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ORIGINAL ARTICLE

Effect of the dynamics of depression symptoms on outcomes after coronary artery bypass grafting

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Abstract

Background: As coronary artery bypass grafting (CABG) remains an important myocardial revascularisation strategy, more attention has been paid to the role of numerous factors affecting outcomes after CABG, including depression and depressive symptoms. However, previous studies on this issue gave inconsistent results, the dynamics of depression has been seldom investigated, and only few reports have specifically addressed this problem in Poland.

Aim: Prospective evaluation of the effect of depressive symptoms and the dynamics of their occurrence on the incidence of cardiac events in patients after CABG during a 2-year follow-up.

Methods: We studied 170 patients aged 63 ± 10 years, including 17 women and 153 men, who underwent CABG. The Beck Depression Inventory (BDI) was used to evaluate the severity of depressive symptoms at 2 weeks (0M), 3 months (3M), and 24 months (24M) after CABG. Based on the BDI findings during subsequent follow-up visits, patients were divided into three groups depending on the dynamics of depressive symptoms: Group I without depression (67 patients), Group II with incidental depression (72 patients), and Group III with chronic depression (31 patients). During the 2-year follow-up, we evaluated the incidence of three combined endpoints that included death, myocardial infarction (MI), coronary angioplasty or redo CABG surgery; recurrent angina; and hospitalisations due to arrhythmia, heart failure or other cardiac causes. We analysed the effect of demographic, clinical, perioperative end psychological parameters to identify independent risk factors for cardiac events.

Results: Among patients with chronic depression, more cardiac events were noted compared to patients without depression or with incidental depression. All combined endpoints were significantly more common in patients with chronic depression compared to those without depression (death, MI, coronary angioplasty or redo CABG surgery: 19.3% in Group III *vs*. 5.9% in Group I, p = 0.0437; recurrent angina: 45% in Group III *vs*. 16.4% in Group I, p = 0.027; hospitalisations due to arrhythmia, heart failure or other cardiac causes: 54.8% in Group III *vs*. 31.3% in Group I, p = 0.0287). Hospitalisation rate was also higher among patients with chronic depression compared to those with incidental depression (54.8% in Group III *vs*. 31.9% in Group II, p = 0.031). In multivariate analysis using a linear regression model, independent risk factors for hospitalisation during the 2-year follow-up included the presence of depressive symptoms in the early postoperative period (p = 0.03) and the BDI score at 3 months after CABG (p = 0.0001). Use of antidepressants at baseline was an independent risk factor for recurrent angina (p = 0.004). Depressive symptoms, regardless of their dynamics, were not found to be a risk factor for the combined endpoint of death, MI, coronary angioplasty or redo CABG surgery.

Conclusions: During a 2-year prospective follow-up of patients after CABG, cardiac events were significantly more common among patients with chronic depression (but not incidental depression) as compared to patients without depressive symptoms. Hospitalisation rate among patients with chronic depression was significantly higher compared to both patients without depression or with incidental depression. Both chronic and incidental depression was not shown to be to be a risk factor for the combined endpoint of death, MI, coronary angioplasty or redo CABG surgery. Severe depressive symptoms that required the use of antidepressants at baseline were an independent risk factor of recurrent angina. The presence of depressive symptoms at baseline and BDI score at 3 months were independent risk factors for rehospitalisation. This suggests that the dynamics of depressive symptoms may have an effect on rehospitalisations in patients after CABG.

Key words: depression, outcomes, coronary artery bypass grafting

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INTRODUCTION

Coronary artery bypass grafting (CABG) remains an important myocardial revascularisation strategy. In the European Society of Cardiology (ESC) guidelines, CABG has been recommended for two main indications: to improve prognosis and to relieve symptoms [1]. Recently, more attention has been paid to the role of numerous factors affecting mortality and morbidity after CABG. In addition to factors directly related to the surgical procedure and patient status [2, 3], sociodemographic parameters and mental condition such as depression and anxiety have been increasingly considered [3]. Depression is diagnosed in about 20% of patients after CABG, and the prevalence of depressive symptoms ranges from 32% to 43% [4]. So far, only few reports have addressed this problem in Poland [5–7]. One study reported depression in 28––32% of patients in the perioperative period and in 26% of patients at 3 months [5], while in other study, depressive symptoms were found in 51.3% of patients after CABG. They were mild in severity in most cases (60%) [6].

