Original article

Analysis of selected risk factors of coronary artery disease in a healthy population aged 35-55 years

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Abstract

Background: This report comprises an analysis of results of examinations performed as a part of a cardiovascular disease prevention programme funded by the National Health Fund.

Aim: To determine the relationship between body mass index (BMI) and blood pressure, blood glucose and lipid metabolism abnormalities in an ethnically homogeneous population of males and females aged 35 to 55 years with sense of full health without prior diagnosis of cardiovascular disease or diabetes.

Methods: The study was carried out in the population of a 175,000-resident city during 9 months, involving 1080 subjects (696 females and 384 males) aged 35 to 55 years (mean age – 47.2±5.4). The following variables were assessed: systolic and diastolic blood pressure, body weight and height, BMI, fasting blood glucose, total cholesterol, triglycerides and HDL cholesterol levels.

Results: The studied male population had significantly higher blood pressure, blood glucose, total cholesterol, triglycerides and lower HDL cholesterol levels compared to age-matched females. The female population was found to have a more prominent relationship between increased BMI and blood pressure, blood glucose and serum cholesterol levels than males. Significant differences in favour of females regarding systolic blood pressure, blood glucose and serum cholesterol failed to be present in the obese women subgroup (no statistically significant differences were found compared to obese males). In females aged 45 to 55 years, significantly higher body weight, blood pressure as well as blood glucose, cholesterol and triglyceride levels were observed than in younger women (35-45 years old).

Conclusions: Overweight and obesity are associated with increase of arterial blood pressure, lipid metabolism disturbances and elevation of blood glucose. The relationship between BMI and studied risk factors was influenced by age and gender. Menopause is associated with increasing body weight and unfavourable evolution of studied risk factors.

Key words: obesity, lipid profile, arterial hypertension, glucose, gender

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Introduction

Hypertension, hypercholesterolaemia, glucose metabolism disturbances and increase of body weight like other risk factors often precede development of cardiovascular disease. Cardiovascular diseases are the leading causes of death in Europe [1]. The European Society of Cardiology recommends the SCORE model for evaluation of risk of adverse events related to these conditions in individual patients. It takes into consideration the four following risk factors: age, smoking, total serum cholesterol in relation to HDL cholesterol level, and systolic blood pressure [2].

For more efficient prophylaxis, the INTERHEART study statistical evaluation included a larger number of modifiable risk factors, and their epidemiological importance was determined for individual countries' populations. Significant cardiovascular risk factors were determined as follows: abnormal ratio of ApoB/ApoA-1, current smoking, diabetes, hypertension, abdominal obesity, unfavourable psychosocial factors, lack of daily

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consumption of fruit and vegetables, alcohol abstinence as well as lack of daily exercise [3]. The study showed abdominal obesity to increase cardiovascular risk and confirmed its relationship with 7 of the 9 above risk factors [3]. There was also a link observed between body weight, blood pressure and carbohydrate and lipid metabolic pathways. Stevens et al. reported that decrease of body weight significantly reduced blood pressure in overweight and prehypertensive individuals [4]. It is also known that the effectiveness of antihypertensive and lipid-lowering agents increased in patients after myocardial infarction along with reduction of body weight [5]. In an overweight population with glucose intolerance, measured weight loss led to the reduction of diabetes occurrence and lowering of serum triglycerides [6].

The above-mentioned reports support the relationship between overweight and hypertension, diabetes and lipid disturbances in affected patients. In this context the question arises whether a similar relationship exists in individuals with various BMI with respect to blood pressure, total serum cholesterol and LDL/HDL cholesterol, triglycerides and glucose levels prior to clinical presentation of cardiovascular disease.

The European Union (EU) has approved a programme aimed at 40% cardiovascular mortality reduction by 2020. It presumes reduction of blood pressure below 140/90 mm Hg, serum cholesterol below 5 mmol/l (190 mg%) and 1% annual reduction of smoking. Cardiovascular mortality rate in the young and middle-aged population in Poland is 2.5 times higher than in the 'old' EU. Therefore, an essential part of this programme to be successful is recognition of the current epidemiological situation of the young and middle-aged population and planning of preventive measures [7].

The aim of this study was to evaluate the prevalence of cardiovascular risk factors in untreated, ethnically homogeneous population aged 35 to 55 years. In search for a cheap method enabling a mass preventive effect through lifestyle modification in females and males, we assessed the relationship between body weight and blood pressure and several metabolic variables.

Methods

During 9 months 1080 subject were enrolled, including 696 females and 384 males, aged 35-55 years (mean 47.2±5.4) with sense of full health and without prior diagnosis of cardiovascular disease or diabetes. The study was performed in the population of a 175,000--inhabitant city in Poland. The study comprises an analysis of results of examinations performed as a part of a cardiovascular disease prevention programme funded by the National Health Fund. Subjects were invited to participate in the project through media such as the Internet, press, radio and television advertisements. The following variables were recorded for further analyses: systolic and diastolic blood pressure, body weight and height, BMI, fasting blood glucose, total cholesterol, triglycerides and HDL cholesterol levels in venous blood serum. Blood was collected in the morning, seven days a week. Body height was measured with a height meter, and body weight was measured without shoes and outer garments when using the medical scales.

Serum lipid profile and glucose were determined with the following methods:

- enzymatic colorimetric method CHOD-PAP with cholesterol esterase, cholesterol oxidase and 4-aminoantipyrine for measurement of cholesterol levels;
- homogeneous enzymatic colorimetric assay using PEG--modified cholesterol esterase and cholesterol oxidase for determination of HDL cholesterol levels;
- enzymatic colorimetric method (GPO/PAD) with glycerophosphate oxidase 4-aminoantipyrine for measurement of triglycerides;
- blood glucose was determined using the reference enzymatic method with hexokinase.

