CAN PSYCHOLOGICAL RISK FACTORS FOR CORONARY HEART DISEASE PREDICT EXTENT AND SEVERITY OF CORONARY ATHEROSCLEROSIS?

ALI LAHKO PSIHOLOŠKI DEJAVNIKI TVEGANJA ZA KORONARNO SRČNO BOLEZEN NAPOVEDUJEJO RAZŠIRJENOST IN TEŽAVNOST KORONARNE ATEROSKLEROZE?

Andrej Marušič[1], Dorjan Marušič[2], Radovan Starc[3]

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Abstract

Objective: *The main objective of the present study was to test prediction of angiographically determined coronary atherosclerosis on the basis of presence of various psychological and other coronary risk factors.*
Methods: *The sample constituted 176 male patients with coronary heart disease (CHD) who underwent coronary angiography. Exploratory variables consisted of psychological (personality traits of neuroticism and sensitisation, and emotional coping style) and other coronary risk factors (age, family history, smoking, hypertension, total, LDL and HDL cholesterol). Outcome variables of the study were extent score of disease and severity score of disease. The goal of statistical analysis was to find best fitting multivariate linear models.*
Results: *Both final models included only LDL and age. Psychological risk factors did not contribute significantly to the prediction of extent and severity of coronary artery disease.*
Conclusion: *We concluded that the clinical entity of CHD should be differentiated from its underlying pathologic process, coronary atherosclerosis, and so should be CHD risk factors distinguished from the risk factors for development of atherosclerosis. Different reasons can be given for the absence of significant associations between important risk factors and extent or severity of disease. For psychological risk factors in particular, a multistage development of CHD with the potential for different risk factors involvement at different stages, is the best explanation. Most probably, psychological risk factors are involved in acute and sudden deteriorations in coronary flow due to coronary vasoconstriction or spasm, which makes them more important in the secondary rather than the primary prevention of coronary heart disease.*

Key words: coronary disease, coronary angiography, risk factors, prevention

Izvirni znanstveni članek
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Izvleček

Namen: *Osnovni namen predstavljene študije je bil preveriti, ali lahko napovemo angiografsko določeno koronarno aterosklerozo na podlagi podatkov o prisotnosti različnih psiholoških in drugih koronarnih dejavnikov tveganja.*
Metode dela: *Vzorec je sestavljalo 176 bolnikov moškega spola s koronarno boleznijo (KB) po koronarni angiografiji. Obravnavane neodvisne spremenljivke so predstavljale psihološki (osebnostni potezi neuroticizma in senzitizacije ter emocionalno obvladovanje stresa) in drugi koronarni dejavniki tveganja (starost, pozitivna družinska anamneza, kajenje, povišan krvni tlak, celokupni, LDL in HDL holesterol). Odvisni spremenljivki sta bila rezultata razširjenosti in težavnosti bolezni. Cilj statistične analize je bil najti ustrezna multivariantna linearna modela.*
Rezultati*: Oba končna modela sta upoštevala le LDL in starost. Psihološki dejavniki tveganja niso pomembno doprinesli k napovedi razširjenosti in težavnosti koronarne arterijske bolezni.*

[1]Institute of Public Health of Republic of Slovenia, Trubarjeva 2, 1000 Ljubljana, Slovenia
[2]Ministry of Health of Republic of Slovenia, Štefanova 5, 1000 Ljubljana, Slovenia
[3]Clinical Centre, Zaloška cesta 7, 1000 Ljubljana, Slovenia
Correspondence to: e-mail: andrej.marusic@ivz-rs.si

