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Depressive symptoms in patients with coronary artery disease after percutaneous coronary interventions (PCIs)

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Summary

Introduction: Studies confirm a strong relationship between depression and coronary artery disease (CAD). Despite this, depressive disorders in CAD patients are often misdiagnosed and under-treated.

Aim: 1) to investigate whether CAD patients qualified for percutanous coronary interventions (PCI) develop any specific type of depressive disorders; 2) to assess the depressive symptoms in CAD patients after the successful PCI.

Subject and methods: of 227 CAD patients, qualified for PCI, 156 with optimal PCI result were included. Patients were assessed with the Hamilton Depression Rating Scale (HDRS), Beck Depression Inventory (BDI), Rosenberg Self-Esteem Scale (RS), Hopelessness Scale (HS), Automatic Thoughts Questionnaire (ATQ) one day before and 1 month after PCI.

Results: The results were compared to the group of 49 depressed patients without CAD, treated in psychiatric setting (group III). Depressive symptoms, observed at the baseline in 75 patients (48.1% – group I) were of mild or moderate severity with the prevalence of somatic complains. A comparison between group I and group III revealed different characteristics of depressive symptomatology, while the severity of depression was comparable. One month after the PCI, depressive symptoms persisted in 33 subjects, in whom at the baseline BDI, ATQ and HS scores were significantly higher as compared to 42 patients in whom depressive symptoms resolved.

Conclusions: Successful PCI is not a sufficient determinant for the improvement of depressive symptoms. Diagnosis of depression in CAD patients needs a special attention, because of a specific clinical picture and tendency to persistence.

coronary angioplasty / **coronary artery disease** / **depression**

INTRODUCTION

Depression contributing to cardiovascular disease is a major clinical problem both due to its frequent occurrence and serious health effects. A wide variety of studies have confirmed a strong relationship between depressive disorders and the risk of development and unfavourable course of coronary artery disease (CAD) and myocardial infarction [1, 2]. The risk of CAD and

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cardiac death seems to be correlated to the severity of depression [3, 4, 5, 6]. Depressive disorders occur more frequently in CAD patients than in the general population. Transient and short-term depressive symptoms are observed in more than half of the patients during the first few days after the myocardial infarction. Moreover, in 16–22% of cases DSM major depression criteria are fulfilled [7, 8, 9].

The association between depression and CAD is not merely coincidental, but proved psychological (isolation, lack of social support), behavioural (lifestyle, compliance) and pathophysiological (stress axis hyperactivity, adrenergic activation, altered autonomic activity, platelet dysfunction, immunological changes) mechanisms underlie this comorbidity.

The comorbidity of depressive disorders and CAD increases the risk of major cardiac episodes, illness' severity, longer-term disability, worse physical capacity and about 50% greater risk of cardiac mortality [6, 10, 11, 12, 13, 14, 15]. Subjective quality of life is also diminished.

Despite these important clinical implications, depressive disorders in CAD patients are rarely well-diagnosed or adequately treated. It is estimated that only 25% of depressive disorders comorbid with CAD are recognized [16]. Usually, mild or moderate levels of depression with nonspecific clinical symptomatology and a predominance of physical complaints may be the reason for misinterpretation of depressive psychopathology as signs of a poor physical state or drug induced side-effects.

The aims of our study were: 1) to investigate whether CAD patients qualified for PCI develop any specific type of depressive symptomatology; 2) to assess the depressive symptoms after the successful PCI in CAD patients.

SUBJECTS AND METHODS

Subjects

227 patients diagnosed with stable CAD (CCS II-III), with no previous history of PCI or coronary artery by-pass grafting (CABG), qualified for an elective PCI (balloon angioplasty, angioplasty with stent implantation, rotational atherectomy) were enrolled in the study. Angiographic and clinical successful outcome of intervention, as well as lack of recurrent symptoms of ischemia during the four weeks following the intervention, made the patient eligible for further analysis. PCIs were performed according to generally accepted standards of practice. The operator's task was to achieve an optimal result for the procedure, which was defined as final diameter stenosis < 30% (estimated in quantitative coronary angiography) without a high grade of dissection with good coronary flow (TIMI 3). Stents were used for an abrupt or threatened vessel closure, as well as in the case of a suboptimal result of balloon angioplasty (final diameter stenosis < 20% was recognized as an optimal result of stent implantation). The operators were allowed to use intravascular ultrasonography for additional optimalization of intervention. The clinically successful PCI was defined as an angiographically effective procedure without serious complications, in conjunction with a reduction of clinical symptoms. Patients with one vessel disease, as well as those with multivessel disease were included in the study. PCIs were performed either as non-staged or staged procedures, during one hospital stay.

