

SIMILARITIES AND DIFFERENCES IN EPIDEMIOLOGY AND RISK FACTORS OF CEREBRAL AND MYOCARDIAL ISCHEMIC DISEASE

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SLIČNOSTI I RAZLIKE U EPIDEMIOLOGIJI I FAKTORIMA RIZIKA CEREBRALNE I MIKARDNE ISHEMIJSKE BOLESTI

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ABSTRACT

Ischemic heart disease and cerebral ischemia represent the leading causes of mortality worldwide. Both entities share risk factors, pathophysiology and etiologic aspects by means of a main common mechanism, atherosclerosis.

The authors aimed to investigate differences and similarities in epidemiology and risk factors that could be found between both entities.

In a retrospective study 403 patients were included and divided into two groups: group of 289 patients with history of myocardial infarction (AMI), and group of 114 patients with history of ischemic stroke (IS). All patients were evaluated for nonmodifiable risk factors, which included age and sex, and modifiable, such as hypertension, dyslipidemia, diabetes, obesity, physical activity and smoking. Differences in some epidemiological aspects were also considered: occupation, marital status, alcohol consumption, exposure to stress.

Patients with history of IS were significantly older than AMI patients (64.0 ± 9.9 vs 64.0 ± 9.9 , $p=0.028$), with higher diastolic blood pressure (87.1 ± 10.2 vs 83.6 ± 10.4 , $p=0.003$) and higher Sokolow-Lyon index in ECG, as also index of left ventricular hypertrophy (19.2 ± 9.1 vs 14.7 ± 6.5). There were no significant differences between groups in the estimated body mass index and waist circumference. Differences between groups in stress exposure, occupation, alcohol consumption or physical activity were not significant. Patients in AMI group were more frequently male (199 (69%) vs 59 (52%), $p=0.001$), married (252 (87%) vs 88 (77%), $p=0.037$), smokers (162 (56%) vs 50 (44%), $p=0.018$) and with higher incidence of dyslipidemia (217 (75%) vs 73 (64%), $p=0.019$) compared with IS group. Incidence of arterial hypertension and diabetes was similar in both groups.

Both entities share similar pathophysiological mechanisms and, consequently, main traditional risk factors. However, incidence of myocardial infarction increases with male sex, dyslipidemia, smoking and marital status, while incidence of ischemic stroke increases with age, higher diastolic blood pressure and also with ECG signs of left ventricular hypertrophy.

Keywords: Ischemic heart disease, mortality, hypertension

SAŽETAK

Ishemijska bolest srca i cerebralna ishemija predstavljaju vodeće uzroke smrtnosti u svetu. Oba entiteta dele faktore rizika, patofiziologiju i etiološke aspekte. Cilj rada je bio razmotriti razlike i sličnosti u epidemiologiji i faktorima rizika za oba entiteta.

U retrospektivnu studiju uključena su 403 bolesnika podeljena u dve grupe: grupa od 289 bolesnika sa istorijom akutnog infarkta miokarda (AMI) i grupa od 114 bolesnika sa istorijom ishemijskog moždanog udara (IS). Kod svih bolesnika su praćeni nekorektibilni faktori rizika, kao što su godine i pol kao i korektibilni faktori, kao što su hipertenzija, hiperlipoproteinemija, dijabetes, gojaznost, fizička aktivnost i pušenje. Razmatrane su i razlike u nekim epidemiološkim aspektima; bračni status, upotreba alkohola i izloženost stresu.

Bolesnici sa istorijom IS bili su značajno stariji u poređenju sa bolesnicima koji su imali AMI (64.0 ± 9.9 vs 64.0 ± 9.9 , $p=0.028$), sa višim dijastolnim pritiskom (87.1 ± 10.2 vs 83.6 ± 10.4 , $p=0.003$) i imali su veće vrednosti indeksa hipertrofije leve komore (Sokolow-Lyon) u EKG-u (19.2 ± 9.1 vs 14.7 ± 6.5). Nije bilo značajnih razlika između grupa u indeksu telesne mase i obima struka. Takođe, razlike između grupa u izloženosti stresu, konzumaciji alkohola ili fizičkoj aktivnosti nisu bile značajne. Bolesnici sa AMI su češće muškog pola (199 (69%) vs 59 (52%), $p=0.001$), oženjeni (252 (87%) vs 88 (77%), $p=0.037$), pušači (162 (56%) vs 50 (44%), $p=0.018$) i sa većom učestalošću hiperlipoproteinemije (217 (75%) vs 73 (64%), $p=0.019$) u poređenju sa IS grupom. Učestalost arterijske hipertenzije i dijabetesa bila je slična u obe grupe.

