

Prevalence of risk factors, population-attributable fraction and risk of stroke among Kaunas middle-aged population

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The aim of the study was to assess the prevalence of risk factors, population-attributable risk fraction and prognosis of multiple risk factors for the risk of death from stroke among middle-aged Kaunas population during 1983–2003.

Patients and methods. The random samples of men and women aged 35–64 years were examined in MONICA-1, 2, 3 (n = 5437). The risk factors were assessed by the standard epidemiological questionnaire. New cases of deaths from stroke were registered from the beginning of every survey until December 31, 2003. During the follow-up period 85 deaths occurred: 45 in men and 43 in women. The Cox proportional hazards model was used to estimate the relative risks for death from stroke. The prevalence of arterial hypertension, physical inactivity, obesity, ischemic changes on electrocardiogram was higher among men who died of stroke as compared to men examined in the MONICA-1 survey.

Results. The highest population attributable fraction of stroke was for arterial hypertension (59.1%) among men and for obesity (55.1%) among women. The risk of death from stroke among men was 2.3-fold higher with arterial hypertension, 4.9-fold with previous stroke, 2.3-fold with ischemic changes on electrocardiogram and 1.9-fold with physical inactivity. Arterial hypertension and impaired fasting glycaemia displayed the risk of death from stroke for women. Arterial hypertension and obesity were showed the highest prevalence among men and women who died from stroke. Arterial hypertension among men and obesity among women showed the greatest population-attributable fraction.

Conclusion. Arterial hypertension, previous stroke, ischemic changes on electrocardiogram and physical inactivity approved the risk for stroke among men; arterial hypertension and impaired fasting glycaemia were independently associated with the risk for stroke among women. The highest population-attributable fractions among middle-aged men were arterial hypertension, physical inactivity and obesity, and among women obesity, arterial hypertension and coronary heart disease.

Key words: stroke, risk factors, population-attributable fraction

INTRODUCTION

Recent statistics on cerebrovascular mortality has shown declining rates since at least the 1980 in most countries in Western Europe and in Lithuania, though not so greatly. Mortality rates from cerebrovascular diseases in 1993 among 25–64-aged males of Finland comprised 35.4 and of Lithuania 78.1 per 100,000, the numbers for females being 20.4 and 38.9 (1). Ten years later, in 2003, the numbers among males in Finland and in

Lithuania indicated 23.7 and 58.7 and among females 11.9 and 28.4, respectively. Stroke is the third most common cause of death in developed countries, exceeded only by coronary heart disease and cancer (2). Worldwide, 3 million women and 2.5 million men die from stroke every year. Inequalities in mortality rates can be attributed partly to the differences in the levels of risk factors – blood pressure, smoking status, serum cholesterol and relative body weight. Certain racial, ethnic and socioeconomic groups are also at a greater risk of stroke. The most modifiable causes of stroke are high blood pressure, smoking, hypercholesterolemia, lack of physical exercise, unhealthy diet, alcohol consumption, high salt intake, previous or underlying heart disease,

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diabetes; nonmodifiable risk factors have been associated with age, gender, heredity, race or ethnicity (3). The relative importance of risk factors can be estimated using the population attributable fraction.

The objective of the study was to compare the prevalence of risk factors among persons who died of stroke using the data from the first examination, to identify factors with the greatest population attributable fraction, and to estimate the differences in the risk of death from stroke among middle-aged men and women.