Symptoms of angina were assessed before PCI and four weeks after the intervention using the Canadian Cardiovascular Society classification (CCS) [17]. In the instances of atypical chest pain after PCI, evaluation of myocardial ischaemia was based on the results of the exercise test. Only patients with complete functional revascularization were included.

Methods

The psychopathological status of the patients was assessed: one day before, one month, 6 months, 12 months after the PCI intervention. In this paper, the subanalysis of results obtained at the first and second examinations is presented. The following instruments were administered: structured medical history, 21-item Hamilton Depression Rating Scale ($HDRS_{21}$), Beck Depression Inventory (BDI), Rosenberg Self-Esteem Scale (RS), Beck Hopelessness Scale (HS), and Automatic Thoughts Questionnaire (ATQ) [18, 19, 20, 21, 22]. A patient was classified as being depressed according to the results of the clinical

examination and BDI, HDRS scores. Since the validity of those scales (especially HDRS) may be problematic in patients with concurrent somatic illnesses, it has been suggested by many authors that the higher cut-off scoring should be chosen for better diagnostic accuracy [23, 24]. In this study it was accepted that a score > 11 points in BDI indicate the presence of depression.

Additionally, the mean BDI, BDI 13 (cognitive – affective subscale) and BDI 14–21 (somatic subscale of BDI) [25], scores of CAD patients were compared with a group of 49 patients with recurrent depressive disorder treated at the outpatient unit of the Department of Psychiatry, Collegium Medicum UJ, and fulfilling ICD–10 criteria for a mild or moderate depressive episode (Group III). The patients from group III were free of severe somatic disorders, including CAD.

The distribution of the age of patients was examined with descriptive statistics (median, mean, standard deviation) and boxplots. If the normality and equality of variance assumptions were present, the difference in the mean age in the two groups was tested using a t-test. If the assumptions were not met, a non-parametric test was used (Wilcoxon rank-sum test). Statistical analysis of psychological tests was based on a comparison of mean results. Before conducting statistical analysis, normal distribution was checked (Shapiro-Wilk test). Mean scores, results and standard deviations of BDI, BDI 13, BDI 14–24, HS, RS, ATQ, HDRS were compared (Mann Whitney U test, Wilcoxon test). Spearman's rank correlation coefficients were calculated to permit examination of the association between cardiovascular function impairment (CCS criteria) and severity of depression. All statistical tests were two-sided. A p value of < 0.05 was considered statistically significant.

RESULTS

Of 227 patients enrolled, 71 were excluded because of: suboptimal result of PCI (n=31); hospitalizations due to non-cardiological reasons during the one-year follow-up (n=14), compliance failure (n=26). The final group consisted of 156 patients (39–71 year-old; mean age: 55.05±8.25) including: 135 males (86.5%) and 21 females (13.5%) who were followed up for one year. 115 subjects (73.3%) had a previous history of cardiac infarction. According to the CAD risk factors: 108 of patients (69%) had hyperlipidemia, 97 (62%) were diagnosed with hypertension and 19 (12%) with diabetes II type. 70 patients (45%) were smokers.

In the entire group of patients (n=156) there were no significant correlations between angina symptoms impairment (CCS criteria) and severity of depression, assessed with HDRS or BDI in; (Spearman rank correlation, HDRSvsCCS r=0.25; BDIvsCCS r=0.27, p- NS). The presence or absence of depressive symptomatology during the first examination was the defining criterion for group I (n=75, 48.1%) – patients depressed before PCI and II (n=81, 51.9%) – patients without the symptoms of depression prior to intervention.

The severity of depression assessed one day before PCI in group I was mild or moderate (20.2 ±5.7 points in BDI, 16.06 ± 5.2 points in HDRS), with a prevalence of somatic symptoms (BDI 13 = 9.77 ± 4.6; BDI 14–21 = 10.38 ± 3.0). The characteristic of thinking style, i.e. negative automatic thoughts, low self-esteem, and feelings of hopelessness, were significantly higher in group I than in group II (Tab.1).