Oba entiteta dele slične patofiziološke mehanizme, a time i glavne tradicionalne faktore rizika. Međutim, učestalost AIM je bila veća kod osoba muškog pola, osoba u braku, pušača i bolesnika sa hiperlipoproteinemijom, dok je učestalost ishemijskog moždanog udara bila povezana sa godinama starosti, višim dijastolnim krvnim pritiskom i sa znacima hipertrofije leve komore u EKG-u.

Ključne reči: Ishemijska bolest srca, smrtnost, hipertenzija



INTRODUCTION

Cerebral and myocardial ischemic disease share similar risk factors and pathophysiology and represent the consequence of atherothrombosis as a main etiological factor. About 87% of all strokes are ischemic strokes, in which blood flow to the brain is blocked [1]. Both entities represent the leading causes of mortality worldwide. Coronary artery disease (CAD) is a leading cause of death or disability in both, men and women. According to the World Health Organization (WHO), in 2002 there were 7.22 million deaths from coronary artery disease globally. [2]

Coronary artery disease alone is the most common cause of death in Europe, accounting for nearly 2 million deaths each year. More than 1 in 5 deaths of women (22 percent) and men (21 percent) are from CAD [3].

Stroke is also a major cause of death and a leading cause of serious long-term disability [4, 5].

According to WHO estimates, 15 million people each year suffer from strokes and 5 million people are left permanently disabled. [2] Based on report of American Heart Association in the Heart Disease and Stroke Statistics – 2012 Update, the average age for the incidence of a stroke is >75 years for women, and 71 years for men [4].

Stroke risk increases with age, but strokes can occur at any age. Compared to older people young adults are at a lower risk of stroke, however incidence of stroke in young people ranges from 60 to 200 new cases per year per million inhabitants. By the age of 75, 1 in 5 women and 1 in 6 men will have a stroke [6, 7].

Previous study [8] reported a yearly increase in frequency of stroke from 2.4 per 100,000 for a person aged between 20 and 24 years, to 4.5 per 100,000 for a person aged between 30 and 34 years, and to 32.9 per 100,000 for a person aged 45–49 years. Incidence of stroke was slightly higher in women younger than 30 years and in men older than 35 years.

Although coronary heart disease and stroke share important risk factors, some risk factors appear to have a stronger association with risk of stroke, such as high blood pressure, whereas others, for example total cholesterol, may have a stronger association with risk of coronary heart disease [9–13].

Luckily, although not curable, cardiovascular diseases are largely preventable. Modification of 9 easily measured clinical and laboratory risk factors can prevent up to 90% of first myocardial infarctions [14]. The long-recognized risk factors include age, sex, blood pressure, cholesterol levels, smoking status, diabetes mellitus, obesity, and a sedentary lifestyle. In addition, chronic kidney disease and insulin resistance (pre-diabetes) can be important risk factors for coronary heart disease, such as atrial fibrillation for stroke.

Unfortunately, the previous studies have demonstrated that coronary artery disease increases the risk for stroke, whereas patients with stroke are more likely to suffer from coronary artery disease [15–18].

In the present study the differences and similarities in epidemiology and risk factors that could be found in between both entities were analyzed and discussed.

MATERIALS AND METHODS

This observational, multicenter, epidemiological study consisted of 403 patients divided into two groups: group of 289 patients with history of myocardial infarction (AMI), and group of 114 patients with history of ischemic stroke (IS).

Patients were recruited from primary care facilities and outpatient cardiology clinics, part of the Hypertension, infarction and stroke prevention association (HISPA).

