, after a relatively fast improvement, showed the recurrent symptoms of depression during the long-term follow-up. Those patients were prone to a significant lowering of the quality of life [33].

The link between post-CABG depression and prognosis

The occurrence of post-CABG depression affects negatively the prognosis in patients undergoing surgery. It appears that the occurrence of the reactive symptoms of depression which are related to the outcomes of the surgery only in the early postoperative period does not affect a long-term prognosis [36]. However, during a 12-year follow-up Blumenthal et al. [37] indicated that in patients who showed the symptoms of depression for six months after CABG, a risk of death was twice as high as in case of patients who did not suffer from depression. The adverse effect of depression on the occurrence of cardiovascular events has also been demonstrated in studies with a shorter medical follow-up. In a study of patients at one year follow-up Connerney et al. [6] revealed that for those who had post-CABG depression the risk of cardiovascular events is two- or threefold higher in comparison with non-depressive patients.

The impact of depression on the mortality was also to be seen during a 10-year follow-up of patients participating in the above mentioned study. The following independent factors: age, reduced LVEF, diabetes have been reported to increase the risk of cardiovascular death, and major depression. All these factors, except from depression, increased the risk of all-cause mortality [14]. In the Polish study, during the two-year follow-up the conditions such as: death, MI, repeat coronary revascularization, recurrent dyspnoea, and hospitalization due to cardiovascular events, occurred significantly more often in patients with chronic depression than in those without the symptoms of depression [27].

The use of pathophysiological and psychological mechanisms which have an impact on a negative prognosis in patients with post-CABG depression is advocated [38]. Among all pathophysiological mechanisms, hormonal fluctuations play a significant role. Depression results in the increase in cortyzol concentration and adrenergic hyperactivity, which lead to angiospasm, activation of the coagulation system and increased heart rate. A significant role in the pathogenesis of arteriosclerosis is assigned to prothrombotic mechanisms. Patients suffering from depression have the elevated β -thromboglobulin levels and *increased* expression of glycoprotein IIb/IIIa and selectin receptors on platelets [38]. They also suffer from leukocytosis, the increased CD4/CD8 ratio, as well as the elevated levels of TNF- α , IL1 and IL6 [39].

Cardiovascular risk factors, such as: nicotineism, hypertension, diabetes, dyslipidaemia, and obesity are more often observed in patients with ischaemic heart disease and depression than in those who do not suffer from depression. The presence of mentioned factors in depressive patients have been reported to intensify the atherosclerosis progression in coronary arteries and peripheral vessels to a more significant extent than in non-depressive patients [38]. It is also claimed that the elevated homocysteine and fibrinogen levels have more influence on the atherosclerosis progression in depressive patients than in non-depressive ones [40].

In CABG patients with postoperative depression numerous factors having the influence on the outcome of ischaemic heart disease might be observed. These are common also for patients without depression, however their influence is stronger in depressive patients.

Summary

Post-CABG depression is a common condition, whose occurrence has an impact on the patient's prognosis. The presence of the symptoms of depression in patients may involve difficulties faced by the physician in the diagnostic process and treatment. These may include following circumstances: the insufficient cooperation with the patient in terms of drug administration and reduction of coronary disease risk factors, frequent admissions to emergency departments due to undiagnosed symptoms, requests for the extension of a sick leave, as well as chronic anxiety or pessimism despite of provided information and confirmation of the improved health condition. Factors predisposing to the occurrence of depression in patients undergoing cardiac revascularization are well recognized. Moreover, their evaluation enables the identification of patients who are particularly prone to depression. Evaluating the risk of depression during the long-term follow-up after CABG also seems to be essential due to the fact that late occurrence or recurrence of the disease results not only in the lowering of the quality of patient's life but more importantly in the significant risk of cardiovascular events.

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