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Prognostic factors in patients who have survived myocardial infarction

Research Article

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Abstract: Patients who have survived myocardial infarction (MI), compared to the general population, have an increased risk of reinfarction, myocardial revascularization, and death. In this study we investigated the prognostic significance of the predictors of the risk for adverse coronary events in 118 patients, both male and female, with a confirmed diagnosis of MI in the last 3 years. The predictors of reinfarction, revascularization and death in patients who survived MI were: poor adherence to hypolipemics (hazard ratio [HR] 3.06, p=0.006), physical inactivity (HR 2.22, p=0.056), the number of variable risk factors (HR 1.29, p=0.025), and age (HR 1.06, p=0.007). After the inclusion of the invariable risk factors in the model of multivariant analysis, the following factors were singled out as significant predictors of the risk: gender (HR 3.86, p=0.0015), physical inactivity (HR 2.38, p=0.007), change in the level of triglycerides (HR 1.49, p=0.040), change in the number of variable risk factors (HR 1.41, p=0.0007), and age (HR 1.05, p=0.009). A 3-year follow-up of the patients who survived the first MI and who were enrolled in this study of secondary prevention demonstrated that physical inactivity, the number of variable risk factors and age significantly contributed to an increased risk of reinfarction, revascularization, and death.

Keywords: *Myocardial infarction • Adverse coronary events • Independent prognostic factors*

1. Introduction

Myocardial infarction (MI) is the cause of a large number of hospitalizations throughout Europe and presents a huge health care problem. Patients who have survived a MI have a potentially poor prognosis. Their mortality rates range from 5% to 30% [1] in the first year and up to 55% in the first 10 years [2].

Advances in the domains of prevention and treatment have reduced mortality rates from coronary disease in developed countries. In developing countries, however, the mortality rates are rising. While the mortality rates from coronary disease are dropping in the Western Europe, they are rising in the Eastern and Central Europe (especially in the countries of the former USSR).

Although age-specific rates of mortality from coronary disease are dropping in developed countries, the absolute number of deaths has not been markedly reduced because of ageing of the general population in most of the countries. Appropriately, timely treatment of

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the first MI has had an impact on reduced mortality rates [3], but it has also increased the number of individuals at high risk for new adverse coronary events, infarction, myocardial revascularization, and death. Depending on the gender and clinical outcome for those who have survived an acute MI, the risk of adverse events and death is 1.5 to 15 times greater than that of the general population [4].

This fact suggests that the measures of secondary prevention in patients who have survived the MI have to be rigorous, aiming to reduce the risk of new cardiovascular events, temporary disability, and morbidity, while prolonging survival and improving the quality of life.

However, despite several studies in the field of secondary prevention, there are few data about its impact on survival and the rates of adverse coronary events, which is probably due to an insufficient average duration of these studies (up to 1 year).

The aim of this study was to assess the prognostic importance of variable and invariable cardiovascular risk factors for adverse coronary events in patients who have survived the MI.

2. Material and Methods

2.1. Patients

For the purposes of this study, we selected 118 patients on the basis of the information in the data base of the multicentric prospective interventional study „Secondary prevention of coronary disease and cerebrovascular diseases“, which was conducted in the first half of 2005 in 38 health care centres in Serbia and involved 1189 patients.

Our group was comprised of both male and female patients aged less than 80 years, with a confirmed diagnosis of a first MI survived within previous 3 years; the confirmation was based on the diagnostic summary formed after the analysis of medical documentation. Those who had had a first MI were enrolled in the study, provided they had not had revascularization (percutaneous transluminal angioplasty or bypass), while those with postinfarction angina or reinfarction as new coronary events were not considered for the study. The study thus enrolled 84 (71.2%) men and 34 (28.8%) women who survived the MI in the period 2003-2005. The average age of the patients was 59.32±10.14 years (59.38±9.86 for men; 59.18±10.98 for women), without a statistically significant difference between the genders ($t=0.099$; $p=0.922$; $p>0.05$).

2.2. Experimental procedure

The data were collected by means of questionnaires, medical records, and physical examination. The follow-up questionnaire contained the criteria for the data on invariable (gender, age, genetic burden) and variable (body mass index, systolic and diastolic blood pressure, heart frequency, glycemia, total, LDL and HDL cholesterol and triglycerides, smoking status, physical activity) cardiovascular risk factors, collected at the beginning of the study and during the secondary prevention after 2, 4, 6, 12, 24, and 36 months. Drug therapy with aspirin, β-blockers, angiotensin converting enzyme inhibitors, hypolipemics, and metformin was also monitored.