Studies on the effect of depression on outcomes after CABG were infrequent, and their results inconsistent. Most authors limited their research to the evaluation of depression in the perioperative period [4, 8–19]. The dynamics of depressive symptoms during follow-up has been rarely taken into account [20–23], and the importance of this phenomenon has not been investigated.

The aim of the present study was to evaluate prospectively the effect of depressive symptoms and the dynamics of their occurrence on the incidence of cardiac events in patients after CABG during a 2-year follow-up.

METHODS

Patients and study protocol

For this study, we recruited subsequent patients after CABG who were hospitalised in the Department of Cardiac Rehabilitation and Noninvasive Electrocardiology at the Institute of Cardiology in Warsaw, Poland in 2003–2005 who fulfilled two inclusion criteria: age > 18 years and CABG performed within 2 preceding weeks. We excluded patients who underwent simultaneous valvular surgery, had an implanted pacemaker, had other cardiac rhythm than the sinus rhythm, or did not give consent for participation in the study. Patients who fulfilled the inclusion criteria underwent an initial assessment including history and physical examination, 24-h ECG Holter monitoring, and a self-assessment of the severity of depressive symptoms using the Beck Depression Inventory (BDI) [24]. The presence of depressive symptoms was defined as the BDI score of > 10. We intended to include equal numbers of patients with or without depressive symptoms at baseline.

The study protocol included assessment at three time points: at baseline (0M), at 3 months (3M), and at 2 years (24M) after the surgery. During each of the follow-up visits, evaluations performed during the initial assessment were repeated. The study was approved by the ethics committee at the Institute of Cardiology.

Endpoints

We evaluated the following cardiac endpoints: death, myocardial infarction (MI), coronary angioplasty, redo CABG surgery, recurrent angina, hospitalisation due to arrhythmia, hospitalisation due to heart failure (HF), and hospitalisation due to other cardiac causes.

Factors and parameters evaluated in the study

To identify independent risk factors for cardiac events, we analysed the following groups of parameters.

Demographic variables: age, gender, place of residence, marital status, children, living alone/with family, education, and source of income.

Clinical factors: body mass index (BMI), smoking, hypertension, dyslipidaemia, diabetes, peripheral arterial disease, previous MI, New York Heart Association functional class, left ventricular ejection fraction, Holter monitoring parameters (mean heart rate, occurrence of significant ventricular arrhythmia), and drug therapy, including antidepressant use.

Perioperative factors: number of grafts, complete revascularisation, use of cardiopulmonary bypass, length of hospital stay after the surgery, and postoperative complications.

Psychological factors: dynamics of depressive symptoms (incidental *vs*. chronic depressive symptoms), BDI score (overall, somatic, and mental).

Statistical analysis

To compare study groups, we used the Student *t* test for unpaired samples and the Mann-Whitney U test. Correlations were established using ANOVA, and independent risk factors were identified using a linear regression model with backward variable elimination. A p value < 0.05 was considered statistically significant.

RESULTS

The study protocol called for recruiting comparable numbers of patients with or without depressive symptoms. Initially, we recruited subsequent patients fulfilling the inclusion criteria, but after the intended number of patients without depressive symptoms was reached, only patients with depressive symptoms were further recruited. Ultimately, we recruited 230 patients, including 114 without depressive symptoms and 116 with depressive symptoms. Among those, 60 patients withdrew consent at various stages of follow-up, including 41 after the initial assessment and 19 after the first follow-up visit (3M). Thus, the final evaluable study group included 170 patients, including 88 without depressive symptoms and 82 with depressive symptoms. Fifteen patients failed to attend the follow-up visit at 2 years (24M), and outcomes in these patients were determined using a mailed questionnaire. Throughout

