ORIGINAL ARTICLES

The association between aggressiveness, clinico-instrumental features and the mortality risk in patients with CAD after percutaneous coronary intervention

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Summary

Objective. *To identify the association between the aggressiveness and clinico-instrumental features in patients with coronary artery disease (CAD) after percutaneous coronary intervention (PCI) and to assess the impact of aggressiveness on mortality risk during one-year follow-up after the surgery.*

Materials and methods. *The study was based on the data of "Prospective Registry of PCI". The registry contains the information about 1080 patients (764 men and 254 women) aged from 33 to 90 years (average age — 58,9±9,7 years). The Russian version of Cook and Medley hostility scale was used to assess the level of aggressiveness. Life status after one year of prospective observation was determined in 986 patients (96.9 %). The statistical analysis included: binary logistic regression and Cox proportional hazards model.*

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Results. *The binary logistic regression analysis revealed significant association between the level of aggressiveness, gender, and the severity of chronic heart failure (CHF). During the follow-up, 24 (2,4 %) of patients died from all causes and 21 (2.1 %) — from cardiovascular diseases (CVDs). Relative risk (RR) for the parameter of aggressiveness, which was assessed in points, for all-cause mortality was 1,05 (95 % CI 0,98–1,13, p=0,04), for cardiovascular mortality — 1,08 (95 % CI 1,01–1,17, p=0,04). The analysis of categorical variables revealed that in patients with high level of aggressiveness the RR for all-cause mortality was 2,28 with 95 % CI from 0,93 to 5,61, p=0,07, and for cardiovascular mortality 3,01 with 95 % CI from 1,14 to 7,94, p=0,03 compared with patients from the control group.*

Conclusion. *The parameter of aggressiveness in patients with CAD after PCI was independently and significantly associated with gender and CHF severity, as well as with the risk of cardiovascular mortality during 1-year follow-up.*

Keywords: *coronary artery disease, aggressiveness, psychosocial risk factors, percutaneous coronary interventions.*

Introduction

Cardiovascular diseases are still the main cause of mortality in developed and most developing countries [1]. In our country psychosocial risk factors (RF) contribute to the development, progression and mortality from cardiovascular diseases [2]. The analysis of the literature data shows that today the main focus is on the association between psychosocial RF and the severity of cardiovascular diseases, in particular coronary artery disease (CAD) and chronic heart failure (CHF) [3]. For example, it has been shown that social isolation, hostility, depression negatively affect the prognosis in patients with cardiovascular pathology and significantly increase their mortality [4].

Objective

To access the prevalence of high level of aggressiveness in patients with coronary artery disease (CAD) according to the data from "Prospective Registry of PCI" that allows to identify the association between the aggressiveness and clinico-instrumental features and to assess its impact on mortality risk during one-year follow-up after the coronary artery stenting (CAS).

Materials and methods

The study was based on the data of "Prospective Registry of PCI" that has state registration database No. 2020621655 [5]. The registry contains the infor-

mation on 1018 patients (764 men and 254 women) aged from 33 to 90 years (mean age 58.9± 9.7 years). The clinical part of the database contains information on medical history, concomitant pathology, smoking, alcohol consumption, basic anthropometric data (office blood pressure (BP), height, weight, body mass index (BMI), waist circumference (WC)), as well as the results of biochemical blood test, including lipid panel. In addition, the electronic database contains the results of ECG, echocardiography and coronary angiography of patients before PCI. The prospective part of the registry contains information on the status of 986 patients (96.9 %) obtained one year after the intervention.