The study was designed so that there was no statistically significant difference between genders in regard to comorbidities (Fisher's exact probability test: $p=0.418$; $p>0.05$). Arterial hypertension (81.4%) and diabetes (29.7%) were the most commonly diagnosed diseases in both genders. We did not observe any statistically significant difference between genders regarding the site of the MI, either inferior ($\chi^2=0.12$; $p=0.726$; $p>0.05$) or anteroseptal ($\chi^2=0.12$; $p=0.726$; $p>0.05$).

At the beginning of the study, there were no statistically significant differences between the observed factors, which was in accordance with the study design, with an exeption for male subjects who had significantly higher values for body mass index ($t=2.188$; $p=0.031$; $p<0.05$) (Mann-Whitney U Test: $U=1050.5$; $Z=2.244$; $p=0.025$; $p<0.05$).

The presence of variable cardiovascular risk factors was verified anamnestically, by measuring blood pressure (with a mercury manometer), measuring body height and weight, and using laboratory assays (lipidogram and glycemia testing). The analyses of medical records and patient interviews were used to monitor the incidence of possible adverse coronary events (reinfarction, myocardial revascularization, death).

At the beginning of the study, all the patients were instructed about lifestyle changes, procedures before blood sampling for laboratory tests, measurement of blood pressure, height and weight, as well as the harmful effects of cardioprotective drugs. Blood-pressure determination and all other anthropometric and laboratory measurements were performed in outpatient settings with the same instruments and measurement techniques.

The resulting effects of the secondary prevention measures were evaluated on the bases of up-to-date European recommendations for the secondary prevention of coronary disease [5].

Table 1. Characteristics of the patients enrolled in the study (the first control).

Parameter	TOTAL	Men	Women
Gender - number (%)	118 (100%)	84 (71.2%)	34 (28.8%)
Age (years)	59.32±10.14	59.38±9.86	59.18±10.98
BMI (kg/m2)	27.01±3.71	27.48±3.85	25.86±3.11
SBP (mmHg)	148.98±24.17	150.18±23.46	146.03±25.96
DBP (mmHg)	90.85±12.43	91.85±11.71	88.38±13.91
CF (beats/min)	77.71±10.23	77.88±9.84	77.29±11.28
Total cholesterol (mmol/l)	6.83±1.54	6.78±1.54	6.96±1.53
LDL-cholesterol (mmol/l)	4.33±1.43	4.30±1.46	4.40±1.38
HDL-cholesterol (mmol/l)	1.36±0.38	1.39±0.38	1.28±0.36
Triglycerides (mmol/l)	2.61±1.92	2.79±2.18	2.17±0.93
Glycose (mmol/l)	6.43±2.31	6.49±2.16	6.27±2.67
Smokers – number (%)	30 (25.4%)	21 (25.0%)	9 (26.5%)
Insufficient physical activity - number (%)	49 (41.5%)	33 (39.3%)	16 (47.1%)
Diabetes in family history	29 (24.6%)	21 (25.0%)	8 (23.5%)

BMI-body mass index, SBP-systolic blood pressure, DBP-diastolic blood pressure, CF-cardiac frequency

Table 2. Independent prognostic factors for adverse coronary events in patients **without** stroke.

Characteristic	B*	SE**	p***	OR(95%CI)****
AGE	0.059	0.022	0.007	1.06 (1.02-1.11)
NON-ADHERENCE TO HYPOLIPEMICS	1.117	0.409	0.006	3.06 (1.37-6.81)
PHYSICAL INACTIVITY	0.798	0.417	0.056	2.22 (0.98-5.03)
CHANGE IN THE NUMBER OF VARIABLE RISK FACTORS	0.253	0.113	0.025	1.29 (1.03-1.61)

** Logistic regression coefficient ** Standard error *** Odds ratio **** Confidence interval (95%) CVI-cerebrovascular insult*

2.3. Statistical analysis

Multivariant analysis was used to analyze the factors associated with adverse coronary events, including only the statistically significant variables obtained by univariant analysis. The backward (Wald) regression model was applied; all the variables and a constant that were significantly associated with adverse coronary events according to this model were included in the equation. Data were then processed by Cox regression analysis, especially for the differences obtained by subtraction of the values at the first control from the values at the last control immediately before the adverse event.