MATERIALS AND METHODS

The World Health Organization Monitoring Trends and Determinants in Cardiovascular Disease as the WHO MONICA Project was carried out in Kaunas in 1983–1992, three random samples of subjects aged 35–64 were selected. The samples were stratified by age and sex. Three population-based surveys of 2,444 (1,162 men and 1,282 women), 1,762 (894 men and 868 women) and 1,231 (610 men and 621 women) patients were carried out in 1983–1984 (MONICA-1), 1986–1987 (MONICA-2) and 1992–1993 (MONICA-3). Response rate in the first survey was 70.2%, in the second 69.6% and in the third 58.6%. The WHO criteria were used to determine risk factors (4). Every survey included examination by standard questionnaires and physical measurements. The standard questionnaire on smoking included questions about smoking behavior (regular smoker, ex-smoker, never smoker, occasional smoker, and number of cigarettes smoked per day). Subjects who smoked at least one cigarette per day were considered to be regular smokers. Physically inactive persons were identified as the mean time (divided by two) at leisure in winter and in summer spent on walking, moderate and hard work, gardening and other physical activities less than 10 hours a week. Heavy drinkers used alcohol two or more times per week or every day. Arterial hypertension (AH) was assessed as systolic blood pressure 140 mm Hg or more and / or diastolic blood pressure 90 mm Hg or more, or normal blood pressure if the person had taken antihypertensive drugs within the last two weeks. The body mass index (BMI) – body weight (kg) divided by height squared (m^2) – was used to determine and classify body weight (obesity – $BMI \geq 30.0 \text{ kg}/m^2$). Serum cholesterol concentration was measured from a venous blood sample and determined by the enzymatic method (5). Serum total cholesterol level $\geq 5.0 \text{ mmol}/l$ was classified as hypercholesterolemia. Fasting plasma glucose values were classified as normal at $\leq 6.0 \text{ mmol}/l$, impaired fasting glycaemia from 6.1 to 6.9 mmol/l and diabetes $\geq 7.0 \text{ mmol}/l$ (6). In every survey, resting 12-lead electrocardiogram (ECG) was performed and evaluated by the Minnesota Code (MC) independently by two coders (7). By means of standard G. Rose questionnaire and ECG coding using MC, the following coronary heart disease (CHD) forms were diagnosed: 1. Previous myocardial

infarction (MI) (MC 1–1, 1–2 and documented MI). 2. Angina pectoris. 3. Ischemic ECG changes : MC 1–3, 4–1, 2, 3, 5–1, 2, 3, 6–1, 2, 7–1, 8–3.

The difference between the parameters compared was considered significant when greater than 1.95 ($p < 0.05$). The estimates of hazards ratio (HR) and 95% confidence intervals (CI) were based on the multivariate Cox proportional hazards model (8). The mean follow-up was 15.0 years for men and 16.2 years for women. Population-attributable fraction (PAF) was calculated by dividing the population-attributable risk by the incidence rate of the disease in the total population and multiplying by 100 (9, 10). Age-adjusted prevalence of risk factors was standardized by the direct method with the European population as a standard (11). Deaths from stroke were defined according to the International Classification of Diseases (ICD)-9, codes 430–438, and ICD-10, codes I60–I69.

RESULTS

In 1983–1993, among the 2,662 middle-aged men and 2,771 women surveyed, initially 88 deaths from stroke occurred, of them 45 among men and 43 among women. The prevalence of variables among those who died from stroke and the initially surveyed middle-aged men and women in MONICA-1, 2, 3 were analyzed. The prevalence of physical inactivity, previous MI, frequent alcohol consumption, hyperglycemia, atrial fibrillation among men was higher in MONICA-1 as compared to MONICA-3 (Table 1). The prevalence of arterial hypertension, physical inactivity, obesity and ischemic ECG changes among dead men from stroke have been observed higher as compared to initially surveyed men in MONICA-1. The prevalence of obesity, arterial hypertension, CHD, physical inactivity and hypercholesterolemia was assessed higher among women in MONICA-1 as compared to women examined in MONICA-3 (Table 2). The prevalence of obesity, CHD, hyperglycemia and ischemic ECG changes among dead women from stroke was higher as compared to initially surveyed women in MONICA-1.

The greatest population-attributable fraction of stroke among men was 59.1% for AH, 35.3% for physical inactivity, 30.1% for obesity. No association was found for hypercholesterolemia, hyperglycemia and atrial fibrillation. Obesity (55.1%), AH (53.8%), CHD (25.0%) were important population-attributable fractions of stroke among women. Smoking and frequent alcohol consumption didn't demonstrate any significance for stroke among women.