All subjects involved in the study went through clinical examination, anthropometry and blood pressure measurements, electrocardiography, and laboratory tests, which included parameters of metabolic control and diabetic status.

The body mass index (BMI) was calculated as body weight (in kilograms) divided by height (in meters squared), while systolic and diastolic blood pressure (SBP/DBP) values were measured in the sitting position. Waist size was measured too in all patients.

Patients were evaluated for nonmodifiable risk factors, which included age and sex, and modifiable, such as hypertension, dyslipidemia, diabetes, obesity, physical activity and smoking. Differences in some epidemiological aspects were also considered: marital status, alcohol consumption, exposure to stress.

STATISTICAL ANALYSIS

All statistical analyses were performed by SPSS for Windows (SPSS version 20.0, Inc., Chicago, IL, USA). All statistical tests were two-tailed, in which a p-value of <0.05 was considered significant.

Continuous data are presented as mean ± standard deviation when normally distributed (as assessed by the Kolmogorov–Smirnov test) and as a median when non-normally distributed. Categorical data are presented as frequencies and percentages.

The data were compared between groups by an unpaired t-test for continuous variables. Categorical variables were compared by nonparametric tests.

RESULTS

The study population consisted of 403 patients, mean age 64.7 ± 9.8 years; 258 (64%) men and 145 (36%) women.

The general characteristics of the study groups are presented in Table 1.

Patients with history of IS were significantly older than AMI patients. Diastolic office blood pressure (DBP)

**Table 1** General characteristics of patients

	Groups		p
	AMI (n=289)	IS (n=114)	
Age (years)	64.0 ± 9.9	66.3 ± 9.3	0.028
Sex, male/female (%male)	199/90 (68.9%)	59/55 (51.8%)	0.001
SBP (mmHg)	139.2 ± 19.9	142.7 ± 22.6	0.127
DBP (mmHg)	83.6 ± 10.4	87.1 ± 10.2	0.003
Heart rate (bit/min)	69.4 ± 9.9	71.3 ± 13.2	0.231
Sokolow-Lyon index in ECG	14.7 ± 6.5	19.2 ± 9.1	0.047
BMI (kg/m ²)	29.0 ± 4.1	28.1 ± 5.0	0.103
Waist size (cm)	100.2 ± 11.7	100.7 ± 14.1	0.791

Results are shown as a mean ± standard deviation, SBP-systolic blood pressure, DBP-diastolic blood pressure, BMI-body mass index, ECG – electrocardiography, (*) significant at the 0.05 level, (*) at the level 0.01

Table 2 Modifiable risk faktors and epidemiological aspects

	Groups		p
	AMI (n=289)	IS (n=114)	
Hypertension, n (%)	270 (93.4%)	106 (93.0%)	0.513
Diabetes, n (%)	77 (26.6%)	29 (25.4%)	0.455
dyslipidemia			
Dyslipidemia, n (%)	217 (75.1%)	73 (64.0%)	0.019
Smoking, n (%)	162 (56.1%)	50 (43.9%)	0.018
Family history, n (%)	238 (82.4%)	98 (86.0%)	0.235
Alcohol consumption, n (%)	20 (6.9%)	7 (6.1%)	0.487
Exposure to stress, n (%)	168 (58.1%)	67 (58.8%)	0.499
Marital status, married n (%)	252 (87%)	88 (77%)	0,037

(*) significant at the 0.05 level, (*) at the level 0.01

was found to be significantly higher in IS patients, and Sokolow-Lyon index in ECG, as a index of left ventricular hypertrophy, also was found to be significantly higher in the same group of patients. There were no significant differences between groups in the estimated body mass index and waist size.

Patients with AMI were more frequently male, while gender distribution in IS group were found to be almost equal.

Table 2 displays comparison of well established modifiable risk faktors and some epidemiological aspects between the groups.

Patients in AMI group were more frequently married, smokers and with higher incidence of dyslipidemia compared to SI group. Incidence of arterial hypertension, diabetes, family history, alcohol consumption and exposure to stress was similar in both groups.

A significant difference in physical activity, which was graded in five levels, was not found ($X^2 = 3.028$, $p = 0.082$).

