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ARTYKUŁ ORYGINALNY / *ORIGINAL ARTICLE*

Prognostic assessment of selected clinical and ultrasonographic indices in patients with non-critical lesions in coronary angiography

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Abstract

Background: Coronary heart disease is the leading cause of mortality, especially in industrialised countries. In the case of detection of significant lesions narrowing the vessel lumen, management is guided by recommendations of international cardiac societies, while in the case of non-critical lesions there are some doubts as to the further prognosis and identification of patients in whom accelerated progression of disease can be expected.

Aim: The aim of this study was to evaluate the prognostic significance of selected clinical and ultrasonographic indices in patients with non-critical lesions in coronary angiography.

Methods: In 100 symptomatic patients with non-critical stenosis in coronary arteries, cardiovascular events after one and three years of follow-up were assessed and analysed compared to a control group.

Results: During the follow-up period there were no deaths. In univariate analysis, factors associated with need for revascularisation in 4% of patients after one year and 7% at three years were: age (odds ratio [OR] 1.16, confidence interval [CI] 0.98–1.35; p = 0.04), fibrinogen concentration (OR 1.01, CI 1.00–1.02; p = 0.05), isovolumetric relaxation time [ms] (OR 1.07, CI 0.79–0.98; p = 0.04), and transmitral flow propagation velocity [cm/s] (OR 0.88, CI 1.01–1.12; p = 0.01). Nearly one third of patients with non-critical lesions despite optimal pharmacotherapy reported symptoms deteriorating quality of life.

Conclusions: Factors predisposing to the occurrence of cardiovascular events in the 12 months of follow-up were: older age, higher plasma fibrinogen concentration, and impaired left ventricular filling pattern.

Key words: coronary angiography, symptoms, echocardiography

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INTRODUCTION

Coronary heart disease (CHD) is one of the most common diseases of the 21st century and one of the most common causes of mortality among adults. Despite achievements in recent years there are still a large number of unsolved issues.

While management in acute coronary syndromes (ACS) has been widely studied, proceedings in stable coronary artery disease (CAD) still raise many questions. An undeniable success was the introduction of coronary angiography to the coronary lesion assessment in order to make further treatment decisions. In the case of critical narrowing of the artery lumen above 70% (> 50% for the left main artery), management is established and defined by cardiac societies while for non-critical lesions (50–70% stenosis) there are some doubts as to the further prognosis, management, and identification of patients in which accelerated progression of disease can be expected and requiring more aggressive treatment. The current guidelines of the European Society of Cardiology (ESC) on stable CAD and ACS suggest an appropriate strategy aimed at achieving therapeutic targets [1–3].

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Table 1. Characteristics of the coronary heart disease (CHD) and control (C) groups taking into account demographic and laboratory findings

Parameter	CHD group (n = 100)		C group (n = 100)		p
	Mean	SD	Mean	SD	
Age [years]	63	8.3	62	8.3	0.12
HR [bpm]	72	7	73	7	0.41
BMI [kg/m^2]	28.9	4.2	27.9	4.5	0.10
RBC [mln/μL]	4.77	0.39	4.87	0.44	0.08
HGB [g/dL]	14.2	1.1	14.4	1.2	0.44
HTC [%]	41.1	2.9	41.5	3.1	0.46
WBC [1000/μL]	7.2	2.1	7.2	2.7	0.85
PLT [1000/μL]	233	55	232	64	0.79
Creatinine [μmol/L]	81	16	77	15	0.08
Fibrinogen [mg/dL]	303	77	296	69	0.53
Na [mmol/L]	141	3	142	3	0.05
K [mmol/L]	4.08	0.43	4.15	0.43	0.25

SD — standard deviation; HR — heart rate; BMI — body mass index; RBC — red blood cells; HGB — haemoglobin; HTC — haematocrit; WBC — white blood cells; PLT — platelets; Na — sodium; K — potassium

Symptomatic patients with critical coronary artery lesions and proven ischaemic area undergo percutaneous coronary intervention or surgical-coronary artery bypass grafting revascularisation. Patients with non-critical lesions in coronary angiography are usually qualified for optimal medical therapy, and their prognosis is not entirely predictable. Simultaneously, there have been the published cases of ACS caused by atherosclerotic plaque rupture in non-critical stenosis. Therefore, the problem of predictive assessment and identification of risk factors in patients with non-critical coronary lesions is still noteworthy.