Sklepne misli: *Na podlagi dobljenih rezultatov smo sklenili, da je potrebno ločevati med klinično entiteto KB in osnovnim patološkim procesom, to je koronarno aterosklerozo. Vzporedno s tem je potrebno razlikovati tudi med dejavniki tveganja za KB in dejavniki tveganja za razvoj ateroskleroze. Različne razloge lahko naštejemo za odsotnost povezanosti med nekaterimi pomembnimi dejavniki tveganja in razširjenostjo ter težavnostjo bolezni. Glede psiholoških dejavnikov velja izpostaviti večstopenjski razvoj KB z vpletenostjo različnih dejavnikov tveganja na različnih stopnjah. Psihološki dejavniki tveganja so najverjetneje vpleteni v akutnem in nenadnem poslabšanju koronarnega pretoka zaradi koronarne vazokonstrikcije ali celo spazma, kar bi pomenilo, da so lahko pomembnejši v sekundarni kot v primarni prevenciji koronarne bolezni.*

Ključne besede: koronarna bolezen, koronarna angiografija, dejavniki tveganja, preprečevanje

Introduction

Psychological coronary-proneness is most probably one of the first recognised risk factors for coronary heart disease (CHD). That the nervous system influences the actions of the heart and blood vessels has been known for at least 4.500 years - ancient Egyptian physicians were aware that the heart and pulse are affected by emotions (1). Nevertheless, the association between psychological factors and CHD has only recently been validated empirically (2). Mechanisms by which these psychological risk factors might exert their influence on the cardiovascular system are less clear than those for biological risk factors. Several hypothesis have been generated to explain such associations: alterations in health-related behaviours, increased oxygen demand of the heart muscle, and decreased blood supply to the heart muscle due to enhanced blood clotting, vasoconstriction or increased atherogenesis (3, 4). In terms of the latter, several studies have shown minimal or no relation between psychological variables and the degree of coronary stenosis in CHD patients undergoing coronary angiography (5, 6, 7, 8). On the other hand, one prospective study found an independent relation between hostility and coronary artery calcification (9).

Another question is which would be the most atherogenic psychological risk factors if the relationship with extent and severity of coronary atherosclerosis were confirmed. Hostility, anxiety and depression are only some of the psychological risk factors that have been demonstrated to be associated with the risk of CHD (10, 11, 12). The multidimensional nature of psychological coronary-proneness could only be complete if some other personality traits and stress-related issues, such as maladaptive coping styles were also considered. For example, emotional coping was found to predict deteriorated health (13, 14). As a personality trait, neuroticism represents increased reactivity to stressors, which may adversely affect bodily homeostasis and, thus, promote progression of CHD in stressful situations (13). Moreover, neuroticism and chronically disturbing emotions have repeatedly been found to be associated with the presence of different forms of CHD (15-18). The notion that neuroticism or emotional instability precede CHD has been criticised by Costa (19), who claimed that neuroticism was related to increased somatic complaints but was not causally related to objective signs or pathophysiological evidence of disease, especially coronary artery disease. The best way to deal with the this dilemma would be to investigate neuroticism together with a variable of over-reporting of emotional reactions as determined by physiological measures of emotional reactivity, referred to as sensitisation. Gudjonsson (20) directly investigated the discordance between physiological and self-reported measures and formed a hypothesis about personality and defensiveness traits. The hypotheses that repressors would have a high defensiveness score or L score and low trait anxiety or N score, and that sensitisers would have the opposite results, notably high N and low L scores, were confirmed (20). A study of Kneier and Temoshok (21) showed sensitisation to be important in cardiovascular disease subjects.

The main aim of the present study was to examine whether neuroticism, sensitisation and emotional coping style independently predict coronary artery disease extent and severity. This study, therefore, tested prediction of angiographically determined coronary atherosclerosis on the basis of presence of psychological and other coronary risk factors. These risk factors were shown to be either more frequent or had more dangerous values in our CHD patients when compared to their control matches (4). We hypothesised that especially directly atherogenic risk factors (e.g. dyslipidaemia and hypertension) will be associated with coronary atherosclerosis extent and severity. Our investigation of relationship between psychological risk factors and atherosclerosis was exploratory in nature.

