

Prevalence of classical risk factors in Polish women with premature coronary artery disease

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Abstract

Background: It is generally believed that in 50% of perimenopausal women several factors other than classical risk factors play a significant role in the development of premature coronary artery disease (CAD).

Aim: To determine the prevalence of five classical risk factors (cigarette smoking, hypertension, diabetes, hyperlipidaemia and obesity) in women aged < 55 years with premature CAD.

Methods: We performed a single-centre, case-control study in women < 55 years with angiographically confirmed CAD or troponin-positive acute coronary syndrome. A total of 330 female patients were enrolled between April 2005 and January 2008. The control group consisted of 347 age-matched healthy women from a similar region selected from the National Health Survey WOBASZ study (Polish Multi-centre Population Health Survey) designed to assess the cardiovascular risk in the Polish adult population.

Results: Compared to age-matched healthy controls, women with premature CAD had a very high prevalence of traditional risk factors — hypercholesterolaemia (82% vs 68%), smoking (current and former) (81% vs 48%), and hypertension (68% vs 42%). Women with premature CAD had 4.3 times more often diabetes, 1.68 times smoking and 1.63 times hypertension compared to controls. At least one of five classical risk factors was present in 98.8% of patients, compared to 89% in controls, while 10% of patients vs 1.4% of controls had all five of them.

Conclusions: Classical risk factors are present in the vast majority of females with premature CAD — in 99% of them at least one CAD risk factor is present. Premature CAD is most frequently associated with smoking, hypertension and hyperlipidaemia.

Key words: premature coronary artery disease, cardiovascular risk factors, gender

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INTRODUCTION

Coronary artery disease (CAD), especially in individuals under 50, is usually regarded as a problem of men and infrequently diagnosed in women.

Cardiovascular (CV) risk in women is notoriously underestimated by both society and physicians [1, 2]. The mortality rate in women with acute coronary syndrome (ACS) younger than 50 is twice that of age-matched men [3]. During the

last ten years, a rise in CAD prevalence among younger women has been observed [4, 5]. Although the importance of classical risk factors is well established, it is commonly suggested that other factors play a significant role in the development of premature CAD in women. Emerging data suggest a unique risk profile in young women, especially those who are perimenopausal or in the early post-menopausal stage, where hypoestrogenaemia, novel risk factors or genetic cau-

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ses may also play leading role [5, 6]. However, some data suggests that conventional risk factors may play a much more significant role in atherogenesis, supporting the validation of the role played by classical risk factors [7, 8]. We therefore sought to determine the prevalence of five classical risk factors (cigarette smoking, hyperlipidaemia, hypertension, diabetes and obesity) in women with well established premature CAD.

METHODS

Study population and design

The study participants were recruited from consecutive women displaying early onset symptomatic CAD who were admitted to our institution. Inclusion criteria for the study group were: women with CAD confirmed by coronary angiography or troponin-positive ACS, and age less than 55 years. As in other studies that have defined premature CAD, an age cut-off of 55 years was used [9].

At least one female control was recruited per case (matched in terms of age and region of residence) via the National Health Survey WOBASZ study (Polish Multi-centre Population Health Survey) designed to assess the CV risk in the community adult population [10]. Out of 14,350 participants, those subjects with a negative history of CV disease and/or negative exertional chest pain were selected for this project. All study participants were ethnically homogenous, being of white, Caucasian race.

Procedures

Structured questionnaires were administered and physical examinations were undertaken in exactly the same manner for both cases and controls. Information about demographic factors, socio-economic status (education, income), risk factors (hypertension, diabetes, hyperlipidaemia), lifestyle (smoking, physical activity), menopausal status and use of hormone replacement therapy, and personal and family history of CV disease was collected (Table 1). Height, weight, waist and hip circumference were measured using standard instruments and protocols. Before blood pressure was measured, subjects were seated for five minutes and asked to relax. The cuff size was based on the individual's arm circumference, and readings were taken from the right arm by an automated digital Omron M5-I apparatus. Three readings were taken, with a one minute rest period between assessments, and the average of the second and third readings was used in the analysis [10].

Fasting blood samples (drawn from every individual and collected for biochemical analyses and DNA isolation) remained stored for further analysis. In patients with ACS, blood samples for plasma glucose analyses were repeated at discharge.

