Association of major cardiovascular risk factors with the development of acute coronary syndrome in Lithuania

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KEYWORDS

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Cardiovascular (CV) disease remains the leading cause of death in Lithuania. Timely recognition of CV risk factors and intervention to reduce these risk factors is of absolute importance to prevent coronary heart disease and reduce its burden on society. This study aimed to compare the prevalence of major CV risk factors in general population and acute coronary syndrome (ACS) patients and to determine their association with the development of ACS. Five hundred and twenty-three ACS patients and 645 age- and gender-matched control subjects were enrolled in the study. Smoking, dyslipidaemia, diabetes, and hypertension, but not overweight or obesity, were significantly more prevalent in the ACS patients, compared with control group. The prevalence of smoking, overweight or obesity, and dyslipidaemia were significantly higher in younger patients. Hypertension was highly prevalent in all age subgroups. More than a half of all patients aged <45 years had three or four CV risk factors. Smoking [odds ratio (OR), 7.03, $P < 0.0001$], hypertension (OR, 1.82; $P = 0.001$), dyslipidaemia (OR, 1.99; $P < 0.0001$), and diabetes (OR, 2.30; $P < 0.001$) were significantly associated with ACS. Significant association of traditional CV risk factors, such as smoking, dyslipidaemia, hypertension, and diabetes with ACS, and high prevalence of these risk factors, especially in younger individuals, calls for attention, and implementation of prevention programmes to reduce the burden of CV morbidity and mortality in Lithuania.

Introduction

Each year cardiovascular disease (CVD) causes over 4 million deaths in Europe and over 1.9 million deaths in the European Union (EU).[1] Death rates from CVD are generally higher in Central and Eastern Europe than in Northern, Southern and Western Europe.[1–3] CVD remains the leading cause of death in Lithuania.

A substantial number of CV risk factors have been recognized to date. The main modifiable CV risk factors, such as hypertension, dyslipidaemia, and smoking, are included into CV risk charts, their targets are set in the national and international guidelines. According to the World Health Organization, in terms of attributable deaths, the leading CVD risk factor is raised blood pressure (to which 13% of global deaths is attributed), followed by tobacco use (9%), raised blood glucose (6%), physical inactivity (6%), and overweight and obesity (5%).[4]

Timely recognition of risk factors and intervention to reduce these risk factors is of utter importance to prevent coronary heart disease and reduce its burden on society. In order to implement prevention measures effectively, analyses of the prevalence of CV risk factors in general population and acute coronary syndrome (ACS)

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patients are required. To date, several epidemiological studies have assessed the prevalence of main CV risk factors in Lithuania. We aimed to compare the prevalence of major CV risk factors in both ACS patients and control group and to determine their association with ACS.

Methods

Five hundred and twenty-three Caucasian patients with ACS were enrolled in the study. All of them were admitted to the Cardiology Department of the Lithuanian University of Health Sciences Hospital from 2007 until 2011.

Written informed consent was obtained from all of the patients, and the study protocol was approved by the ethics committee of the hospital.

Acute myocardial infarction (AMI) and unstable angina were defined according to the standard criteria based on clinical symptoms, electrocardiograph findings, and cardiac enzyme abnormalities.[5] Family history, CV risk factors, and current treatment were obtained from each patient using a standard questionnaire. Hypertension was defined as the presence of elevated systolic ($\geq$140 mmHg) and/or diastolic ($\geq$90 mmHg) blood pressure or current use of antihypertensive drugs. A patient was considered a smoker if he was a current smoker or was a smoker in the past. Diabetes mellitus was identified when dietary treatment and/or medical therapy was required to control blood glucose levels. Hypercholesterolaemia was defined as a total serum cholesterol level of 5.2 mmol/L or more and low density cholesterol >2.6 mmol/L, and/or triglycerides equal to or more than 1.7 mmol/L, or use of statin medication. Overweight or obesity was defined as body mass index (BMI) equal to or higher than 25 kg/m². Patients were excluded from the study if they had stable angina, or previous MI, severe underlying organic or mental illness, or refused to participate in the study.

Control group involved 645 age- and gender-matched subjects free from CVD. Control group was selected from a random sample of the Lithuanian population screened within the international HAPPIE (Health, Alcohol, and Psychosocial factors In Eastern Europe) project, CINDI (Countrywide Integrated Non-communicable Disease Intervention) project and 'Kaunas Healthy Ageing Study'.