Besides classic cardiovascular (CV) risk factors such as older age, sex, lipid disorders, tobacco smoking, and diabetes mellitus (DM), the Polish Forum for Prevention lists new risk factors, including resting heart rate, fibrinogen concentration, intima-media thickness (IMT), homocysteine level, C-reactive protein (CRP), degree of expansion, and coronary artery calcification index [4].

The aim of this study was to assess prognosis in symptomatic patients whose angiography revealed non-critical lesions, and to determine the classic, demographic, biochemical, or echocardiographic markers of risk factors for CV events.

METHODS

The study included 200 patients consecutively admitted to the Department of Cardiology. Subjects were divided into two groups: the CHD group and the control group (C group), based on the result of coronary angiography. To the study group (CHD group) 100 patients in which coronary angiography revealed non-critical narrowing lesions not eligible for invasive treatment were enrolled, while the C group included 100 persons with no lesions in coronary angiography.

Medical history, physical examination, laboratory tests, transthoracic echocardiography (TTE), and carotid artery ultrasonography to assess IMT were performed in every subject. After one and three years following coronary angiography, occurrence of CV events was assessed. Obtained data were statistically analysed using MedCalc software (version 11.2.0.0). $P < 0.05$ was considered to be statistically significant.

RESULTS

The characteristics of the studied group of patients regarding demographic and laboratory data are presented in Table 1.

In the CHD group there were 44% and in the C group 63% of women. There were no significant differences in age and body mass index between the two groups. The basic biochemical parameters in the peripheral blood of both groups were comparable. The characteristics of the CHD and C groups involving the occurrence of risk factors are shown in Table 2.

The CHD was burdened with more risk factors for CAD, including arterial hypertension (AH), DM, and tobacco smoking, as compared to the C group. The characteristics of the CHD and C groups with regard to echocardiography findings are presented in Table 3.

Transthoracic echocardiography showed significant differences between groups in the following parameters: end systolic volume of the left ventricle was significantly greater and left ventricular ejection fraction (LVEF) was significantly lower in the CHD group compared with the C group. It should be noted, however, that assessed values in both groups were within normal limits.

Table 2. Characteristics of groups regarding risk factor occurrence

Parameter	CHD group		C group		p
	N	%	N	%	
Arterial hypertension	95	95	85	85	0.008
Type 2 diabetes	25	25	12	12	0.03
Hyperlipidaemia	41	41	29	29	0.10
Stroke/TIA	4	4	2	2	0.67
Tobacco smoking	32	32	8	8	< 0.0001
Familiar history of CVE	29	29	20	20	0.19
Sex (female/male)	45/55	44/55	63/37	63/37	0.02

C — control; CHD — coronary heart disease; CVE — cardiovascular event; TIA — transient ischaemic attack

Table 3. Echocardiographic parameters in the coronary heart disease (CHD) and control (C) groups of patients with non-critical coronary artery lesions

Parameter	CHD group (n = 100)		C group (n = 100)		p
	Mean	SD	Mean	SD	
Aorta [mm]	32	3	31	3	0.21
LA [mm]	37	4	36	4	0.19
RV [mm]	26	2	27	3	0.06
IVS [mm]	11.1	1.2	10.8	1.3	0.07
LVEDD [mm]	50	5	50	4	0.81
LVESD [mm]	31	5	32	4	0.83
PW [mm]	10.8	1.1	10.7	4.4	0.73
LVEDV [mL]	127	32	119	32	0.08
LVESV [mL]	55	17	49	16	0.01
LVEF [%]	57	4	59	4	0.008
LVM [g]	211	49	199	53	0.08
LVM index [g/m^2]	110	22	106	23	0.30
Vmax A wave [m/s]	0.77	0.2	0.75	0.2	0.59
Vmax E wave [m/s]	0.65	0.2	0.66	0.2	0.71
E/A	0.9	0.37	0.91	0.26	0.38
E wave DT [ms]	231	43	243	51	0.1
E/E'	9.1	2.3	9.4	3.8	0.47
Vp [cm/s]	51	12	49	11	0.32
IVRT [ms]	89	19	90	16	0.55
LA area [cm^2]	19.2	3.1	19.1	3.1	0.84