Table 2 displays general characteristics of patients and nonmodifiable and modifiable cardiovascular risk faktors adjusted by gender.

Men who suffered from AMI were significantly older, more frequent smokers and alcohol users, while men who suffered from IS had higher values of diastolic blood pressure and also were more alcohol users compared to women.

DISCUSSION

Overall, results indicates substantial similarities of modifiable risk faktors with coronary heart disease (CHD) and stroke.

Table 3 General characteristic and cardiovascular risk factors adjusted by gender

	AMI			IS		
	male	female	p	male	female	p
Age (years)	63±9.87	66±9.47	0.004	65±11.1	67±6.7	0.262
SBP (mmHg)	138±18.9	141±21.9	0.329	146±22.5	140±22.4	0.156
DBP (mmHg)	84±9.7	83±11.9	0.396	89±10.9	85±9.0	0.014
Heart rate (bit/min)	70±10.9	68±7.4	0.245	71±8.7	72±16.8	0.778
Sokolow-Lyon index	14.9±6.8	14.3±6.2	0.812	16±8.4	21±9.4	0.296
BMI (kg/m ²)	29±3.7	29±4.8	0.456	29±4.2	28±5.7	0.264
Waist size (cm)	102±11.2	96±11.6	<0.001	106±13.6	96±13.2	0.007
Hypertension, n (%)	184(92.5)	86(95.6)	0.239	54(91.5)	52(94.5)	0.398
Diabetes, n (%) dyslipidemia	51(25.6)	26(28.9)	0.329	15(25.4)	14(25.5)	0.583
Dyslipidemia, n (%)	151(75.9)	66(73.3)	0.373	35(59.3)	38(69.1)	0.187
Smoking, n (%)	123(61.8)	39(43.3)	0.003	30(50.8)	20(36.4)	0.085
Family history, n (%)	165(82.9)	73(81.1)	0.413	52(88.1)	46(83.6)	0.337
Alcohol consum., n (%)	20(10.1)	0	<0.001	7(11.9)	0	0.008
Stress, n (%)	117(58.8)	51(56.7)	0.416	31(52.5)	36(65.5)	0.113
Married n (%)	180(90.5)	72(80.0)	0.013	47(79.7)	41(74.5)	0.334

Results are shown as a mean ± standard deviation, SBP-systolic blood pressure, DBP-diastolic blood pressure, BMI-body mass index, (*) significant at the 0.05 level, (*) at the level 0.01



MODIFIABLE RISK FACTORS AND EPIDEMIOLOGICAL ASPECTS

Previous investigations have found that hypertension has a generally stronger association with risk of stroke versus CHD, whereas cholesterol has a generally stronger influence on risk of CHD [19, 20].

Hypertension is a main risk factor not only for hemorrhagic stroke but also for IS [21]. According to data from the Sagrat Cor of Barcelona Stroke Registry (2704 patients with ischemic stroke), hypertension was the main risk factor in the different age groups [7].

In a study conducted by Ihle-Hansen et al [23] 60% of patients with stroke (126/210) had hypertension, while in a study conducted by Putaala et al. [24] 39% of patients (389/990) had hypertension.

In our study incidence of hypertension in group of IS patients was significantly higher in comparison to previous investigations, even 93% of patients with IS had hypertension (106/114). Incidence of hypertension was similar in both our study groups, but value of diastolic blood pressure was significantly higher in IS group. Men who suffered from IS in our study had higher values of diastolic blood pressure and also were more alcohol users compared to women.

Dyslipidemia is a major risk factor for atherosclerosis and atherosclerotic based diseases [25]. Serum cholesterol has generally strong influence on risk of CHD [19], and is positively related to coronary heart disease morbidity and mortality [26].

In our study dyslipidemia was significantly frequent in group of AMI patients compared to patients who suffered from IS.

Diabetes mellitus is well-established risk factor for cardiovascular disease, but also an independent risk factor of ischemic stroke of atherothrombotic cause [27]. Dyslipidemia, hypertension and obesity are atherogenic risk factors frequently found in type 2 diabetes patients [28, 29]. The combination of hypercholesterolemia and hypertension increases the frequency of vascular complications in patients with diabetes.