Statistical analysis

Statistical analysis was carried out using STATA/IC 11.0 (College Station, TX). Normally distributed continuous variables were expressed as mean $\pm$ standard deviation (SD). Continuous variables were assessed using the unpaired Student's t test. Categorical variables were presented as absolute numbers and percentages, and were compared using the χ^2 test. Variables with statistical significance at univariate analysis were further analysed at multivariate analysis. A P-value of <0.05 was considered statistically significant.

Results

Data of 523 ACS patients and 645 control subjects were analysed. Smoking ($P < 0.0001$), dyslipidaemia ($P < 0.0001$), diabetes ($P = 0.002$), and hypertension ($P < 0.0001$) were significantly more prevalent in the ACS patients, compared with control group (*Table 1*). All four CV risk factors (smoking, hypertension, dyslipidaemia, and overweight or obesity) were present in almost one-third (28.9%) of ACS patients.

Analysis in age subgroups demonstrated significantly higher prevalence of smoking (92.5% vs. 36.9% in $\leq$45 years and $\geq$75 years age subgroups; $P < 0.0001$, respectively), obesity (83.3% vs. 74.3%; $P = 0.003$), and dyslipidaemia (85.7% vs. 67.1%; $P = 0.015$) in younger patients. No differences were found in the prevalence of diabetes and hypertension between the groups. Hypertension was highly prevalent in all age categories. More than a half of all patients aged <45 years had four or three CV risk factors (*Table 2*).

Univariate and multivariate logistic regression analyses were performed to evaluate association of traditional CV risk factors with the development of ACS. In age- and gender-adjusted analyses smoking increased the odds for ACS more than 7 times (OR 7.03; $P < 0.0001$) (*Table 3*). Analyses by gender demonstrated that this association was stronger in women, compared with men (OR 10.35 vs. 6.71, respectively) (*Table 4*).

Presence of hypertension significantly increased ACS risk (OR, 1.82, $P = 0.001$), and although this association did not reach statistical significance in men (OR, 1.3, $P = 0.195$), it was strong in women (OR, 5.42, $P < 0.0001$). On the contrary, dyslipidaemia and diabetes were significantly associated with ACS in men (OR, 2.19, $P < 0.0001$ and OR, 2.40, $P = 0.005$, respectively), compared with women (OR, 1.31, $P = 0.452$ and OR, 2.45, $P = 0.052$, respectively) (*Table 4*). Overweight or obesity was not associated with the development of ACS (OR, 1.06, $P = 0.756$).

Discussion

Our study demonstrated high prevalence of CV risk factors among patients with ACS compared with the control group. Also, differences in the association of traditional CV risk factors with ACS between the genders and age groups

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Table 1 Prevalence of major cardiovascular risk factors in ACS patients compared with control group

	ACS group ($n = 523$)	Control group ($n = 645$)	P-value
Age (SD)	60.8 (11.6)	60.6 (12.0)	0.715
Gender (male %)	72.8	70.7	0.417
Dyslipidaemia (%)	80.3	69.1	<0.0001
Diabetes (%)	11.8	6.6	0.002
Smoking (%)	59.7	30.2	<0.0001
Hypertension (%)	82.6	71.1	<0.0001
Overweight or obesity (%)	78.6	76.0	0.531

Table 2　Prevalence of cardiovascular risk factors in acute coronary syndrome patients by age categories

	Age categories				P-value
	<45 (n = 42)	45–54 (n = 125)	55–74 (n = 282)	≥75 (n = 74)	
Hypertension (%)	71.4	80.0	84.4	86.5	0.130
Gender (male %)	88.1	88.0	69.5	51.4	<0.0001
Dyslipidaemia (%)	85.7	79.2	83.3	67.1	0.015
Diabetes (%)	9.5	7.2	13.8	13.5	0.255
Smoking (%)	92.5	76.7	53.1	36.9	<0.0001
Family history (%)	45.2	46.7	40.8	37.9	0.639
Overweight or obesity (%)	83.3	89.6	74.1	74.3	0.003
Four risk factors (%)[a]	51.2	36.4	26.9	11.3	<0.0001
Three risk factors (%)[b]	57.5	41.3	35.3	18.6	<0.0001

[a]Smoking, hypertension, dyslipidaemia, and overweight or obesity.
[b]Smoking, hypertension, and dyslipidaemia.