Lipid levels and glucose levels were measured in fasting serum, both for patients and controls in one institutional central laboratory, certified by the CDC (Center for Disease Control — Lipid Standardization Program) in Atlanta, USA, and

RIQAS (Randox International Quality Assessment Scheme). Total cholesterol, high-density lipoprotein cholesterol (HDL-C), directly obtained low-density lipoprotein cholesterol (LDL-C) and triglycerides levels were measured with reagent from Roche Diagnostics, using an INTERGRA 800 Roche analyser. Fasting blood glucose was determined by a hexokinase assay procedure. Coronary angiography assessment included quantification of coronary artery stenosis as significant $\geq 50\%$ in any of the major epicardial coronary arteries.

The study protocol was approved by the Institutional Review Board and Local Bioethics Committee. All participants gave their informed consent to participate in the study.

Definition of risk factors

Hypertension was defined as blood pressure of 140/90 mm Hg or higher, or use of blood pressure lowering medication.

Current smokers were defined as those who had smoked at least one cigarette a day in the previous 12 months; former smokers were those who had stopped smoking more than one year earlier.

Participants were classified as physically active if they reported moderate or strenuous exercise lasting at least 30 minutes for four or more days a week.

Hypercholesterolaemia was defined as a history of high cholesterol level or statins/fibrate treatment before hospital admission, or fasting cholesterol level ≥ 5.2 mmol/L.

Diabetes was defined as a reported treating physician diagnosis, use of insulin, oral hypoglycaemic or insulin sensitising agent, or fasting glucose level ≥ 7 mmol/L [11].

Obesity was defined as body mass index (BMI) > 30.0 ; abdominal obesity was measured as waist-to-hip ratio (WHR), or as waist circumference ≥ 88 cm.

Menopause was defined as lack of menstrual bleeding for at least 12 months, or history of hysterectomy or oophorectomy, and age of menopause was defined as the age at last menstruation [12]. Information on the use of hormone replacement therapy was classified as 'current', 'past' or 'never used'.

Statistical analysis

Categorical data are presented as numbers and percentages and continuous data — as means \pm SD. Frequencies were analysed by χ^2 tests and continuous variables were analysed using the Wilcoxon test. Premenopausal women served as the reference group for further menopausal analyses. A p value < 0.05 was considered significant. Statistical analyses were performed using SAS software version 8.2.

RESULTS

Between April 2005 and January 2008, 330 women with premature CAD and 347 controls were enrolled. Two patients did not have true CAD, and another five had insufficient data. Therefore, 323 patients and 347 controls were included in the analysis.

Table 1. Characteristics of study group: prevalence of risk factors and mean values of continuously defined variables

Categorical variables	Patients; n = 323 (%)	Controls; n = 347 (%)	P
Current cigarette smoking	158 (48.9)	95 (28.0)	< 0.001
Current and former cigarette smoking	263 (81.4)	168 (48.4)	< 0.001
History of hypertension	204 (67.3)	111 (32.0)	< 0.001
Hypertension	220 (68.1)	145 (41.8)	< 0.001
Body mass index ≥ 30 kg/m ²	113 (35.0)	93 (26.8)	< 0.001
Physical activity	125 (38.7)	199 (57.3)	< 0.001
Diabetes history or treatment	56 (17.1)	17 (4.9)	< 0.001
Diabetes or fasting glucose ≥ 7.0 mmol/L	88 (27.2)	22 (6.3)	< 0.001
History of hypercholesterolaemia	237 (73.4)	90 (25.9)	< 0.001
Hypercholesterolaemia	264 (81.7)	237 (68.3)	< 0.001
Menopause (including surgical)	225 (69.7)	141 (40.6)	< 0.001
Continuous parameters	Mean (SD)	Mean (SD)	
Mean age [years]	49.4 (4.68)	49.5 (3.71)	0.82 (NS)
Body mass index [kg/m ²]	28.13 (5.54)	27.15 (5.24)	< 0.05
Waist circumference [cm]	92.2 (14.0)	87.58 (12.66)	< 0.001
Waist-to-hip ratio	0.86 (0.07)	0.82 (0.06)	< 0.001
Fasting glucose [mmol/L]	6.24 (2.39)	4.97 (1.43)	< 0.001
Total cholesterol [mmol/L]	5.23 (1.25)	5.62 (1.06)	< 0.01
HDL cholesterol [mmol/L]	1.42 (0.38)	1.58 (0.43)	< 0.001
LDL cholesterol [mmol/L]	3.45 (1.18)	3.43 (0.95)	0.93 (NS)
Triglycerides [mmol/L]	1.57 (1.04)	1.33 (0.65)	< 0.01

HDL — high-density lipoproteins; LDL — low-density lipoproteins

The age of patients at entry ranged from 30 to 55. Overall, 186 (57.6%) patients were admitted because of ACS whereas the remaining 138 (42.7%) patients had a history of myocardial infarction. Significant stenosis of two or three coronary arteries was found in 167 (51.7%) patients, 123 (38%) had one vessel disease and 33 (10%) had nonsignificant coronary stenosis. The mean age of patients at onset of the disease was 46.5 years.