Incidence of diabetes in our study was equal in both groups. Abdominal obesity is defined by a waist circumference > 102 cm in men and 88 in women [41]. Unfortunately a lot of our patients were overweight and obese. This is an important finding due to the fact that weight and abdominal fat reduction is associated with a lowering in blood pressure, and may thereby reduce the risk of stroke,

A great deal of evidence over the last few decades has confirmed that cigarette smoking is an independent predictor of cerebrovascular disease in both gender. Smokers have a significantly higher risk of ischemic stroke compared to non-smokers. Finally, there is an indication that passive cigarette smoker have highest risk of stroke. It is known that smoking increases the risk of atherosclerosis, also causing thrombosis in narrow arterial vessels. Smoking have contrabutin in the onset of endothelial dysfunction,

increase in blood viscosity, and platelet aggregation [30-32].

Patients who suffered from AMI in our study were more frequently smokers compared to IS group, predominantly men who were significantly older, more frequently smokers and alcohol users compared to women.

Physical activity reduces the risk of cardiovascular disease, premature death and stroke [33].

Based on data from a large population-based case-control study conducted in Stockholm, Sweden, 1992-1994 investigators concluded that aerobic physical activity such as exercise or walking at work seemed to reduce the risk of myocardial infarction, whereas anaerobic activity such as heavy lifting at work were related to increased risk of myocardial infarction.

According to data collected from 23 corresponding studies, there is strong evidence that subjects with high physical activity as compared to those with low physical activity had a lower stroke risk [34].

A significant difference in physical activity, which was graded in five levels, was not found between groups in our study.

The evidence from previous studies suggest that stressful life events, specially acute psychological stress factors contribute independently to the risk of coronary heart disease [35, 36] and have been shown to be independent predictive factors of CHD [37].

Stress may be a trigger for neuroendocrine and platelet activation and directly affect CHD, or may cause adverse health behaviors such as smoking, poor diet, and sedentary lifestyle, which increases the risk of CHD [38].

In our study stress exposure were significant, almost equal in both groups, 58.1% in AMI and 58,8% in IS group.

In the study conducted by Tulio et al. [39], left ventricular hypertrophy and abnormal left geometry were independently associated with increased stroke risk. Left ventricular hypertrophy is strongly associated with ischemic stroke in all age, sex, and race-ethnic subgroups.

In our study left ventricular hypertrophy was estimated with Sokolow-Lyon index by electrocardiography, as an index of left ventricular hypertrophy which was significantly higher in IS group.

NONMODIFIABLE RISK FACTORS

Incidence of coronary heart disease in male is well recognised. Cardiovascular disease develops 7 to 10 years later in women than in men [39].

In accordance with previous studies, in our study patients in AMI group were more frequently male and significantly younger compared to female.

The coronary heart disease event rate in women is low and predominantly attributed to smoking before menopause, Smoking increases the risk of a first acute myocardial infarction more pronounced in females compared to male [42].



However, in our study male were more frequent smokers compared to female.

The incidence of stroke increases significantly with age, and is higher in men up to age 75, similar in the 75-84 age group, and higher in women in the age group greater than 85 [43].

Despite the higher risk in men, the lifetime risk of stroke is higher in women. The Framingham study calculated lifetime risk of stroke among middle age men and women and found that the lifetime risk in women age 55 was 21% and in men age 55, 17% [44].

In our study IS patients were significantly older compared to AMI group, but without significant difference in age between men and women in IS group. Men who suffered from IS had higher values of diastolic blood pressure and were more alcohol users compared to women.

Hypertension associated with age represents leading risk factors for cerebrovascular disease and also multiply the risk for stroke [45, 46].

CONCLUSION

Both entities share similar pathophysiological mechanisms and, consequently, main traditional risk factors. However, the majority of cardiovascular risk factors show no important differences between the groups. Incidence of myocardial infarction increases with male sex, dyslipidemia, smoking and marital status, while incidence of ischemic stroke increases with age, higher diastolic blood pressure and also with ECG signs of left ventricular hypertrophy.

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