Method

Subjects

The sample constituted 176 consecutive male patients with CHD (Mean Age 57.1 year old; SD 9.4) who underwent coronary angiography at the Clinical Centre in Ljubljana prior to bypass surgery or other therapeutic procedures. They had at least 50 percent narrowing of at least one coronary artery. Due to the lower percentage of women with CHD only men were included in the study. The exclusion criteria were a history of terminal illness, head injury and mental illness.

Outcome variables

Lesperance et al. (22) suggested that characterisation of plaque morphology could provide useful information beyond those generally yielded by the more traditional methods of interpretation of coronary angiograms based on assessment of severity of stenoses and number of diseased vessels. The information derived from the morphologic analysis can be extended to the chronic phase of disease by calculating the extent score of disease (it marks more severe disease and predicts future progression) and severity of stenosis (more severe lesions will occlude more frequently although most often without clinical consequences) (22), both being outcome variables of our study:

1. extent score of disease ... sum of coronary artery segments showing a narrowing of any severity marks divided by number of all angiographically examined segments;
2. severity score of disease ... an average narrowing of all angiographically examined coronary artery segments.

Assessment of outcome variables

Ideally, the number of all investigated segments was 15: left main coronary artery (LCA) as one segment, and left anterior descending artery (LAD), left circumflex artery (LCX) and right coronary artery (RCA) (all divided into proximal, intermediate and distal segments), two diagonal branches of LAD and three marginal branches of LCX. Other branches were not included as they vary in size, number and distribution or origin [23]. In patients with left coronary dominance (less than 10 percent of cases) RCA is smaller with only two segments. A segment here defined as the distal RCA would in these cases form a longer distal part of LCX (23). Any of these 15 segments could be missing or could remain undetected in the case of occlusion. The agreement before the beginning of our analyses was to determine all segments distal to an occlusion as immeasurable. Because of its ease, rapidity, and somewhat lower complication rate, the Judkins technique was used (24). Two independent experts visually assessed coronary angiograms. Each of the 15 segments had to be assessed for presence and severity of stenosis coded from 0 to 100 percent with 5 percent accuracy. The intraobserver reliabilities for presence (Phi > 0.9) and degree of stenosis ($r > 0.9$) were high enough to continue with our analysis.

Exploratory variables

The 10 exploratory variables constituted of 3 psychological and 7 other risk factors for CHD:

1. neuroticism (N) or emotional lability/stability as measured by the Eysenck Personality Questionnaire (EPQ) (25); the alpha coefficient for N in the present study was 0.87;
2. the presence or absence of sensitisation of emotion or over-reporting of emotional reactions as determined by physiological measures of emotional reactivity; according to Gudjonsson's criteria Š20Ć, sensitisation is present when the subject has the N score above and the L (EPQ-lie scale) score below the median;
3. emotional coping with stress as measured by the Coping Styles Questionnaire (CSQ) (26); the alpha coefficient for emotional coping in the present study was 0.69;
4. age on the day of the assessment;
5. family history of CHD as the percentage of first-degree relatives with CHD;
6. the presence or absence of smoking history;
7. the presence or absence of hypertension;
8. total cholesterol, high-density lipoprotein (HDL) and low-density lipoprotein (LDL) as 3 measurements of lipid profile.

Assessment of exploratory variables

Psychological factors were assessed by psychological questionnaires. Information for other variables were obtained from structured interview, medical history, medical records, clinical examination and laboratory testing. All laboratory testing were performed using the same reagents and standards throughout the study.

Statistical analysis

First, correlation coefficients (Pearson for continuous and Phi for categorical variables) were calculated to

investigate associations between risk factors on one side, and extent and severity score of atherosclerosis lesions on the other. The goal of further analysis was to find two best fitting multivariate linear models to describe predictability of both extent and severity of coronary artery disease on the basis of the studied risk factors.