Comparison of patients and control subjects

The characteristics of patients and control subjects are presented in Table 1. For the study population, the median age of CAD subjects and controls at study entry did not differ significantly. Although the age at menopause was not significantly lower in patients than in the controls (46.8 ± 4.7 ; and 47.5 ± 4.0 , respectively, $p = 0.13$), women with CAD had a significantly higher prevalence of menopause (prevalence ratio 1.7) at the time of enrolment.

There was a discrepancy in some risk factors' prevalence being dependent on risk factor definition. Relying on patient self-report only, the prevalence of diabetes and hypercholesterolaemia was much lower than the definition based also on blood examination. A smaller such discrepancy was found in hypertension diagnosis (Table 1).

Patients with premature CAD had a very high prevalence of smoking, hypercholesterolaemia and hypertension (Table 1). The highest prevalence ratio between subjects and controls was calculated for diabetes (4.3), followed by smoking (1.68), hypertension (1.63), obesity (1.3), and hypercholesterolaemia (1.2). Patients had lower levels of HDL-C, higher fasting triglycerides, and higher levels of fasting glucose than controls. Total cholesterol was lower in patients than in controls, but LDL-C did not differ significantly between the groups, probably because of the higher proportion of patients (43.9% vs 4%) using lipid-lowering medication. Obesity (defined as BMI ≥ 30) was found in 35% of patients and almost 27% of controls. Waist circumference or WHR which define abdominal obesity better, were significantly higher in patients than in controls (Table 1).

At least one of the five classical risk factors was present in 98.8% of patients, and in 89% controls (Table 2). Four or more risk factors were noted in almost 30% of patients, and 7.5% of controls.

DISCUSSION

Our data indicate that traditional risk factors analysed according to the described definition were present in almost 99% of women with premature CAD, and 89% of controls, sho-

Table 2. Total number of classical risk factors of coronary artery disease

No. of risk factors	Cases n = 323 (%)	Controls n = 347 (%)
0	4 (1.24)	35 (10.09)
1	22 (6.81)	85 (24.5)
2	94 (29.1)	132 (38.0)
3	107 (33.1)	69 (19.9)
4	63 (19.5)	21 (6.05)
5	33 (10.2)	5 (1.44)

wing a high atherosclerosis risk threatening in Polish women. Cigarette smoking seems to play a critical role in the development of premature CAD in women. The majority of former smokers among patients had quit smoking at the first symptoms of heart disease; that is why we analysed former and current smokers together. Only 18.5% of patients had never smoked, compared to more than 50% of the controls. Recent publications have shown the prevalence of smoking in women in older groups to be much lower than among younger patients [13, 14]. A paper by Rosenberg et al. [15] stressed the role of smoking in myocardial infarction etiology in young women, regardless of other risk factors. The critical role of smoking in the development of premature CAD was stressed also by Khot et al. [7] who showed in smokers reduced age at trial entry by about 1 decade in every risk factors subgroup. Smoking, when associated with other classical risk factors, particularly hyperlipidaemia and hypertension, may interact with them, thereby magnifying the baseline risk associated with each risk factor individually [7].

Overall, 68% of patients had diagnosed and/or treated hypertension, compared with less than 42% of controls. The prevalence of hypertension in our study was much higher than in the INTERHEART case-control study [16], but lower than the 81.8% found in the REACH study [17].

Diabetes is also an important risk factor of early CAD onset in women. Relying on study participants' report only, diabetes prevalence would be lower, both in patients and controls, by about 10% and 1.5% respectively. In our study, the patients' reported prevalence of diabetes was similar to that reported in the INTERHEART study [16]; but the true prevalence of diabetes in our study was higher. However, the REACH study reported [17] a marked geographic variation in the prevalence of diabetes, ranging from 52% in the Middle East to 27.7% in Eastern Europe.

The role of lipid levels was difficult to assess in our study because of previous statin treatment in 44% of patients. In spite of this, patients had significantly lower HDL-C and higher triglycerides levels than the controls.