Table 1. Clinical characteristics of the study subgroups

	Group I (without depression) N = 67	Group II (incidental depression) N = 72	Group III (chronic depression) N = 31	P — II *vs.* I	P — III *vs.* I	P — III *vs.* II
BMI [kg/m^2]	27 ± 3	27 ± 3	28 ± 4	NS	NS	NS
Female gender	4.4%	11%	19%	NS	0.02	NS
Smoking	28%	39%	43%	NS	NS	NS
Hypertension	70%	71%	86%	NS	NS	NS
Hyperlipidaemia	92%	87%	96%	NS	NS	NS
Diabetes	22%	22%	29%	NS	NS	NS
Previous MI	52%	61%	64%	NS	NS	NS
Peripheral arterial disease	21%	10%	32%	NS	NS	0.007
Previous revascularisation	13%	20%	29%	NS	NS	NS
NYHA class	2 ± 0.4	2 ± 0.4	2 ± 0.6	NS	NS	NS
LVEF (%)	54 ± 10	52 ± 13	53 ± 10	NS	NS	NS
Medications:						
Beta-blocker	100%	100%	100%	NS	NS	NS
ACE-I	94%	95%	97%	NS	NS	NS
Statin	100%	96%	97%	NS	NS	NS
Aspirin	100%	100%	100%	NS	NS	NS
Antidepressant	1.5%	9.7%	16%	0.04	0.01	NS

BMI — body mass index; MI — myocardial infarction; NYHA — New York Heart Association; LVEF — left ventricular ejection fraction; ACE-I — angiotensin-converting enzyme inhibitor

this report, terms of depressive symptoms and depression are used interchangeably, although the authors are aware of the fact that the BDI score of > 10 is not synonymous with a clinical diagnosis of depression.

Dynamics of depressive symptoms

Based on the BDI scores at baseline and during follow-up visits (0M, 3M, 24M), the study group was divided into three subgroups; with Group I including patients without depression (BDI score ≤ 10 at all time points, i.e. 0M, 3M, and 24M), Group II including patients with incidental depression (BDI score > 10 at one or two time points), and Group III including patients with chronic depression (BDI score > 10 at all time points, i.e. 0M, 3M, and 24M). In Group II, depressive symptoms were present at only one time point in 35 (49%) patients (20 patients at 0M, 5 patients at 3M, and 10 patients at 24M), and at two time points in 36 (51%) patients (11 patients at 0M and 3M, 20 patients at 0M and 24M, and 5 patients at 3M and 24M).

Clinical characteristics of the study group

The study group included 17 women and 153 men aged 63 ± 10 years. Clinical characteristics of the three subgroups (I, II, and III) are shown in Table 1. Significant differences between subgroups were noted only for age, the presence of peripheral arterial disease, and the use of selective serotonin uptake inhibitors (SSRI). The first two factors did not materially affect o our findings, and SSRI use was a significant prognostic factor as discussed below.

Table 2. Cardiac events in the study group

Death	6 (3.5%)
Myocardial infarction	3 (1.8%)
Coronary angioplasty	6 (3.5%)
Redo CABG surgery	1 (0.5%)
Recurrent angina	47 (27.6%)
Hospitalisation due to arrhythmia	16 (8.8%)
Hospitalisation due to HF	13 (7.6%)
Hospitalisation due to other cardiac causes	32 (16%)

CABG — coronary artery bypass grafting; HF — heart failure

Cardiac events

Cardiac events noted in the overall study group during the 2-year follow-up are summarised in Table 2.

Due to a low number of events, we ultimately defined three combined endpoints: (1) death, MI, coronary angiopla-

Table 3. Cardiac event rates in relation to the presence and dynamics of depressive symptoms

	Group I (without depression) N = 67	Group II (incidental depression) N = 72	Group III (chronic depression) N = 31	P — II *vs*. I	P — III *vs*. I	P — III *vs*. II
1. Death, MI, PCI, redo CABG	5.9%	8.3%	19.3%	NS	0.0437	NS
2. Recurrent angina	16.4%	30.5%	45%	NS	0.0027	NS
3. Hospitalisation due to arrhythmia, HF, or other cardiac causes	31.3%	31.9%	54.8%	NS	0.0287	0.031

MI — myocardial infarction; PCI — percutaneous coronary intervention; CABG — coronary artery bypass grafting; HF — heart failure

sty or redo CABG surgery; (2) recurrent angina; and (3) hospitalisations due to arrhythmia, HF or other cardiac causes.

Rates of the combined endpoints in the study subgroups are shown in Table 3.