Qualitative analysis of the severity of depressive symptoms, based on BDI items, per-

Table1. Mean and standard deviation of BDI, HS, RS, ATQ scores in group I and II at first examination point

	Group I (n=75)	Group II (n=81)	Group I vs. II* (p value)
HDRS	16.06 ± 5.2	4.46 ± 2.71	p< 0.001
BDI	20.2 ±5.7	7.0 ± 3.2	p< 0.001
HS	9.8 ± 4.6	4.2± 2.8	p< 0.001
RS	70.4 ± 14.6	85.0 ± 10.5	p< 0.001
ATQ	64.1 ± 14.3	49.2 ± 12.5	p< 0.001

*Mann-Whitney U test

formed on group I revealed the highest rating (mean score >1.0) in the following items: 2 (Pessimism), 12 (Social withdrawal), 13 (Indecisiveness), 15 (Retardation), 16 (Insomnia), 17 (Fatigability), 19 (Loss of Weight), 20 (Somatic preoccupation) and 21 (Low level of energy). The lowest rated (mean < 0.5) were: 5 (Guilt), 6 (Expectation of punishment), 7 (Dislike of self) and 9 (Suicidal ideation).

A comparison between group I and group III revealed different characteristics of depressive symptomatology, while the severity of depression, as measured by BDI, was comparable. There was a predominance of somatic complaints (BDI 14–21 subscale) in group I, while patients from group III presented more severe affective-cognitive symptoms, reflected by significantly higher BDI 1–13 subscale scoring (Tab.2).

One month after the PCI procedure (second examination), depressive symptoms were observed in 45 patients (28.9%). Depressive symptoms were still present in 33 subjects from group I, while in the rest of group I (n=42) spontaneous improvement was observed. Moreover, in group II (patients free of depressive symptoms a day before PCI) twelve patients developed depressive symptomatology during the 4 weeks after the procedure. Based on these findings, the following subgroups were identified for further analysis: Ia (n=33) – patients with depressive symptoms persisting one month, Ib (n=42) – patients in whom depressive symptoms abated, IIa (n=12) – patients without depression before PCI in whom depressive symptoms developed prior to the second examination, IIb (n=69) – patients without depression both before and one month after PCI. The aim of further analysis was to investigate the presence of qualitative or quantitative features predicting a high risk of depression and its persistence after the PCI.

At the first examination (before PCI), more severe both affective-cognitive (BDI 13) and somatic symptoms (BDI 14–21) of the depressive syndrome were detected in subgroup Ia in comparison with subgroup Ib. Moreover, in subgroup Ia, a significantly higher frequency of negative automatic thoughts (ATQ) and more pronounced hopelessness (HS) were observed. A comparison of RS scores revealed no statistically significant difference between subgroups Ia and Ib (Tab.3).

The qualitative comparison of severity of depressive symptoms measured by BDI items showed that symptoms included in items: 2 (Pessimism), 7 (Dislike of self), 8 (Self Accusation), 9 (Suicidal ideation), 11 (Irritability), 15 (Retardation), 16 (Insomnia), and 19 (Loss of Weight),

Table 2. Comparison of mean BDI and BDI subscales rates between group I and III (Mann Whitney test)

	Group I (n=75)	Group III (n=49)	Group I vs. III (p value)
BDI	20.2 ±5.7	21.1 ±6.5	NS
BDI 13	9.8 ± 4.6	13.9 ± 4.0	p< 0.001
BDI 14–21	10.4 ± 3.0	7.2 ± 3.2	p< 0.001

Table 3. Mean and standard deviation of BDI, HS, RS, ATQ scores in subgroup Ia and Ib at first examination point.