Data on the stable character trait — aggressiveness, were obtained using the Cook-Medley Hostility Scale adapted by Sobchik L.N. [6]. The scale is highly reliable and valid [7]. The questionnaire includes 27 questions and 3 subscales: subscale of cynicism, subscale of aggressiveness and subscale of hostility. The Cook-Medley scale adapted by L.N. Sobchik uses the Likert scale that consist of 6 items that grades from 1 ("Never") to 6 ("Usually"). The final score was calculated by summing the scores of aggressiveness subscale questions. The scores were split into 2 categories according to percentiles. Patients with the score of over 75th percentiles by the aggressiveness subscale were assigned to the group with high aggressiveness. Patients with the total score less than

the 75th percentile were assigned to the comparison group. The "Prospective Registry of PCI" contains complete information on 947 patients. Thus, the survey response rate was 93 %. The study was approved by the local Ethics committee, informed consent was waived from all the participants before the study.

Statistical analysis was performed using SPSS software (SPSS Inc., version 21). The results are presented as M± SD (mean± standard deviation). The normality of distribution was assessed using Kolmogorov — Smirnov test. Student's t-test was used to compare normally distributed quantitative variables, and nonparametric Mann — Whitney test — for the variables that significantly deviated from the normal distribution. The Chi-squared test (χ^2) was used to assess the significance of differences between qualitative variables. Multivariate analysis was performed using binary logistic regression, and the odds ratio (OR) with 95 % confidence interval (CI) were calculated. A multivariate analysis by Cox proportional hazard regression model was performed to estimate the relative risk (RR) of death and its 95 % CI. Confounding factors included: gender, age, alcohol abuse, smoking, BMI and blood pressure (systolic and diastolic), total cholesterol, atrial fibrillation (AF), diabetes mellitus (DM), left ventricular (LV) ejection fraction, the severity of CHF (functional class (FC) according to NYHA)), as well as acute coronary syndrome (ACS) during admission and the severity of coronary stenosis according to the SYNTAX score.

Results

The mean of aggressiveness by Cook-Medley hostility scale was 29.6±6.6 points. High level of aggressiveness was observed in 217 patients (22.9 %). Clinical and instrumental characteristics of patients depending on the level of aggressiveness are presented in Table 1.

Compared groups significantly differed by gender. The proportion of men was higher in group with high level of aggressiveness (p=0.004). Patients with high level of aggressiveness had lower values of systolic blood pressure (p=0.058) and higher functional class of chronic heart failure (p=0.058). Patients with high level of aggressiveness had lower LV ejection fraction (p=0.009). Other parameters did not differ significantly between groups.

The results of coronary angiography and PCI did not differ significantly between groups with different levels of aggressiveness (Table 2). There was a tendency towards more frequent lesion of the anterior

Table 1. **Clinical and instrumental parameters in patients depending on the level of aggressiveness**

Parameters		Comparative group (n=730)	Group with high level of aggressiveness (n=217)	p
Men, %		74,4	83,9	0,004
Age, years		58,3±9,0	58,4±9,5	0,96
Postinfarction cardiosclerosis, %		44,1	43,3	0,84
Smoking, %		40,1	40,1	0,99
Alcohol abuse, %		8,4	8,8	0,85
BMI, kg/m²		30,4±5,2	30,9±5,0	0,38
WC, cm		101,3±12,7	102,2±11,0	0,29
Arterial hypertension, %		89,7	87,6	0,37
Systolic BP, mmHg		135,7 20,4	131,6/20,3	0,058
Diastolic BP, mmHg		83,7 11,2	82,0/12,8	0,21
Hypercholesterolemia, %		61,4	63,6	0,56
Total cholesterol, mmol/l		4,98±1,27	5,02±1,32	0,73
Low-density lipoproteins, mmol/l		3,18±1,11	3,24±1,17	0,73
High-density lipoproteins, mmol/l		1,16±0,37	1,11±0,31	0,10
Triglycerides, mmol/l		1,74±1,06	1,80±1,14	0,51
Chronic Heart Failure FC (NYHA), %	I–II	79,3	73,1	0,058
	III–IV	20,7	26,9	
DM, %		20,8	22,6	0,58
AF, %		9,2	11,1	0,42
ACS at admission, %		31,8	35,5	0,31
LV ejection fraction, %		54,1±8,4	52,2±9,3	0,009

ACS — acute coronary syndrome, AF — atrial fibrillation, DM — diabetes mellitus, FC — functional class, BMI — body mass index, BP — blood pressure, LV — left ventricular, WC — waist circumfluence.

interventricular artery in patients with high level of aggressiveness (p=0.07).