Of note, the dynamics of depressive symptoms had an effect on the cardiac event rate, as more events were noted in the chronic depression group as compared to both patients without depression and patients with incidental depression. In patients with chronic depression, the rate of all three combined endpoints was increased compared to patients without depression, while no significant differences were noted when groups with incidental depression and without depression were compared. In addition, hospitalisation rate was significantly increased in the chronic depression group as compared to patients with incidental depression.

Factors affecting cardiac event rates during the 2-year follow-up

We evaluated the relationship between cardiac events and demographic, clinical, perioperative, and psychological factors. In multivariate analysis (linear regression model), independent risk factors for hospitalisation during the 2-year follow-up included the presence of depressive symptoms during the early postoperative period (β = –0.336, t = –2.249, p = 0.03) and the BDI score at 3 months (β = 0.59, t = = 3.985, p = 0.0001) (R^2 = 0.39). Baseline use of antidepressants was an independent risk factor for recurrent angina (β = 0.394, t = 3.034, p = 0.004, R^2 = 0.33). Depressive symptoms, regardless of their dynamics, were not found to be a risk factor for the combined endpoint of death, MI, coronary angioplasty or redo CABG surgery. Somatic and mental scores on the BDI had no significant effect on the outcomes.

DISCUSSION

Depression or depressive symptoms are quite frequent in patients after CABG [4, 6, 7, 25]. Some authors indicated an adverse effect of depression on mortality [8–12, 20] or morbidity [13–18, 21, 22] after CABG but others were unable to confirm such a relationship [4, 26], with differences attributable to varying methodology used, including the diagnostic criteria and timing of the diagnosis of depression, as well as details and duration of the follow-up. There are no published reports that would specifically address this issue in Poland. In addition, only few authors considered the dynamics of depressive symptoms during a longer follow-up [20, 22]. In our previous report on this issue [23], we found dynamic changes of the depressive symptoms during a 2-year follow-up in most patients with depressive symptoms noted in the early postoperative period and in about 25% of patients without depression at baseline. Question remains, however, whether this dynamics of depressive symptoms has a clinical significance.

Dynamics of the depressive symptoms and cardiac event rate

Saur et al. [21] and Borowicz et al. [22] showed that chronic depressive symptoms (that were, however, not evaluated using the BDI) were related to more frequent rehospitalisations at 6 months after CABG and recurrent angina during a 5-year follow-up. They did not perform, however, any comparative analyses regarding different dynamics of the depressive symptoms during the follow-up. Our 2-year prospective study showed a significantly higher rate of all cardiac events in the group with chronic depression compared to patients without depression. No such relationship was found for incidental depression. In addition, rehospitalisations were significantly more frequent in the group with chronic depression compared to patients with incidental depression. These findings suggest a significant effect of the dynamics of depressive symptoms (chronic *vs*. incidental) on outcomes in patients after CABG.

Are depressive symptoms and their dynamics independent risk factors for cardiac events?

In our study, we found that neither chronic nor incidental depressive symptoms had a significant effect on the occurrence of a combined endpoint of death, MI, coronary angioplasty or redo CABG surgery. Connerney et al. [13] also did not find a relationship between postoperative depressive

symptoms (as evaluated using the BDI) and outcomes. However, when the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria were used, cardiac event rate was increased more than twofold in patients with depression after CABG at 1-year follow-up, although without any significant effect on mortality. Pirraglia et al. [26] were also unable to confirm a relationship between postoperative depressive symptoms as evaluated using the Centre for Epidemiologic Studies-Depression Scale (CES-D) and outcomes during a 6-month follow-up, in contrast to findings reported by Peterson et al. [15] and Rafanelli et al. [11]. The latter authors showed that mild depression (by the DSM-IV criteria) at one month after CABG was a risk factor for cardiac events including cardiac death and MI during a 6- to 8-year follow-up. Similarly, Connerney et al. [19] recently reported that perioperative depressive symptoms as evaluated using the BDI were an independent risk factor for cardiac mortality during a 10-year follow-up. Blumenthal et al. [20] were the only ones who evaluated the dynamics of depressive symptoms. These authors showed that depressive symptoms persisting for 6 months (as evaluated using the CES-D) were an independent risk factor for mortality during a 12-year follow-up. In our study, despite significant quantitative relationships found between the form of depression (chronic or incidental) and major cardiac event rate, we did not confirm a statistically significant independent effect of depression on the occurrence of a combined endpoint of death, MI, coronary angioplasty or redo CABG surgery. This may have resulted from low rates of cardiac events in our study population (death 3.5%, MI 1.8%, coronary angioplasty 3.5%, redo CABG surgery 0.5%) and a relatively short follow-up period.