SD — standard deviation; LA — left atrium diameter; RV — right ventricle diameter; IVS — interventricular septum diastolic thickness; LVEDD — left ventricular end-diastolic diameter; LVESD — left ventricular end-systolic diameter; PW — posterior wall thickness; LVEDV — left ventricular end-diastolic volume; LVESV — left ventricular end-systolic volume; LVEF — left ventricular ejection fraction; LVM — left ventricular mass; Vmax A wave — maximal mitral A wave velocity; Vmax E wave — maximal mitral E wave velocity; E/A — mitral inflow E/A ratio; E wave DT — mitral E wave deceleration time; E/E' — ratio between early mitral inflow velocity and mitral annular early diastolic velocity; Vp — transmitral flow propagation velocity; IVRT — isovolumetric relaxation time

Analysis of the topography of the coronary arteries in the CHD group (total of 135 lumen narrowing lesions from 30% to 60%; 95% CI 39–42%) revealed the presence of lesions of three coronary arteries in five patients, lesions in two vessels in nine patients, and stenosis in one coronary artery in 76 individuals.

IMT was assessed in the CHD and C groups. The results are shown in Figure 1.

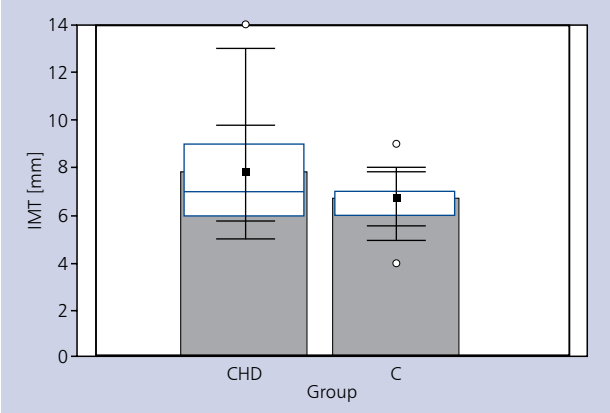

Figure 1. Mean values and standard deviation of intima-media--thickness (IMT) in the study group. CHD — coronary heart disease group, C — control group

Carotid IMT in the CHD group (0.78 ± 0.19 mm) was larger compared with the C group (0.67 ± 0.11 mm; $p < 0.001$). IMT above 0.7 mm identified non-critical lesions in the coronary arteries in women with sensitivity of 38% and specificity of 84.1%, and a value greater than 0.9 mm in men with sensitivity of 29.1% and specificity of 100%. Data are presented in Figure 2.

After 12-month follow-up there were no deaths. Due to the severity of chest pain, despite optimal medical therapy, four patients from the CHD group had control coronary angiography. Progression of atherosclerotic stenosis was observed and coronary angioplasty with stent implantation was performed in these patients (4% vs. 0%; $p = 0.13$). Recurrent chest pain occurred in 35 (35%) patients from the CHD group and in 29 (29%) patients of the C group ($p = 0.44$). Angina severity in the CHD group was significantly greater: 52%, 38%, 9%, and 1% for Canadian Cardiovascular Society (CCS) I, II, III, and IV class, respectively, whereas in the C group CCS class I angina was in 79% and CCS II class in 6% ($p = 0.03$). Factors affecting angina were: female sex (odds ratio [OR] 1.84, 95% confidence interval [CI] 0.99–3.38; $p = 0.04$), and localisation of non-critical lesions in the left anterior descending artery (LAD) (OR 2.54, 95% CI 1.31–4.92; $p = 0.006$) and left atrium (LA) area (OR 0.89, 95% CI 0.80–0.99; $p = 0.02$; Table 4).

Analysis of the assessed markers and need for revascularisation are presented in Table 5.