Table 3　Association of cardiovascular risk factors with ACS in multivariate analysis

	OR[a]	95% CI	Unadjusted P-value	Age- and gender-adjusted P-value
Hypertension	1.82	1.28–2.58	<0.0001	0.001
Dyslipidaemia	1.99	1.43–2.75	<0.0001	<0.0001
Diabetes	2.39	1.46–3.93	0.003	0.001
Smoking	7.03	5.01–9.9	<0.0001	<0.0001
Overweight or obesity	1.06	0.75–1.49	0.531	0.756

OR, odds ratio; CI, confidence interval.
[a]Adjusted for age and gender.

Table 4　Association of cardiovascular risk factors with ACS by gender[a]

	Men			Women		
	OR	95% CI	P-value	OR	95% CI	P-value
Hypertension	1.30	0.87–1.94	0.195	5.42	2.31–12.73	<0.0001
Dyslipidaemia	2.19	1.51–3.17	<0.0001	1.31	0.65–2.66	0.452
Diabetes	2.40	1.31–4.39	0.005	2.45	0.99–6.07	0.052
Smoking	6.71	4.67–9.61	<0.0001	10.35	3.55–30.19	<0.0001
Overweight or obesity	1.06	0.70–1.60	0.702	0.95	0.49–1.83	0.869

OR, odds ratio; CI, confidence interval.
[a]Adjusted for age.

were found. Indeed, the contributions of the different components of the metabolic syndrome differ between genders and in different populations.[6,7] Acute coronary syndrome was associated with diabetes both in men and in women; however, hypertension increased the odds of ACS only in women, and dyslipidaemia reached statistical significance only in men. Literature suggests that low-density lipoprotein (LDL) cholesterol may be a less important risk factor in women, especially in premenopausal age, because oestrogen protects the arterial wall against LDL deposition.[8] The association of overweight or obesity with ACS was insignificant in our study. Smoking was highly prevalent in the ACS subgroup, especially in younger age subgroups, and significantly increased the risk of ACS. The association was particularly strong in women. The association of smoking with CVD was

confirmed in numerous studies.[9] Although the prevalence of smoking declined since implementation of tobacco control strategies, in Lithuania the decline was smaller, compared with other countries, and smoking remained prevalent in young individuals.[10,11]

In our study younger patients were more likely to be males, smokers, overweight or obese, and to have dyslipidaemia. More than a half of young ACS patients possessed four risk factors. The prevalence of hypertension did not differ between age categories. Several other studies have investigated the impact of age on the prevalence of CV risk factors.[12] A recent prospective multicentre study by Ahmed *et al.* found that younger patients with ACS were more often obese, smokers, and had a positive family history of coronary heart disease (CHD), whereas older patients were more likely to have diabetes mellitus,

hypertension, and dyslipidaemia. Diabetes was far more prevalent in this study compared with ours, reaching 30.9% in patients <50 years and over 45% in individuals aged >70 years.[13] A retrospective Lithuanian study in 606 coronary patients found that only 2.3% of patients aged <55 did not have any of the four CV risk factors (i.e. smoking, hypertension, diabetes, or dyslipidaemia) and 66.5% possessed at least two risk factors.[14]

We did not find any association of overweight or obesity with ACS. The 'obesity paradox' was also demonstrated by several other studies. No association was found between change in BMI and all-cause or CVD mortality in 14 345 men.[15] Uretsky et al.[16] investigated the effects of obesity on CV outcomes in 22 576 treated hypertensive patients with known CHD. During a 2-year follow-up, all-cause mortality was 30% lower in overweight and obese patients, despite less effective blood pressure control in these patients compared with the normal weight group. In another study of 800 elderly hypertensive patients, total mortality and CV and non-CV major events were highest in those with the leanest BMI quintile.[17] Recently, interesting results were published from a cohort study of 11 240 participants, followed up for 12 years, suggesting that prevention of smoking and physical inactivity, not a change in BMI would prevent 13% of deaths.[18] Some studies suggest that although obesity may be a powerful risk factor for hypertension and left ventricular hypertrophy, obese hypertensive patients may paradoxically have a better prognosis, possibly because of having lower systemic vascular resistance and plasma renin activity compared with leaner hypertensive patients.[19]

Conclusions

Significant association of major CV risk factors, such as smoking, dyslipidaemia, hypertension, and diabetes, with ACS was demonstrated, especially in younger individuals. A half of ACS population in the <45-year-age subgroup possessed all four CV risk factors. These results call for attention and implementation of prevention programmes to reduce the burden of CV morbidity and mortality in Lithuania.

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