Approximately 2% of patients and 10% of controls with hypertension were unaware that they were hypertensive.

Relying on patient self-report only, the true prevalence of risk factors would be frequently underestimated when compared to more objective measurements involving physical examination and laboratory testing. Higher rates of unawareness, approaching 10–40% in our study, were found for hyperlipidaemia and diabetes.

The unawareness of CV risk can lead to earlier CAD manifestation. Because CAD typically presents ten years later in women than in men, a very high prevalence of risk factors in young women leads to the development of CAD at a younger age. Also, our control group does not seem to be at low CV risk. About 65% of them had more than one risk factor, but only 28% of them presented as current smokers.

Physicians typically underdiagnose classical risk factors. Eliminating smoking alone would be of dramatic public health importance, because it could diminish CV risk and delay the onset of CAD by ten years. Most of the CAD associated risk factors described are preventable. Thus, robust promotion of a healthy lifestyle could reverse the tendency towards an epidemic of CV disease.

CONCLUSIONS

Our study confirms the very high prevalence (99%) of classical risk factors in women with an early onset of CAD. Premature CAD in women was related mainly to cigarette smoking, hypercholesterolaemia and hypertension.

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Częstość występowania klasycznych czynników ryzyka u polskich kobiet z przedwczesną chorobą wieńcową

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Streszczenie

Wstęp: Powszechnie uważa się, że u 50% kobiet w wieku okołomenopauzalnym przyczyną przedwczesnej choroby wieńcowej (CAD) są inne niż klasyczne czynniki ryzyka.

Cel: Celem pracy była ocena częstości występowania 5 klasycznych czynników ryzyka CAD u kobiet z przedwczesną CAD przed 55. rokiem życia.

Metody: Przeprowadzono jednoośrodkowe badanie typu *case-control study*, do którego włączono kobiety z objawową, potwierdzoną angiograficznie przedwczesną CAD (< 55 rż.) lub troponinododatnim ostrym zespołem wieńcowym. Grupę kontrolną stanowiły kobiety w tym samym wieku z negatywnym wywiadem bólów wysiłkowych i/lub chorób sercowo-naczyniowych, wybranych losowo spośród uczestników Wieloośrodkowego Ogólnopolskiego Badania Stanu Zdrowia Ludności (WOBASZ). Analizowano występowanie klasycznych czynników ryzyka CAD: palenia tytoniu, nadciśnienia tętniczego, cukrzycy, hipercholesterolemii i otyłości.

Wyniki: Od kwietnia 2005 do stycznia 2008 roku do badania włączono 330 kolejnych kobiet. Z badań wykluczono 7 pacjentek z powodu braku części badań lub innego rozpoznania. Do analizy zakwalifikowano 323 kobiety chorych i 347 kobiet z grupy kontrolnej. U pacjentek z przedwczesną CAD zaobserwowano istotnie większą częstość występowania klasycznych czynników ryzyka w porównaniu z osobami z grupy kontrolnej. U znacznej części kobiet już wcześniej nie rozpoznano hipercholesterolemii i cukrzycy. Najczęściej stwierdzano hipercholesterolemię (82% chorych v. 68% w grupie kontrolnej) oraz palenie tytoniu (aktualne i były palaczki, odpowiednio: 81% v. 48%). Nadciśnienie tętnicze występowało u 68% chorych i u 42% osób z grupy kontrolnej, a otyłość (BMI ≥ 30 kg/m²) u odpowiednio 35% v. 26.8%. W grupie badanej cukrzyca występowała ponad 4-krotnie częściej niż w grupie kontrolnej (27.2% v. 6.3%). Przynajmniej 1 z 5 klasycznych czynników ryzyka był obecny u 98,8% chorych oraz u 89% osób z grupy kontrolnej, a u 10% chorych i 1,4% kobiet z grupy kontrolnej stwierdzono obecność wszystkich 5 klasycznych czynników ryzyka.

Wnioski: Klasyczne czynniki ryzyka CAD u młodych kobiet są niedoszacowane. Wbrew konwencjonalnemu myśleniu niemal u 99% pacjentek z przedwczesną CAD występuje przynajmniej 1 z 5 klasycznych czynników ryzyka. Przedwczesna CAD jest najczęściej związana z paleniem tytoniu, nadciśnieniem tętniczym i hipercholesterolemią.

Słowa kluczowe: przedwczesna choroba wieńcowa, czynniki ryzyka miażdżycy, płeć

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