Parameters associated with the need for revascularisation were: older age (OR 1.16; $p = 0.04$), increased fibrinogen level (OR 1.01; $p = 0.05$), and worse indices of left ventricular (LV) diastolic function: isovolumetric relaxation time (IVRT; OR 1.07; $p = 0.04$) and released propagation velocity of mitral inflow (Vp; OR 0.88; $p = 0.01$). Other demographic or clinical factors (gender, AH, DM, stroke, smoking) and biochemical markers (WBC, haematocrit [HCT], platelets [PLT], hyperlipidaemia) did not correlate with occurrence of symptoms resulting from progression of atherosclerosis. No correlation with the need for revascularisation showed other echocardiographic indices (left ventricular mass [LVM] index, left ventricular ejection fraction [LVEF], ratio between early mitral inflow velocity and mitral annular early diastolic velocity [E/E'], deceleration E wave, pulmonary vein systolic to diastolic velocity ratio [S/D], mitral inflow E/A ratio [E/A], LA area, posterior wall thickness [PW], interventricular septum thickness [IVS], left ventricular end-diastolic volume [LVEDV],

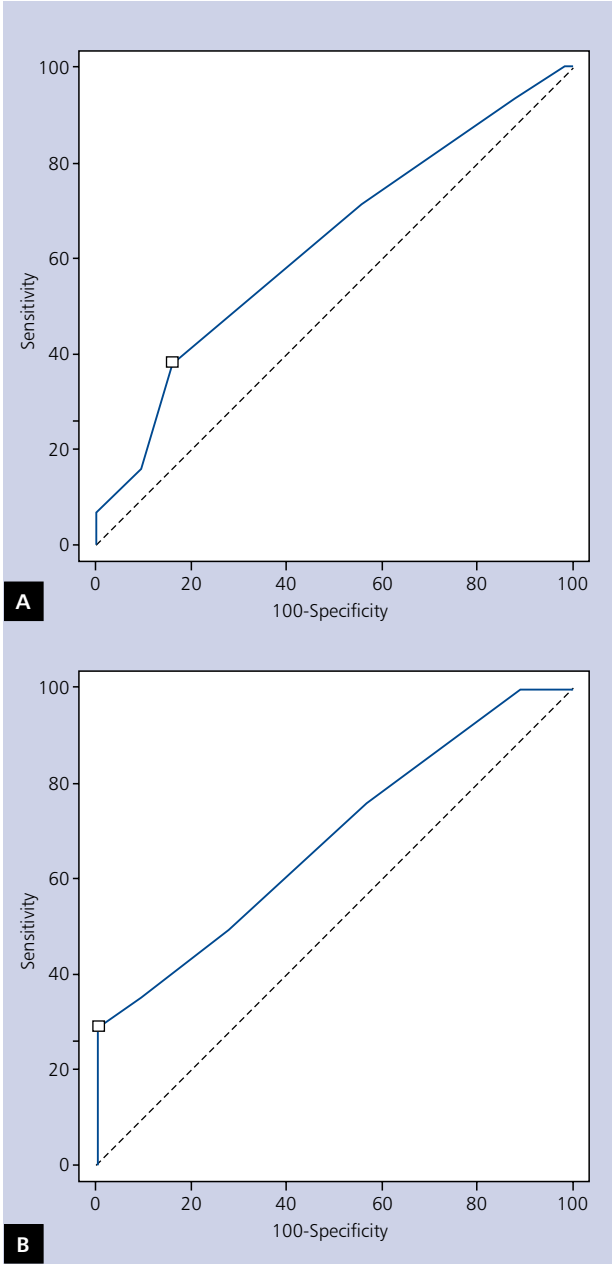

Figure 2. Relationship between intima-media-thickness and occurrence of non-critical coronary artery lesions regarding gender — in women (**A**) and in men (**B**)

Table 4. Results of univariate analysis of parameters associated with the occurrence of pain in the chest in12-month follow-up