Results

The extent score of disease was defined as a sum of all coronary artery segments showing a narrowing of any severity marks divided by number of all angiographically examined segments. Our patients that underwent routine coronary angiography prior to bypass surgery or other therapeutic procedures had about a half of the whole coronary artery system at least to a certain extent affected (Mean Extent Score = 0.50; SD = 0.26).

The severity score of disease was defined as an arithmetic mean of percent narrowing of all angiographically examined coronary segments. Angiogram analysis showed high average degree of severity (Mean Severity Score = 0.28 or 28% narrowing; SD = 0.16 or 16%).

Table 1. *Correlations (r) between CHD risk factors and disease extent and severity scores in the sample of 176 CHD patients.*
Tabela 1. *Korelacije (r) med dejavniki tveganja za KB in rezultatoma razširjenosti in težavnosti bolezni na vzorcu 176 bolnikov.*

	Extent score / Razširjenost bolezni		Severity Score / Težavnost bolezni	
	r	p	r	p
Neuroticism / Nevroticizem	-0.04	0.602	-0.01	0.892
Sensitisation / Senzitizacija	0.02	0.766	0.03	0.660
Emotional coping / Emocionalno obvladovanje stresa	0.01	0.887	0.01	0.913
Age / Starost	0.14	0.057	0.16	0.040
Hypertension / Povišan krvni tlak	0.15	0.047	0.14	0.057
Cholesterol / Holesterol	0.15	0.043	0.17	0.024
LDL	0.19	0.012	0.22	0.004
HDL	0.07	0.337	0.08	0.266
Family CHD / KB v družini	0.03	0.672	-0.01	0.873
Smoking / Kajenje	-0.13	0.086	-0.12	0.102

Next, Table 1 shows all correlation coefficients between both scores of disease and 10 studied risk factors. Altogether, two sets of 10 coefficients were calculated and in each set at least three significant coefficients were obtained which is more than it would be expected by chance. No significant associations were obtained for the suggested psychological risk factors.

Table 2. *Multiple regression analysis predicting the extent of coronary atherosclerosis.*
Tabela 2. *Napovedovanje razširjenosti bolezni na podlagi analize multiple regresije.*

Variable / Spremenljivka	B	SE B	Beta	T	p
LDL	3.78	1.17	0.24	3.22	0.002
Age / Starost	0.29	0.12	0.18	2.38	0.018
Constant / Konstanta	-3.64	8.74		-0.42	0.677

Analysis of Variance / Analiza variance: F=7.46; df=2; p=0.001;
Multiple R=0.28 / Multipli R; R^2=0.08.

Finally, we analysed the multivariate linear regression models using the forward stepwise method with the ten risk factors. Both final models (the one for extent and the other for severity of coronary artery disease) included LDL and age. On both occasions, hypertension was left out, once with borderline significance (Table 2 and Table 3). Again, psychological risk factors did not contribute significantly to the prediction of extent and severity of coronary artery disease.

Table 3. *Multiple regression analysis predicting the severity of coronary atherosclerosis.*
Tabela 3. *Napovedovanje težavnosti bolezni na podlagi analize multiple regresije.*

Variable / Spremenljivka	B	SE B	Beta	T	p
LDL	3.72	1.19	0.23	3.13	0.002
Age / Starost	0.30	0.12	0.18	2.42	0.017
Constant / Konstanta	-3.14	8.83		-0.36	0.723

Analysis of Variance / Analiza variance: F=7.28; df=2; p=0.001;
Multiple R=0.28 /Multipli R; R^2=0.08.