The age-adjusted multivariate hazard ratios (HR) and 95% confidence intervals (CI) of various factors were calculated using the Cox proportional hazards regression model. At the time of initial survey, from all variables included into the Cox model, only AH and physical inactivity were associated with the risk of death from stroke among middle-aged men and women (Table

Table 1. The prevalence of variables among dead from stroke and initially surveyed middle-aged men in MONICA-1, 2, 3 and population-attributable fraction (PAF)

Variables	Dead from stroke (%) n = 45	PAF (%)	Prevalence (%) ¹		
			MONICA-1 n = 1162	MONICA-2 n = 894	MONICA-3 n = 610
Arterial hypertension	76.4 ^{°°°}	59.1	54.2	48.6*	55.0
Physical inactivity	70.6 [°]	35.3	53.9	59.9**	32.9***
Obesity	43.3 ^{°°}	30.1	22.3	24.8	19.8
Coronary heart disease	20.4	13.8	10.2	11.7	12.0
Ischemic ECG changes	18.5 [°]	13.2	5.3	4.7	6.0
Smoking	33.3	9.6	38.3	37.1	34.0
Previous stroke	5.8	8.0	1.5	0.5*	0.9
Previous MI	3.8	6.6	2.2	3.3	4.1*
Frequent alcohol consumption	17.6	4.7	16.3	7.4***	8.4***
Hypercholesterolemia	74.4	0	82.3	82.9	79.4
Hyperglycemia	6.5	0	4.9	10.3**	28.3***
Atrial fibrillation	0	0	0.1	0.5	1.8*

ECG – electrocardiogram, MI – myocardial infarction.

* p < 0.05, ** p < 0.01, *** p < 0.001 as compared with MONICA-1

[°] p < 0.05, ^{°°} p < 0.01, ^{°°°} p < 0.001 as compared with MONICA-1

¹ – standardized by age

Table 2. The prevalence of variables among dead from stroke and initially surveyed middle-aged women in MONICA-1, 2, 3 and population-attributable fraction (PAF)

Variables	Dead from stroke (%) n = 45	PAF (%)	Prevalence (%) ¹		
			MONICA-1 n = 1162	MONICA-2 n = 894	MONICA-3 n = 610
Obesity	61.7 [°]	55.1	45.4	44.6	33.1***
Arterial hypertension	62.4	53.8	51.3	44.7**	43.2***
Coronary heart disease	35.3 [°]	25.0	16.9	16.8	13.4*
Hyperglycemia	32.8 ^{°°°}	23.3	5.0	6.7	15.0***
Physical inactivity	41.8	20.4	47.1	52.1*	26.9***
Ischemic ECG changes	28.5 [°]	18.3	10.9	10.9	8.7
Hypercholesterolemia	87.5	9.0	86.1	87.9	82.2*
Atrial fibrillation	6.9	6.7	0.7	0.2	0.5
Previous stroke	2.8	6.4	0.4	0.8	1.1
Previous MI	4.9	3.5	1.1	2.0	1.2
Smoking	2.3	0	4.1	3.8	4.2
Frequent alcohol consumption	0	0	0.9	0.5	0.7

ECG – electrocardiogram, MI – myocardial infarction.

* p < 0.05, ** p < 0.01, *** p < 0.001 as compared with MONICA-1

[°] p < 0.05, ^{°°} p < 0.01, ^{°°°} p < 0.001 as compared with MONICA-1

¹ – standardized by age

3). The risk of death from stroke among men with AH was higher than among men without AH (HR 2.3, 95% CI 1.28–4.23). The risk of death from stroke among physically inactive men was 1.9-fold higher than among physically active men. The risk of death from stroke among men with ischemic ECG changes and previous MI was 2.3-fold and 4.9-fold higher than among men without ischemic ECG changes and previous MI. At the same time the evaluation of the risk of death from stroke among women revealed only two risk factors –

AH (HR 2.9, 95% CI 1.20–7.27) and impaired fasting glycemia (HR 3.3, 95% CI 1.10–10.26).

DISCUSSION

Detection of risk factors for stroke and strategies for reducing the prevalence of risk factors continue to be relevant in most studies of cerebrovascular disease (12). Major risk factors for stroke include high blood pressure, physical inactivity, smoking, hyperglycemia, hy-

Table 3. Prognostic value of different variables for the death from stroke in middle-aged population (multivariate analysis)