Variable	OR	95% CI	p
Sex [female = 1]	1.84	0.99–3.38	0.04
Age	1.03	0.99–1.07	0.06
Diabetes type 2	1.38	0.65–2.89	0.40
Hypertension	2.73	0.77–9.75	0.09
Smoking	0.55	0.25–1.25	0.14
Hyperlipidaemia	0.57	0.29–1.01	0.08
Fibrinogen	1.00	0.99–1.00	0.29
IMT	1.10	0.92–1.29	0.28
LVEF	1.02	0.95–1.11	0.54
E/E'	0.97	0.87–1.08	0.57
Vp	1.01	0.98–1.04	0.39
LAD lesions	2.54	1.31–4.92	0.006
RCA lesions	0.84	0.31–2.26	0.72
Cx lesions	0.63	0.22–1.82	0.38
Number of affected vessels	0.98	0.53–1.81	0.98
S/D	1.75	0.47–6.51	0.40
E/A	0.40	0.14–1.14	0.08
E wave DT	1.00	0.99–1.01	0.18
IVRT	1.01	0.99–1.03	0.19
LA area	0.89	0.80–0.99	0.02
IVS	0.79	0.61–1.01	0.06
PW	0.96	0.83–1.01	0.48

OR — odds ratio; CI — confidence interval; IMT — intima-media thickness; LVEF — left ventricular ejection fraction; E/E' — ratio between early mitral inflow velocity and mitral annular early diastolic velocity; Vp — transmitral flow propagation velocity; LAD — left anterior descending artery; RCA — right coronary artery; Cx — circumflex artery; S/D — pulmonary vein systolic to diastolic velocity ratio; E/A — mitral inflow E/A ratio; E wave DT — mitral E-wave deceleration time; IVRT — isovolumetric relaxation time; LA — left atrium; IVS — interventricular septum thickness; PW — posterior wall thickness

Table 5. Results of univariate analysis evaluating the correlation of assessed indices with the onset of angina symptoms requiring percutaneous intervention at 12-month follow-up

Variable	OR	95% CI	p
Sex	–	–	0.99
Age	1.16	0.98–1.35	0.04
BMI	1.09	0.88–1.35	0.44
Lipid disorders	0.61	0.06–1.01	0.66
Heart rate	0.95	0.83–1.08	0.47
Creatinine	1.00	0.94–1.07	0.98
WBC	1.03	0.72–1.48	0.87
HTC	0.78	0.59–1.03	0.10
PLT	0.99	0.98–1.01	0.67
Fibrinogen	1.01	1.00–1.02	0.05
IMT	1.22	0.77–1.92	0.43
LVEF	1.04	0.80–1.35	0.75
E/E'	0.97	0.66–1.41	0.86
Group (study vs. control)	–	–	0.99
Vp	0.88	0.79–0.98	0.01
LAD lesions	–	–	0.99
RCA lesions	–	–	0.99
Cx lesions	–	–	0.98
Number of affected vessel	2.82	0.90–8.80	0.08
LVM index	1.01	0.97–1.05	0.63
S/D	22.79	0.28–1854.28	0.16
E/A	0.01	0.00–2.16	0.02
E wave DT	1.01	0.99–1.03	0.29
IVRT	1.07	1.01–1.12	0.01
LA area	0.74	0.49–1.12	0.12
PW	1.05	0.91–1.21	0.57
IVS	1.43	0.66–3.08	0.36
LVEDV	0.99	0.97–1.03	0.84
LVESV	0.99	0.93–1.05	0.72

OR — odds ratio; CI — confidence interval; BMI — body mass index; WBC — white blood cells; HTC — haematocrit; PLT — platelets; IMT — intima-media thickness; LVEF — left ventricular ejection fraction; E/E' — ratio between early mitral inflow velocity and mitral annular early diastolic velocity; Vp — transmitral flow propagation velocity; LAD — left anterior descending artery; RCA — right coronary artery; Cx — circumflex artery; LVM — left ventricular mass; S/D — pulmonary vein systolic to diastolic velocity ratio; E/A — mitral inflow E/A ratio; E wave DT — mitral E wave deceleration time; IVRT — isovolumetric relaxation time; LA — left atrium; PW — posterior wall thickness; IVS — interventricular septum thickness; LVEDV — left ventricular end-diastolic volume; LVESV — left ventricular end-systolic volume

left ventricular end-systolic volume [LVESV]) as well as localisation of lesions in coronary arteries during the first coronary angiography (LAD, circumflex artery [Cx], and right coronary artery [RCA]).