Another endpoint in our study was recurrent angina during the 2-year follow-up. Many authors reported the effect of both preoperative [10, 14, 16] and postoperative depression [11, 13, 22] on the occurrence of anginal symptoms after CABG. Wellenius et al. [27] attempted to clarify this issue and showed that postoperative depressive symptoms correlated with the severity of proliferative changes in venous grafts and their lumen reduction during a 4- to 5-year follow-up. In our study, baseline SSRI use was one of the independent risk factors for this endpoints ($p = 0.004$). Use of these medications may suggest previous severe depressive symptoms and thus outcomes may have been affected by this mechanism. Similar observations were made by Xiong et al. [12] who showed in a retrospective analysis that antidepressant use (mostly of SSRI) before CABG was related to increased mortality and morbidity during 3–6 years of follow-up. In an analysis of the Nurses Health Study data (in a population without cardiovascular disease at baseline), Whang et al. [28] found that antidepressant use was associated with a significantly increased risk of sudden cardiac death. Thus, an adverse effect of medications cannot be ruled out when evaluating the relationship between drug therapy and outcomes.

The presence of depressive symptoms in the early postoperative period was found to be a significant risk factor for the third endpoint evaluated in our study, hospitalisations during 2 years of follow-up after CABG ($p = 0.03$). This is consistent with views expressed by some authors [21] while others [17, 18] held that only preoperative depression and anxiety symptoms after CABG, but not postoperative depression, were risk factors for hospitalisation during 6 months of follow-up. Another independent risk factor for rehospitalisation in our study was the BDI score at 3 months ($p = 0.0001$). Thus, it may be suspected that increasing severity of postoperative depression (as reflected by worse BDI scores at 3 months) increased the risk of rehospitalisation. This would argue for the significance of the dynamics of depressive symptoms in regard to this issue.

Depressive symptoms and female gender

Depression was reported to be more common among women both in the general population and among patients with cardiovascular disease, including those who underwent CABG [6, 25, 29]. Our findings confirmed these reports but only regarding chronic depression. Female gender was not a significant risk factor for cardiac events but due to a very low number of women in our study (only 17 patients, or 10% of the study population) we were unable to perform any detailed analyses of this subgroup.

Limitations of the study

Limitations of our study included a relatively small study sample, short follow-up period, and a low number of cardiac events. It is likely that due to these factors we were unable to show a significant effect of depressive symptoms and their dynamics on the occurrence of a combined endpoint of death, MI, coronary angioplasty or redo CABG surgery.

CONCLUSIONS

During a 2-year prospective follow-up of patients after CABG: (1) Cardiac events were significantly more common among patients with chronic depression (but not incidental depression) as compared to patients without depressive symptoms. (2) Hospitalisation rate among patients with chronic depression was significantly higher compared to both patients without depression or with incidental depression. (3) Both chronic and incidental depression was not shown to be to be a risk factor for the combined endpoint of death, MI, coronary angioplasty or redo CABG surgery. (4) Severe depressive symptoms that required the use of antidepressants at baseline are an independent risk factor of recurrent angina. (5) The presence of depressive symptoms at baseline and BDI score at 3 months were independent risk factors for rehospitalisation. This suggests that the dynamics of depressive symptoms may have an effect on rehospitalisations in patients after CABG.

Conflict of interest: *none declared*

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Wpływ dynamiki występowania objawów depresyjnych na rokowanie pacjentów po operacji pomostowania tętnic wieńcowych

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Streszczenie

Wstęp: Pomostowanie tętnic wieńcowych (CABG) to nadal istotna metoda rewaskularyzacji mięśnia sercowego. Podnosi się rolę wielu czynników wpływających na rokowanie pacjentów po CABG, wśród nich depresji i objawów depresyjnych. Wyniki badań dotyczących tego zagadnienia są niejednoznaczne, rzadko ocenia się dynamikę depresji, nieliczne doniesienia uwzględniają polskie realia.