Scores at first examination point	Subgroup Ia (n=33)	Subgroup Ib (n=42)	Subgroup Ia vs. Ib* (p value)
HDRS	17.8 ± 5.18	14.69 ± 4.85	p<0.05
BDI	22.5± 5.8	18.3± 4.9	p<0.05
BDI 13	11.2±4.8	8.7±4.2	p<0.05
BDI 14–21	11.4± 2.6	9.6± 3.1	p< 0.05
ATQ	68.1± 15.9	61.0± 12.2	p<0.05
RS	67.2 ± 16.8	73.0± 12.2	NS
HS	11.7± 4.7	8.2± 3.9	p<0.001

*Mann-Whitney U test

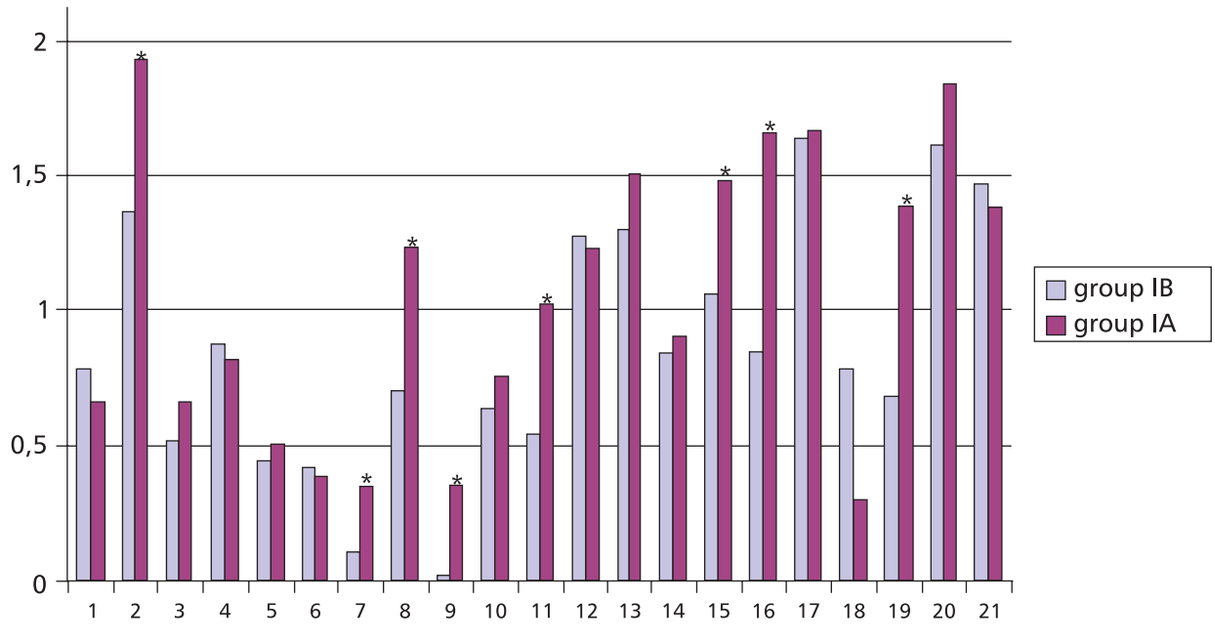

Figure 1. Mean BDI items rating in subgroups: Ia and Ib; comparison between subgroups (Mann-Whitney test; * – $p<0.005$)

were scored significantly more highly noted in subgroup Ia than in subgroup Ib ($p<0.05$ Mann-Whitney U test), (Fig. 1).

The comparison of subgroups Ia and Ib showed that the tendency towards persistent depressive symptomatology at the further follow-up was associated with more severe affective-cognitive and somatic symptoms, more frequent negative automatic thoughts, and higher levels of hopelessness.

In subgroup IIa, the depressive symptoms before the intervention (first examination) were mild, although more severe than in subgroup IIb, and statistically significant differences between subgroups was observed in both BDI subscales (BDI 13; BDI 14–21). Moreover, the frequency of negative automatic thoughts measured with ATQ was significantly higher in subgroup IIa. There were no significant differences in RS scoring and HS scoring between subgroups IIa and IIb (Tab.4).

DISCUSSION

The present study confirms that non-specific depressive symptoms are very common in CAD

Table 4. Mean and standard deviation of BDI, HS, RS, ATQ scores in group IIa and IIb at first examination point

scores at first examination point	Subgroup IIa (n=12)	Subgroup IIb (n=69)	Subgroup IIa vs. IIb (p value)
HDRS	6.0±1.27	4.20±2.81	$p<0.05$
BDI	10.0 ±0.8	6.5±3.2	$p<0.05$
BDI 1–13	3.7±2.2	2.4±1.7	$p<0.05$
BDI 14–21	6.3±2.8	4.1±2.8	$p<0.05$
ATQ	60.7±12.6	47.2±11.4	$p<0.05$
HS	5.5±3.8	4.0± 2.6	NS
RS	82.5±11.9	85.5±10.3	NS

*Mann-Whitney U test

patients requiring revascularization. Mild and moderate depressive disorders with the prevalence of somatic symptoms were observed one day before PCI in 48% of the enrolled patients. Similarly to a study by Freedland et al [7] apart from somatic complaints the most frequent depressive symptoms were: concern about the future, loss of interest in other people, difficulties with decision-making, sleep disorders, fatigue and diminished libido.