Variables	The risk for death from stroke in men and women		The risk for death from stroke in men		The risk for death from stroke in women	
	HR*	95 % CI*	HR	95% CI	HR	95% CI 95
Age	1.101	1.058–1.146	1.092	1.048–1.139	1.088	1.022–1.158
Gender	0.571	0.316–1.031				
Arterial hypertension						
³ 160/95 mm Hg	2.438					
	1.373–4.329	1.285–4.235	2.965	1.209–7.271		
Glucose concentration, mmol/l						
£6.0 mmol/l	1.0					
6.1–6.9 mmol/l	0.874	0.338–2.2264			3.363	1.102–10.262
³ 7.0 mmol/l	1.447	0.437–4.791				
Body mass index, kg/m ²	1.028	0.969–1.091			1.040	0.965–1.121
Physical activity	2.070	1.148–3.733	1.949	1.021–3.723		
Coronary heart disease					1.022	0.216–4.843
Ischemic ECG changes	1.754	0.537–5.730	2.334	1.069–5.096	1.362	0.239–7.768
Previous MI	2.784	0.639–12.138	4.925	1.737–13.963	4.294	0.514–35.903

Continuous variables and their measuring units in the model: age, 1 yr; body mass index – 1 kg/m². Categorical variables: gender – 1. Men, 2. Women, arterial hypertension – 1. Yes, 2. No; physical activity – 1. Sufficient, 2. Insufficient, ischemic heart disease – 1. Yes, 2. No; previous stroke – 1. Yes, 2. No; ischemic ECG changes – 1. Yes, 2. No. HR – hazard ratio; CI – confidence interval.

percholesterolemia. In our study, the prevalence of AH among men who died from stroke was higher as compared with initially surveyed men. The risk for death from stroke in men was assessed 2.3-fold and in women 3.0-fold greater as compared to men and to women with normal blood pressure. It has been widely demonstrated that elevated blood pressure is firmly established as a risk factor for death from stroke (13, 14). Both elevated systolic and diastolic blood pressure was positively associated with the risk of mortality from stroke. However, the relative influence of systolic and diastolic blood pressure on mortality from stroke varied. The risk of stroke is almost twice as high in men and women in Novosibirsk than in northern Sweden. The risk of stroke is associated with increased systolic blood pressure, independently of the level of diastolic blood pressure (15, 16).

In the present study, there was no relationship between cholesterol and risk of stroke in men and women. High plasma levels of lipids are an important modifiable risk factor for CHD, but they are not confirmed as a risk factor for stroke. Many studies have found no relationship between cholesterol and overall stroke, but this could mask the positive relation of cholesterol with ischemic stroke and the negative association with hemorrhagic stroke. Low cholesterol and lower triglyceride concentrations predict a higher mortality after stroke (17–19).

In the present study, glucose concentration 6.1–6.9 mmol/l was found to be positively related to the death from stroke in women but not in men. The Framingham Study observed a two-fold higher risk of mortality from

stroke among diabetic patients, although a study in California didn't prove it (20, 21). It has been shown that hyperglycemia directly increases regional brain damage as a result of acute vascular insufficiency. The association between the risk of death from stroke and smoking in men and women was not determined in this study. In contrast, a statistical overview of 32 epidemiological studies provided information on a relationship between cigarette smoking and the occurrence of stroke; the relative risk of death from stroke increases with the number of smoked cigarettes (22, 23).

The prevalence of physical inactivity among men was higher as compared to initially surveyed men in MONICA-1, and the risk of death from stroke was assessed as 1.9-fold higher. Evidence from longitudinal studies demonstrated that physical activity was inversely related to the risk of ischemic stroke, but multivariate analyses showed no significant association between exercise and a decreased risk of stroke in women (12, 24). Alcohol consumption has been reported to have both beneficial and harmful effects on the incidence of stroke (25, 26). The beneficial effect on mortality from stroke has been demonstrated when consumption of 1–20 g ethanol daily protects against the risk of mortality from stroke, but consumption of ethanol exceeding of 300 g/week increases the risk of brain infarction, particularly among young and middle-aged people.