Cel: Celem pracy była prospektywna ocena wpływu objawów depresyjnych i dynamiki ich występowania na pojawienie się zdarzeń sercowych u pacjentów po CABG w trakcie 2-letniej obserwacji.

Metody: Grupę badaną stanowiło 170 pacjentów (17 kobiet i 153 mężczyzn) w wieku 63 ± 10 lat po przebytym CABG. Nasilenie objawów depresyjnych oceniano za pomocą Kwestionariusza Depresji Becka (BDI) w ciągu 2 tygodni po zabiegu (0M) oraz po 3 (3M) i 24 (24M) miesiącach od CABG. Na podstawie wyników BDI uzyskiwanych w czasie kolejnych kontroli pacjentów podzielono na trzy podgrupy uwzględniające dynamikę objawów depresyjnych: I — bez depresji (67 osób), II — z depresją incydentalną (72 osób), III — z depresją przewlekłą (31 osób). W czasie 2-letniej obserwacji oceniano występowanie 3 złożonych punktów końcowych — 1. zgon, zawał serca, angioplastyka wieńcowa, ponowne CABG; 2. nawrót dławicy; 3. hospitalizacje z powodu zaburzeń rytmu serca, niewydolności serca i innych przyczyn kardiologicznych. W celu ustalenia niezależnych czynników ryzyka wystąpienia zdarzeń sercowych analizowano wpływ parametrów: demograficznych, klinicznych, okołooperacyjnych i psychologicznych.

Wyniki: W podgrupie z depresją przewlekłą zanotowano więcej zdarzeń sercowych w porównaniu zarówno z podgrupą bez depresji, jak i z depresją incydentalną. Wszystkie złożone punkty końcowe występowały znamiennie statystycznie częściej w podgrupie z depresją przewlekłą w porównaniu z podgrupą bez depresji (1. III *v.* I — 19,3% *v.* 5,9%; p = 0,0437; 2. III *v.* I — 45% *v.* 16,4%; p = 0,027; 3. III *v.* I — 54,8% *v.* 31,3%; p = 0,0287). Częstotliwość hospitalizacji była istotnie wyższa również w podgrupie z depresją przewlekłą w porównaniu z grupą z depresją incydentalną (III *v.* II — 54,8% *v.* 31,9%; p = 0,031). W analizie wieloczynnikowej (model regresji liniowej) niezależnymi czynnikami ryzyka hospitalizacji podczas 2-letniej obserwacji okazały się: występowanie objawów depresyjnych we wczesnym okresie pooperacyjnym (p = 0,03) oraz wynik BDI po 3 miesiącach od CABG (p = 0,0001). Przyjmowanie leków antydepresyjnych na początku obserwacji było niezależnym czynnikiem ryzyka nawrotu dławicy (p = 0,004). Objawy depresyjne, bez względu na dynamikę nie okazały się czynnikiem ryzyka pierwszego, złożonego punktu końcowego, tj. zgonu, zawału serca, angioplastyki wieńcowej i ponownego CABG.

Wnioski: W prospektywnej 2-letniej obserwacji chorych po CABG zdarzenia sercowe istotnie częściej występują wśród pacjentów z depresją przewlekłą (a nie incydentalną) w porównaniu z osobami bez objawów depresyjnych. Częstotliwość hospitalizacji w podgrupie z depresją przewlekłą jest istotnie wyższa niż w podgrupie bez depresji i z depresją incydentalną. Nie wykazano, aby depresja (przewlekła lub incydentalna) była niezależnym czynnikiem ryzyka zgonu, zawału serca, angioplastyki wieńcowej i ponownego CABG. Nasilone objawy depresyjne wymagające przyjmowania leków antydepresyjnych na początku obserwacji stanowią niezależny czynnik ryzyka nawrotu dolegliwości dławicowych. Występowanie objawów depresyjnych na początku obserwacji i wynik skali Becka oceniany 3 miesiące po zabiegu są niezależnymi czynnikami ryzyka rehospitalizacji. Może to przemawiać za wpływem dynamiki objawów depresyjnych na ponowne hospitalizacje pacjentów po CABG.

Słowa kluczowe: depresja, rokowanie, pomostowanie tętnic wieńcowych

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