Discussion

There is no a priori reason to suppose that the risk factors affecting the presence of CHD are the same as those affecting the extent or severity of its underlying cause or atherosclerosis. Some studies have attempted to discriminate between them. For example, Vlietstra et al. (27) presented the results of multivariate analyses, which show that several risk factors correlate with angiographic presence of coronary artery disease but not all of these are associated with extent and severity of coronary artery disease. In the present study, only LDL and total cholesterol were found to be related to both extent and severity of coronary artery disease. These results go in line with the lipid hypothesis of atherogenesis, which states that dyslipidaemia is central to the initiation (investigated by the extent) and propagation (studied by the severity) of atherosclerotic plaque and coronary disease (28). Several other studies reported associations between cholesterol and LDL and angiographically assessed degree of atherosclerosis (29, 30). By multiple regression analysis, LDL was the best predictor of atherosclerosis progression, there being no advantage in measuring other variables (31). In terms of age as the second strongest predictor, the prevalence and severity of coronary atherosclerosis increase so dramatically with age that more than one-half of all deaths in persons aged 65 years or older are due to CHD and about three-fourths of all deaths from CHD occur in older individuals (32). Our results are similar to the findings reported by Budde et al. (33). They studied the severity and extension of coronary lesions in male patients with suspected CHD. With multivariate analyses, besides dyslipidemia, only patient's age showed a significant correlation to severity and length-extension of all coronary lesions.

The remaining strong predictors of presence of CHD (e.g. low HDL and smoking history) did not show any degree of association with coronary artery disease indicators. All these negative results came as a surprise, although it is possible to find some reasonable explanations for such outcome. First, angiographic studies may not be the most suitable method of assessing the relation between the known coronary risk factors and coronary artery disease, largely because of a skewed population with late-stage, severe disease. Second, it is clear that the coronary anatomy as revealed by coronary angiography is a poor predictor of the clinical presentation of individual patients with myocardial ischaemia (34). Even absolutely accurate and reproducible angiographic method for estimating the significance of stenosis may fail to predict behaviour of a coronary lesion (35). Finally, Vlietstra et al. (27) suggested the multistage development of CHD, which gives a potential for different risk factors involvement at different stages. Some of the factors that are related to the overall risk for CHD, but are not related to atherosclerosis extent and severity, are most probably risk factors for acute and sudden deteriorations in coronary flow. For example, in myocardial infarction, coronary flow may be as well impaired by a thrombus (36) or by a coronary vasoconstriction or a spasm (37). In the latter smoking [38] and psychosocial variables (39) might be important.

In fact, psychological factors might be more significant in terms of temporary deterioration as it is the alpha-adrenergic vasoconstriction of coronary arteries that is thought to play a role in the development of

coronary spasm. Legault et al. (39) suggested that vulnerability to ischaemia during mental stress might not be determined solely by severity of anatomic disease. Yeung et al. (40) argued that mental stress can cause ischaemia by precipitating vasoconstriction of atherosclerotic epicardial coronary arteries. In subjects with stable angina pectoris, mental stress caused dilation of the arteries with normal endothelium but constriction of vessels with evidence of endothelial dysfunction (41). A similar pattern of response has been observed with other stimuli that are also accompanied by activation of the sympathetic nervous system (34).

There are several limitations to our data. In a sample of CHD patients undergoing coronary angiography there is an under presentation of low degrees of coronary artery disease (disease-spectrum bias) and, possibly, an under presentation of psychological dysfunction, which could have led to an underestimation of any relation between the studied variables. It is also possible that our psychological scales were not sensitive enough to dynamic psychological states and thus missed possible associations. However, these are valid psychometric tools that have also shown sufficient internal reliability. Finally, our results are based on male only sample and cannot be generalised to both sexes.

In conclusion, the clinical entity of CHD should be differentiated from its underlying pathologic process, coronary atherosclerosis, and so should be CHD risk factors distinguished from the risk factors for development of atherosclerosis. Only LDL and age were found to be related to extent and severity of coronary artery disease. Different reasons were given for the absence of significant associations between important risk factors and extent or severity of disease. For psychological risk factors in particular, a multistage development of CHD is the best explanation. Most probably, psychological risk factors are involved in acute and sudden deteriorations in coronary flow due to coronary vasoconstriction or spasm, which makes them relatively more important in the secondary rather than the primary prevention of coronary heart disease.

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