3. Results

The study enrolled 118 patients who have survived a first MI. Their baseline characteristics are shown in Table 1.

During the 3 years' follow-up, there were 49 registered cardiovascular events. Out of those 49, 21 (17.8%) patients had myocardial reinfarction. Myocardial revascularization was registered in 22 (18.6%) patients; bypass surgery in 14 patients, 6 patients underwent stenting, while 2 patients underwent both procedures. A fatal outcome after surviving the first MI was observed in 6 (5.1%) patients.

The method of backward (Wald) Cox regression multivariate analysis which involved gender, age, and seven other characteristics demonstrated that physical inactivity, temporal changes of the total and LDL cholesterol, non-adherence to hypolipemics, change in the number of variable risk factors, and status after a cerebrovascular insult (post-CVI status) were statistically significant ($p<0.05$). This regression model applied to patients without stroke eliminated (at the lowest level of significance) the variables of gender and change in the levels of total and LDL cholesterol. Independent prognostic factors for adverse coronary events in patients without stroke were non-adherence to hypolipemics (HR 3.06, 95% CI 1.37-6.81, p=0.006), physical inactivity (HR 2.22, 95% CI 0.98-5.03, p=0.056), change in the number of variable risk factors (HR 1.29, 95% CI 1.03-1.61, p=0.025), and age (HR 1.06, 95% CI 1.02-1.11, p=0.007) (Table 2).

For the patients who survived CVI, the backward (Wald) method eliminated the variables of gender, change in the levels of total and LDL cholesterol, and post-CVI status; the variables retaining statistical significance

Table 3. Independent prognostic factors for adverse coronary events in patients **with** stroke (CVI).

Characteristic	B*	SE**	p***	OR(95%CI)****
AGE	0.059	0.022	0.007	1.06 (1.02-1.11)
NON-ADHERENCE TO HYPOLIPEMICS	1.117	0.409	0.006	3.06 (1.37-6.81)
PHYSICAL INACTIVITY	0.798	0.417	0.056	2.22 (0.98-5.03)
CHANGE IN THE NUMBER OF VARIABLE RISK FACTORS	0.253	0.113	0.025	1.29 (1.03-1.61)

** Logistic regression coefficient ** Standard error *** Odds ratio **** Confidence interval (95%)*

Table 4. Independent prognostic factors for adverse coronary events (**without** the number of invariable risk factors).

Characteristic	B*	SE**	p***	OR(95%CI)****
GENDER	0.350	0.424	0.0015	3.86 (1.68-8.85)
AGE	0.045	0.017	0.009	1.05 (1.01-1.08)
CHANGE IN TRIGLYCERIDE LEVELS	0.396	0.193	0.040	1.49 (1.02-2.17)
PHYSICAL INACTIVITY	0.866	0.320	0.007	2.38 (1.27-4.45)
CHANGE IN THE NUMBER OF VARIABLE RISK FACTORS	0.342	0.101	0.0007	1.41 (1.15-1.71)

** Logistic regression coefficient ** Standard error *** Odds ratio **** Confidence interval (95%)*

Table 5. Independent prognostic factors for adverse coronary events (**with** the number of invariable risk factors).

Characteristic	B*	SE**	p***	OR(95%CI)****
GENDER	0.350	0.424	0.0015	3.86 (1.68-8.85)
AGE	0.045	0.017	0.009	1.05 (1.01-1.08)
CHANGE IN TRIGLYCERIDE LEVELS	0.396	0.193	0.040	1.49 (1.02-2.17)
PHYSICAL INACTIVITY	0.866	0.320	0.007	2.38 (1.27-4.45)
CHANGE IN THE NUMBER OF VARIABLE RISK FACTORS	0.342	0.101	0.0007	1.41 (1.15-1.71)

** Logistic regression coefficient ** Standard error *** Odds ratio **** Confidence interval (95%)*

were non-adherence to hypolipemics (HR 3.06, 95% CI 1.37-6.81, p=0.006), physical inactivity (HR 2.22, 95% CI 0.98-5.03, p=0.056), change in the number of variable risk factors (HR 1.29, 95% CI 1.03-1.61, p=0.025), and age (HR 1.06, 95% CI 1.02-1.11, p=0.007) (Table 3).