In multivariate analysis the rate of propagation Vp, which reflects the speed of blood flow and diastolic compliance of the LV, was the only independent factor that showed correlation with the necessity of coronary angioplasty, in four patients from the CHD group (OR 0.89, 95% CI 0.84–0.96; p = 0.02).

In three-year follow-up there were no deaths from CV causes. In the CHD group one patient had myocardial infarction and two patients had ischaemic stroke. In the C group two patients experienced transient ischaemic attack. Due to recurrent chest pain and progression of stenosis seven coronary angioplasty procedures were performed, including six in the CHD group (6% vs. 1%; p = 0.003). In this case, angina was also significantly more severe — 49%, 35%, 15%, and 1% of subjects were in CCS class I, II, III, and IV, respectively in the CHD group, while in the C group 80%, 19%, and 1% of patients were CCS class I, II, and III, respectively (p = 0.04).

After three years follow-up chest pain occurred in 43 persons in the studied group (43% vs. 33%; p = 0.05). Factors affecting occurrence of angina among respondents in the multivariate logistic regression analysis were: female sex (OR 14.8, 95% CI 1–218; p = 0.05) and location of non-critical lesions in the LAD (OR 2.62; p = 0.004). Among echocardiographic parameters, lower Vp proved to be associated with need for revascularisation (OR 0.88, 95% CI 0.78–0.98; p = 0.017).

DISCUSSION

The results of this study indicate quite good prognosis of patients with non-critical lesions in coronary arteries, similarly to results obtained by other authors [5]. However, some data in recent years show that occurrence of angina even in the case of absence of significant lesions in coronary angiography is associated with worse prognosis compared to the asymptomatic population. Jaspersen et al. [6] showed that symptomatic patients with normal coronary angiography and those with scattered non-critical lesions have a relatively high risk of major cardiovascular events (MACE) up to 57% and 85%, respectively, as well as increased risk of death from all causes by 29% and 52% compared to asymptomatic subjects with no differences between women and men. However, Canadian authors showed that outcomes depend on gender [7]. They pointed out that among symptomatic patients with non-obstructive lesions (≤ 49%) over one-year follow-up women had higher risk of MACE than men (HR 2.43, 95% CI 1.08–5.49). Women with lesions between 1% and 49% had 2.55 higher risk compared to women without any lesions at angiography (95% CI 1.33–4.88). Recent reports from the WISE study [8] documented increased risk of future CV events in stable CHD women compared to asymptomatic women and pay attention to additional negative value of standard risk factors in this population. Over the analysed period of five years the incidence of CV events in the case of diffuse non-critical lesions (1–49% stenosis) and for patients with normal vessels in coronary angiography were 16.0% and 7.9%; 2.5%, respectively, for asymptomatic women (p < 0.002). In the presence of four or more risk factors percentages of CV events were 25.3%, 13.9%, and 6.5%, respectively, (p = 0.003).

The WISE study investigators suggest that early damage of the endothelium leads to small vessel disease resulting in ischaemic symptoms, and increases the risk of future CV events despite minimal or even no lesions in coronary arteries in symptomatic compared to asymptomatic patients.

The CHD group consisted largely of men (66%) and to a much greater extent was burdened with risk factors such as AH, DM, and tobacco smoking, which could explain the higher incidence of atherosclerotic non-critical lesions and is consistent with population-based studies [9]. Noteworthy is the relatively high incidence of AH in both studied (95%) and control (85%) groups. DM was ascertained, respectively, in 25% and 12%. In the general population percentages of AH and DM were estimated at 32% and 5%, relatively. Smoking was significantly more frequent in the study group (32% vs. 8% compared to the general population — 27%) dominated by men among whom cigarette smoking is more prevalent. In the study by Jaspersen et al. [6] covering, similar to our CHD group, the incidence of factors such as DM, smoking, AH, or hyperlipidaemia were: 13.6%, 23%, 45.8%, and 51.2%, respectively. Men more often than women were smokers (28% vs. 20%) and slightly more often suffered from DM (16% vs. 12%) while women more often took AH (49% vs. 43%) and hyperlipidaemia (53% vs. 50%) medication. Data from the WISE study showed that among patients with so-called non-obstructive CAD (narrowing of ≤ 49%) the incidence of DM, smoking, AH, and hyperlipidaemia were 19.8%, 57.7%, 60.8%, and 39.6%, respectively.