Multivariate analysis regression model included as covariates all variables with statistically significant differences or with tendency for this difference. The binary logistic regression analysis showed independent association between high level of aggressiveness, sex and FC of CHF (Figure 1). Thus, the probability of high level of aggressiveness was approximately 2 times lower in women compared with men
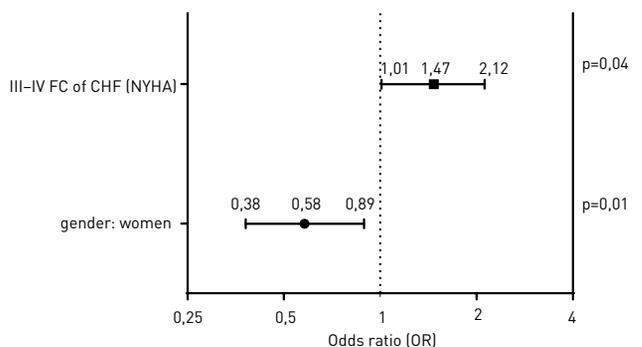

Figure 1. Independent associations between parameters and high level of aggressiveness in patients with coronary artery disease after PCI.

Table 2. **Comparative characteristics of coronary angiography and PCI results depending on the level of aggressiveness**

Parameters		Comparison group (n=730)	Group with high level of aggressiveness (n=217)	p
Stenosis of the trunk of the left coronary artery	%	1,5	1,4	0,89
Stenosis of the anterior intraventricular artery	%	57,3	64,1	0,07
Stenoses of the circumflex artery	%	25,3	26,7	0,68
Stenoses of the right coronary artery	%	44,2	43,3	0,81
Stenosis of second-order coronary arteries	%	26,4	27,6	0,72
Single-vessel coronary artery disease	%	60,8	58,5	0,41
Double-vessel coronary artery disease	%	25,8	24,4	
Multivessel coronary artery disease	%	13,4	17,1	
SYNTAX score	units	10,1±7,4	11,1±8,7	0,25
Number of stents	number	1,33±0,67	1,33±0,69	0,93
Optimal PCI outcome	%	98,1	98,2	0,94
Arterial dissection	%	2,6	1,9	0,51

(p=0.01). Patients with III–IV FC of CHF had 1.5 times greater chance of high aggressiveness compared with lower FC (p=0.04).

During the prospective follow-up, 24 (2.4%) patients died from all causes and 21 (2.1%) patients from cardiovascular diseases. As seen from Fig. 2–3, after adjusting for associated factors, aggressiveness was statistically significantly associated with cardiovascular mortality. Thus, with the increase of aggressiveness by one point, the risk of death from cardio-
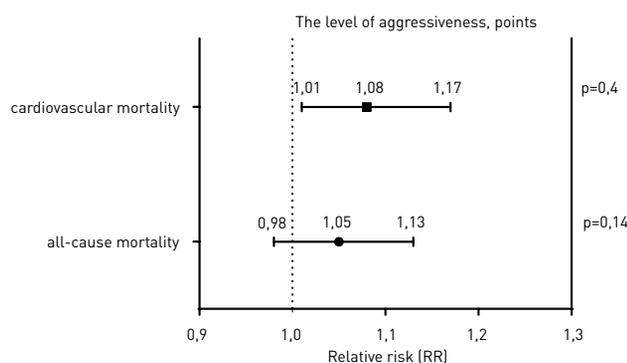