Cox regression analysis was then applied to all events, together with the differences obtained by subtraction of the values at the first control from the values at the last control immediately before the adverse event. Backward (Wald) regression multivariate analysis which involved gender, age, and six other characteristics demonstrated statistical significance at the p<0.05 level for physical inactivity, change in the levels of total and LDL cholesterol and triglycerides, change in the number of variable risk factors, and the number of invariable risk factors.

By taking into account the number of invariable risk factors, we eliminated with this method the variables of change in the levels of total and LDL cholesterol and the number of invariable risk factors. Table 4 shows the variables that retained their statistical significance: gender (HR 3.86, 95% CI 1.68-8.85, p=0.0015), physical inactivity (HR 2.38, 95% CI 1.27-4.45, p=0.007), changes of trigyceride levels (HR 1.49, 95% CI 1.02-2.17, p=0.040), change in the number of variable risk factors (HR 1.41, 95% CI 1.15-1.71, p=0.0007), and age (HR 1.05, 95% CI 1.01-1.08, p=0.009).

Excluding the number of invariable risk factors, backward (Wald) regression mutivariate analysis included gender, age, and five more characteristics and demonstrated physical inactivity, change in the levels of total and LDL cholesterol and triglycerides, and change in the number of variable risk factors to be statistically significant (p<0.05). With this method, the change in the levels of total and LDL cholesterol was eliminated. Independent prognostic factors for adverse coronary events in patients who survived the first MI (without the number of invariable risk factors) were gender (HR 3.86, 95% CI 1.68-8.85, p=0.0015), physical inactivity (HR 2.38, 95% CI 1.27-4.45, p=0.007), change in triglyceride levels (HR 1.49, 95% CI 1.02-2.17, p=0.040), change in the number of variable risk factors (HR 1.41, 95% CI 1.15-1.71, p=0.0007), and age (HR 1.05, 95% CI 1.01-1.08, p=0.009) (Table 5).

4. Discussion

Using the backward (Wald) Cox regression multivariate analysis, the independent prognostic factors for adverse coronary events in patients who survived MI were gender, age, physical inactivity, change in triglyceride levels, non-adherence with hypolipemics, and change in the number of variable risk factors.

Numerous studies [6-13] have demonstrated sometimes conflicting results regarding gender and age as risk factors associated with reinfarction, revascularization, and death after MI. Nevertheless, these factors are considered to be significant prognostic factors for adverse coronary events. Most authors have shown that short-term and long-term mortality rates were higher in older patients. The TRAndolapril Cardiac Evaluation (TRACE) study group investigated the impact of age and cardiac insufficiency on mortality in the first year and in the first three years after MI. They have established that mortality rates were significantly elevated in patients with an ejection fraction (EF) below 35% and in those older than 65 years. Other authors have obtained similar results. Deaner et al. have established that the risk of death is 3% per year in those below 50 years of age. In comparison, the risk of death after surviving the MI was 15% in those older than 70 years; however, compared to other causes of death in this age group, this risk was relatively modest [14]. Gender, as an independent risk factor, affects short-term and long-term mortality after survival of an MI [15].

Recent evidence indicates that other lipid variables besides LDL cholesterol, such as elevated triglycerides and low HDL cholesterol, markedly contribute to cardiovascular risk [16-18]. In several studies, the substantial benefit of achieving target triglyceride levels in patients with coronary disease (including surviving the MI) has been stressed [19-21].

The importance of hypolipemics, especially statins, in the secondary prevention of MI has been suggested in both recent and earlier studies [22-25]. In all these studies, as in this study, the use of hypolipemics in patients after the MI as a secondary prevention measure reduced the percentage of adverse coronary events.

As early as the 1950s, it was hypothesized that insufficient physical activity was a risk factor for adverse coronary events, but it was not evident as one of the principal risks until the 1990s [26]. Numerous authors have investigated the association of physical activity and post-MI status [27-30]. Even the slightest lifestyle changes with moderate physical activity have been found to reduce the percentage of adverse coronary events in patients after the MI, which we also confirmed in this study.

Several large studies of years' duration [6,31,32] have shown that the reduction of adverse coronary events in patients who have survived the MI can be attributed mostly to the reduction or elimination of variable risk factors, which, in addition to adequate therapy, was the most important goal in secondary prevention. All these results were confirmed in this study, as well.

In conclusion, our 3-year follow-up of patients who have survived the MI and who were enrolled in this study of secondary prevention demonstrated that physical inactivity, the number of variable risk factors, and age significantly contributed to an increased risk of reinfarction, revascularization, and death.

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