In this study fibrinogen concentrations did not differ significantly between the study and control groups. In univariate logistic regression analysis, it proved to be a parameter related to the frequency of revascularisation (OR 1.01, 95% CI 1.00–1.02, p = 0.05). Noteworthy in this context is the study evaluating effects of lifestyle modification to reduce the high baseline levels of fibrinogen and other standard CV risk factors [10]. In a two-year observation, in the intensive treatment group, reduction of fibrinogen concentration was average by 31 mg/dL. However, it did not result in changes of total cholesterol levels and decrease of other CV risk factors. It was possibly because of the very low level of plasma fibrinogen that was the threshold for intervention. In this study, it was slightly above 300 mg/dL, which is the boundary for patients from both the C and CHD groups. Other researchers suggest that only fibrinogen concentration higher than 402 mg/dL reveals the effect of long-term prognosis and leads to an increase in mortality, respectively, from 3.1% to 7.7% within a year [11]. Another meta-analysis confirmed that increase of fibrinogen concentration by 1 g/L depending on age and sex differences was associated with higher risk of CHD by 2.42 (95% CI 2.24–2.60) and stroke by 2.06 (95% CI 1.83–2.33) [12].

The type of medication used to overcome associated modifiable CV risk factors is very important. Fibrates and niacin lower fibrinogen concentrations whereas statin therapy does not have such an effect. This is important because current guidelines of the European Society of Cardiology recommend statins in primary and secondary prevention. There have been published so far three large clinical trials on that issue. In the first, despite obtaining a significant decrease in fibrinogen levels as a result of active therapy with bezafibrate (BIP study), there was no decline in incidence of CV events [13]. In the next, as a result of fenofibrate therapy, fibrinogen concentration decreased by 13%, and again with no positive impact on clinical outcomes. Use of hormone replacement therapy (HERS study) reduced fibrinogen levels but again did not translate into positive clinical effects [14]. Therefore,

despite the fact that some data indicate elevated levels of plasma fibrinogen as an important, independent predictor of future CV events, there are still no conclusive data showing improvement in prognosis of patients after lowering its concentration. It may result from fluctuations of fibrinogen concentrations depending on concomitant diseases or clinical conditions such as female sex, oestrogen usage, older age, obesity, or DM. It may also depend on the type of stimulants, for example smoking increases while alcohol intake lowers plasma fibrinogen concentrations.

In our study TTE showed significant differences between the CHD and C groups. Although the studied parameters were within the normal range, the obtained differences could be explained by higher prevalence of traditional risk factors such as AH and predominance of males in the study compared to the control group. In multivariate analysis the only independent factor associated with coronary revascularisation in the follow-up period proved to be colour M-mode flow propagation velocity — Vp (OR 0.88, 95% CI 0.79–0.97; $p = 0.02$). Vp is fairly sensitive indicator of LV diastolic dysfunction. Among many other indices of LV diastolic function, only Vp proved to be, in many studies, an early indicator of improving diastolic function in patients who underwent successful percutaneous coronary intervention in stable CAD [15]. Other studies also demonstrated improvement of other LV diastolic function parameters [16].

Diastolic function parameters correlate well with the size of necrosis area during myocardial infarction. Relaxation of the heart muscle is an energetically costly process and therefore seems to be more sensitive to ischaemia. Recurrent ischaemia can induce structural changes in the myocardium revealing deterioration of early diastolic wall motion of the heart. Hoffman et al. [17] report that it is best seen in anterior and anteroseptal segments in patients with one- and two-vessel disease, respectively, relating to the LAD and Cx and LAD. Possibly this may be due to the fact that segments located in the centre of regions supplied by narrowed arteries are most vulnerable to ischaemia. Peripheral segments are usually supplied by collaterals leaving from unchanged vessels. At this stage, longitudinal contractility decrease may be offset by a radial function. It is a possible explanation of maintenance of the normal LVEF in the early stages of ischaemic heart muscle.