Figure 2. Associations between the quantitative variable aggressiveness in points and the risk of cardiovascular and all-cause mortality (multivariate model)
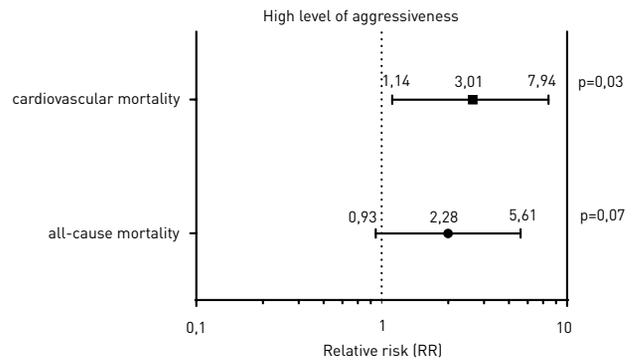

Figure 3. Associations between the categorical variable of aggressiveness and the risk of cardiovascular and all-cause mortality (multivariate model).

vascular disease increased by 8% (p=0.04). Patients with high level of aggressiveness had 3 times higher relative risk of cardiovascular mortality compared with the control group (p=0.03).

Discussion

Several studies have shown that male gender is associated with higher aggressiveness [8] that can be explained by greater level of sex hormone testosterone. Nowadays the connection between aggressive behavior and high level of testosterone is unambiguous [9, 10].

According to the literature data, aggressiveness is the risk factor for the development of arterial hypertension [11]. However, according to the results of the analysis, there is a tendency towards the decrease of systolic blood pressure in patients with higher level of aggressiveness. However, the influence of confounding factors cannot be excluded. For example, patients with high level of aggressiveness had higher CHF class and, accordingly, lower LV ejection fraction, which probably caused lower systolic blood pressure in this group of patients. The most common mechanisms of the effect of aggressiveness on the development and progression of cardiovascular diseases include endothelial dysfunction, platelet and proinflammatory cytokines activation [12, 13]. On the other hand, behavioral mechanisms such as low compliance, resistance to lifestyle changes and insufficient cardiac rehabilitation, which are common in patients with high aggressiveness, can also aggravate the clinical picture of cardiovascular diseases, including CHF. This, probably, can explain the association between aggressiveness and a more severe course of CHF, according to the data of binary logistic regression [14]. There are studies that show the relationship between aggressiveness and the frequency of admissions of patients with CHF [15]. Thus, it can be

assumed that high level of aggressiveness serves as an independent RF for more severe course of CHF.

Present study demonstrates that high level of aggressiveness is independently associated with threefold increase of cardiovascular mortality. K.M. Appleton et al. [16] also found an independent association between the Cook-Medley hostility score and all-cause mortality (RR 1.14, 95% CI 1.01–2.29). According to the results of the meta-analysis by Y. Chida et al., aggressiveness and hostility were associated with increased risk of cardiovascular complications in both healthy controls (1.19; 95% confidence interval [CI]: 1.05 to 1.35, p=0.008)), and patients with cardiovascular pathology (1.24; 95% CI: 1.08 to 1.42, p=0.002) [17]. According to other studies, the relationship between hostility and adverse events is not clear [12] or completely absent [18]. For example, Wong J.M. et al. showed that aggressiveness was associated with a poor prognosis (RR 1.68, p<0.0001), but this association lost its statistical significance when behavioral risk factors such as smoking and physical inactivity were added to the multivariate model (RR 1.25, p<0,13) [18]. The authors, who in their

studies did not confirm the independent association of aggressiveness with cardiovascular mortality, assume that aggressiveness realizes its negative effect through other biological and behavioral risk factors [12], such as unhealthy lifestyle (insufficient physical activity, excessive alcohol consumption, smoking, unhealthy diet, etc.) [17]. A number of studies have demonstrated the connection between hostility / aggressiveness and low socioeconomic status, low educational level and social support, as well as with general dissatisfaction with family relations [19]. These aspects could also exacerbate negative influence of considered risk factors.

Conclusion

Thus, the parameter of aggressiveness in patients with CAD after PCI was independently and significantly associated with gender and CHF severity, as well as with the risk of cardiovascular mortality during 1-year follow-up.

Conflict of interest: None declared.

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