One month after successful PCI depressive symptoms were still present or newly developed in 28.9% of patients. The tendency towards persistent depressive symptomatology , observed one month after PCI, was associated with more severe affective-cognitive and somatic symptoms of the depressive syndrome; more frequent negative automatic thoughts, and stronger hopelessness. The depressive symptoms in the group of patients without depression before PCI in whom depressive disorders developed on second examination, before the intervention were mild, although stronger than in the subgroup of patients who were free of depression during the follow-up. These findings confirm the observation by Hance et al [8] concerning the CAD patients fulfilling DSM criteria for a major depression. In the study by Hance, patients with higher BDI rating were more likely to have persistent depressive symptoms.

These findings indicate that depressive disorders in patients with CAD – even after successful intervention – have a tendency to persist or develop, and because of clinical peculiarities, may be a source of major diagnostic difficulties. Such difficulties are the result of the overlapping of "pure" depressive symptoms with signs of acute emotional reaction and non-specific signs of somatic disease which may be similar one to another [26]. For example, symptoms such as: fatigue, sleep problems, anorexia, weight change – may reflect both mental and somatic pathology.

Several authors have pointed out some differences between depressed patients with affective disorders and patients suffering from somatic diseases comorbid with depression. The severity of depression in patients who have no family history of affective disorders and are hospitalized in non-psychiatric units is usually less, and the risk of its development is the same for both sexes [27, 28, 29]. However, although worrying about health and future, sleep disorders, and appetite loss are quite common in somatic diseases, they are more frequent and more severe in cases of concomitant depression [28, 29]. On the other hand, worrying associated with severe somatic disease and waiting for the operation or any procedure (e.g. PCI) may induce or exacerbate the depression-like symptoms, e.g.: problems with concentration, insomnia, isolation, fatigue, appetite loss and anhedonia [30].

The predominance of somatic symptoms in depressed CAD patients may be a result of specific features of the non-psychiatric medical interview. Patients who have become accustomed to being asked only about their somatic complaints may be convinced that doctors are not concerned about the patients' emotions, and that only somatic signs are important and worth mentioning during the interview. This may result in the somatization of depressive symptoms.

Many authors [31, 32] have noticed that after myocardial infarction patients show low self-esteem, low tolerance of frustration, suppressed hostility, dependence, passivity, and inability to express anger adequately. These non-specific symptoms were named vital exhaustion syndrome by Appels, and found to be negative prognostic factors for CAD patients [33]. It is unclear whether vital exhaustion is a separate psychopathological syndrome induced by cardiological disease, or a type of depressive disorder. According to current diagnostic criteria for psychiatric disorders (DSM IV and ICD–10), diagnosis of depression is based on the presence of a required number of symptoms, but not on their chronology. This is why vital exhaustion is probably synonymous with depression. It seems that the replacement of synonyms with one universal term – depression – may contribute to an easier diagnostic process, better education, and better cooperation between psychiatrists and cardiologists.

CONCLUSIONS

These facts, together with the results of the present study, strongly suggest that diagnosis of depression in patients suffering from serious somatic disorders such as CAD needs special attention, and should be based on a clini-

cal examination supported by instruments detecting the severity and predominance of some depressive symptoms (BDI and its subcscales, HDRS), as well as describing dimensions of depressive thinking like hopelessness (HS) and low self-esteem (RS). The common psychological and pathophysiological background, and overlapping of etiopathogenetic factors, are suggestive of the important role of the psychopathological symptoms in the treatment and rehabilitation of CAD patients. Successful intervention is not a sufficient determinant of improvement in the mental state. An optimized comprehensive approach to CAD patients with concomitant depressive symptoms may require inclusion of psychological intervention, and, in justified cases, even psychiatric treatment.

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