In the study of Mogelvang et al. [18], reduced S' and A' and E'/A' were significantly associated with increased risk of mortality in patients from Copenhagen Heart Study, similarly to the general population. However, in the group of patients with LVEF ≥ 50%, in more than 98% such a relationship was not confirmed for E' and E/E', which confirms the smaller utility of these parameters in patients with preserved LVEF and is consistent with observations from our study. Authors found combination of systolic and diastolic function parameters in tissue Doppler imaging (TDI): E', A', and S in so-called *eas index* [E'/(A' × S')] to be best correlated with the global risk in the low-risk population. In multivariate analysis, it was associated with a 2.7-fold increased risk (95% CI 1.5–4.9; $p < 0.001$). Some authors reported that in patients with CHD, TDI indices can be associated with endothelial damage and increased platelet activity [19]. A recently published meta-analysis of eight studies [20] confirms that the rest TDI test is helpful in identifying patients with CHD.

It has been shown that IMT above the threshold value correlates with the presence of non-critical lesions in coronary arteries. Kim et al. [21] analysed relationship between IMT and the properties of atherosclerotic plaques visualised with IVUS, in particular the total area (total plaque area [TPA]) and total volume (total plaque volume [TPV]). IMT, as in our group, averaged 0.90 ± 0.26 mm. Although the authors found a significant correlation of average values for couples IMT:TPA, IMT:TPV, and TPA:TPV with correlation indices, respectively, 0.448, 0.587, and 0.873 ($p < 0.005$); however, the value of IMT was not correlated with the severity of coronary lesions. In multivariate analysis IMT was associated only with hypertension, the prevalence of which in the subgroup of patients without CHD was similarly high (80%) as in our study.

The meta-analysis of Simon et al. [22] including eight large clinical trials involving 37,197 patients showed that an increase of IMT by 0.1 mm increases risk of myocardial infarction by 10–15% and risk of stroke by 13–18%. IMT predicts CHD and cerebral stroke regardless of age, gender, race, and conventional risk factors; however, it is best suited for predicting cerebral stroke in women [23]. Prediction of CHD is rather moderate and is associated with an absolute risk of 1–2%/year.

Although significant correlation between indicators of early vascular remodelling and SCORE in low-risk populations has been shown, unfortunately IMT is not a good marker of epicardial vascular lesions, especially in younger populations (≤ 55 years). It seems that only in patients of intermediate risk for major CV events (6–20% in 10 years) IMT ≥ 1.0 mm allows qualifying a patient as a high CV risk subject and justifies appropriate diagnosis and optimal therapy. There are reports drawing attention to the fact that not only the presence of lesions in the common carotid artery expressed with measurement of IMT but also its morphology (echolucency — translucency, calcification, local inflammation indices) and other markers such as surface of the plaque could be important in predicting future events [24]. Reports suggest that the baseline IMT as well as the dynamic changes over the period of observation can improve the risk stratification, although earlier reports and meta-analyses did not show relationships between change in thickness and the occurrence of serious vascular complications. In the study of 868 men aged 40 to 74 years without history of CAD, the overall risk of CHD within 10 years was associated with the value of IMT as follows: ≥ 2.0% for IMT 0.88 ± 0.18 and ≥ 5.0% for IMT 0.95 ± 0.19 [25].

Limitations of the study

The prevalence of CV risk factors was analysed only at the beginning of the study while in the follow-up mainly the occurrence of CV events was assessed. Low incidence of MACE could be due to good control of CV risk factors in these subjects as well.

CONCLUSIONS

Prognosis of patients with CHD and non-critical lesions on angiography is good. In some patients there is increased risk of CV events, of which the risk factors were: older age, elevated concentrations of fibrinogen, and impaired left ventricular filling pattern. In women there is marked correlation between existing lesions in coronary arteries and IMT. Despite pharmacological treatment consistent with current recommendations in more than one third of patients with non-critical coronary artery lesions, angina impairing quality of life is still present.

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