The present study proved a relationship between ischemic ECG changes and the risk of death from stroke among men, but not among women. Men with ischemic ECG changes had a 2.3-fold higher age-adjusted relative risk of death from stroke than did those without

such abnormalities. Our results are in accordance with data of T. Ohira et al. (27) who found that men had a 2.3-fold higher risk of ischemic and hemorrhagic stroke, but among women there was no relation between minor ST-T abnormalities and stroke incidence. The most important predictors for death from stroke were indicated as ischemia-like ECG changes, long Q, arrhythmia, abnormal U wave, S-T segment changes (28, 29). Men in this study with previous MI had a 4.9-fold higher risk of death from stroke as compared with men without previous MI. Cardiac diseases, as CHD, atrial fibrillation, previous MI are the dominant cardiac sources of ischemic strokes (12, 30). The most common reason for cerebral embolism is nonrheumatic atrial fibrillation. Our data have not been able to confirm this conception, because the prevalence of atrial fibrillation among the initially surveyed population was very low.

The relative importance of risk factors can be estimated using the population-attributable risk fraction, which is the theoretical proportion of disease "caused" by the risk factor. Our data have demonstrated that AH, physical inactivity and obesity among men and obesity, AH and CHD among women are the most important risk factors to be diminished in stroke prevention.

CONCLUSIONS

The prevalence of the main risk factors among middle-aged men who died from stroke, as compared with those initially surveyed were arterial hypertension, physical inactivity, obesity, ischemic electrocardiographic changes, and among women these were obesity, arterial hypertension, coronary heart disease, hyperglycemia and ischemic electrocardiographic changes. The risk for death from stroke among men was the history of myocardial infarction, ischemic electrocardiographic changes, arterial hypertension and physical inactivity; among women these were impaired fasting glycemia and arterial hypertension. The highest population-attributable fraction was found to be arterial hypertension, physical inactivity and obesity among middle-aged men, and obesity, arterial hypertension and coronary heart disease among women.

Received 4 April 2005

Accepted

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RIZIKOS VEIKSNIŲ PAPLITIMAS, ETIOLOGINĖ POPULIACIJOS FRAKCIJA IR MIRTIES NUO GALVOS SMEGENŲ INSULTO PROGNOZĖ TARP VIDUTINIO AMŽIAUS KAUNO GYVENTOJŲ

Santrauka

Tikslas. Nustatyti rizikos veiksnių paplitimą, etiologinę populiacijos frakciją bei riziką numirti nuo galvos smegenų insulto tarp vidutinio amžiaus Kauno gyventojų remiantis 1983–2003 m. tyrimo duomenimis.

Pacientai ir metodai. Vykdam programą MONICA, atsitiktiniu principu patikrinti trijų skirtingų imčių 35–64 metų gyventojų sveikata: MONICA 1, 2, 3 (N = 5437). Visi tiriamieji buvo apklausiami pagal standartinę epidemiologinę klausimyną. Mirtys nuo galvos smegenų insulto buvo registruojamos kiekvienam nuo sveikatos patikrinimo datos iki 2003 m. gruodžio 31 d. Mirtis nuo galvos smegenų insulto buvo vertinama pagal Tarptautinės statistinės ligų ir sveikatos problemų klasifikacijos 9 peržiūros 430–438 ir 10 peržiūros I60–I69 kodus.

Rezultatai. Per stebėjimo laikotarpį nuo galvos smegenų insulto 88 žmonės mirė. Rizika numirti nuo galvos smegenų insulto buvo vertinta pagal Cox'o modelį. Vyrams, mirusiems nuo galvos smegenų insulto, dažniau nustatyta arterinė hipertenzija, nutukimas, išeminiai pokyčiai elektrokardiogramoje, nepakankamas fizinis aktyvumas; moterims – nutukimas, išeminės širdies ligos, hiperglikemija, išeminiai pokyčiai elektrokardiogramoje yra dažnesni lyginant su pirminio patikrinimo duomenimis. Didžiausią etiologinę populiacijos frakciją tarp vyrų sudarė arterinė hipertenzija – 59,1% tarp moterų – nutukimas – 55,1%. **Išvados.** Daugiaveiksnių regresinės analizės duomenimis, arterinė hipertenzija ir išeminiai pokyčiai elektrokardiogramoje vyrų riziką numirti nuo galvos smegenų insulto didino 2,3, nepakankamas fizinis aktyvumas – 1,9 ir persirgęs miokardo infarktas – 4,9 karto. Moterims reikšmingiausia arterinė hipertenzija ir hiperglikemija.

Raktažodžiai: galvos smegenų insultas, rizikos veiksniai, etiologinė populiacijos frakcija