The Roche INTEGRA 800 analyzer and Roche reagents were used for all assays. Total cholesterol level ≥190 mg/dl (5.0 mmol/l) was defined as abnormal [8]. Other results were interpreted according to the International Diabetes Federation guidelines. Triglycerides were found increased if ≥150 mg/dl (1.7 mmol/l), low HDL cholesterol level was diagnosed if <40 mg/dl (0.9 mmol/l) for males and <50 mg/dl (1.1 mmol/l) for females, and elevated blood glucose was diagnosed at ≥100 mg/dl (5.6 mmol/l) [9].

Blood pressure measurement was performed twice in the sitting position, following a 5-minute rest. The following blood pressure readings were defined as elevated: systolic ≥140 mmHg, and diastolic ≥90 mmHg [10].

Subjects were divided into two groups with respect to gender. For another analysis subjects were divided into three subgroups depending on their BMI:

- first subgroup comprised individuals with normal body weight – BMI <25 kg/m^2.
- second subgroup comprised overweight subjects with BMI of 25-29.9 kg/m^2.
- third subgroup comprised individuals with obesity and BMI of 30-34.9 kg/m^2.

In 11 subjects BMI was above 35 kg/m^2. However, they were not enrolled in the statistical analysis due to the low number of subjects.

Statistical analysis

Statistical analysis of the results was performed using STATISTICA 7.1 software (StatSoft Inc. Tulsa, OK., USA) [11]. Mean, minimum, maximum and standard

deviation were calculated for each study parameter. Normal distribution of analysed variables was verified with Shapiro-Wilk test, whereas homogeneity of variance was evaluated using the Bartlett's and Brown-Forsythe tests [12, 13].

Significance of differences between means of parameters following normal distribution and homogeneity of variance criteria were assessed using Student's t-test (two populations) or analysis of variance (ANOVA) when comparing means from more than two populations. For parameters not following normal distribution or variable variances Mann-Whitney U test and Kruskal-Wallis test respectively were used [14, 15]. A p value <0.05 was considered significant.

Results

In the study population, BMI over 25 kg/m^2 was found in 48% of subjects. Overweight was found in 33% of females and 51% of males, and obesity in 9 and 11%, respectively. The three groups for both genders showed no differences with respect to body height. Hypertension was found in 18.3% of females and 35.2% of males. Serum cholesterol above 190 mg% was confirmed in 70.3% of females and 77.1% of males. Increased levels of serum triglycerides were observed in 12.2% of females and 34.1% of males, and abnormally low HDL cholesterol levels were seen in 6.0% of females and 4.2% of males. Serum glucose higher than or equal to 100 mg% was found in 6.2% of females and 10.2% of males.

Mean systolic and diastolic blood pressure values were significantly higher in males (p <0.001) (Table I). In studied females the analysed biochemical parameters apart from serum HDL cholesterol were significantly lower (p <0.001), whereas serum HDL cholesterol was significantly higher (p <0.001) compared to males.

Comparison using analysis of variance (ANOVA) between the normal weight population and overweight and obese subgroups showed that increased body weight was associated with higher systolic and diastolic blood pressure as well as serum total cholesterol, triglycerides and glucose in females (Table II). The HDL cholesterol levels were significantly lower along with increase of BMI both for males and females.

In males only diastolic blood pressure did not increase significantly with higher body weight. Mean cholesterol levels in overweight males were higher than in obese ones. The difference was insignificant, and cholesterol levels were significantly dependent on body weight as well as serum glucose and triglycerides. Comparison of males and females according to their weight revealed that blood pressure and serum triglycerides were higher in males than in females (p <0.001) in subgroups with normal and increased weight (Table III).

The HDL cholesterol levels were higher in the female group (p <0.001). Serum glucose and cholesterol did not differ significantly between males and females with normal weight. Serum glucose and cholesterol levels were significantly lower in the subgroup of overweight females than males. Systolic blood pressure, serum glucose and cholesterol levels did not differ significantly between obese males and females. Triglyceride levels in obese males were significantly elevated (p=0.003) and HDL cholesterol was significantly lower than in females (p <0.001).

In males, no statistically significant differences were observed for any parameter when comparing the group aged >45 years and younger subjects (<45 years old). Females aged >45 years significantly differed from those aged <45 years with respect to higher body weight by 2.0 kg and higher BMI. The differences appeared in tandem with significantly higher blood pressure, serum total cholesterol, triglycerides and glucose in younger females (Table IV).

Discussion

Increased blood pressure was more often found in studied males than females. In the WOBASZ study, involving randomly selected individuals aged 20-74 years,

Table I. Mean values of analysed variables in males and females

Variables	Females n=696	Males n=384	p
Body weight [kg]	65±10	81±12	<0.001
Body height [cm]	162±5.9	176±6.6	<0.001
Body mass index [kg/m^2]	25±3.4	26±3.3	<0.001
Systolic blood pressure [mmHg]	119±14	126±16	<0.001
Diastolic blood pressure [mmHg]	76±9.3	82±9.7	<0.001
Glucose [mg/dl]	82±16	85±18	<0.001
Cholesterol [mg/dl]	213±40	221±41	<0.001
Triglycerides [mg/dl]	100±67	142±87	<0.001
HDL cholesterol [mg/dl]	71±16	62±16	<0.001

Table II. Mean values of analysed parameters with respect to BMI in the entire study population as well as male and female subgroups

Variables	Total				Females				Males			
	Normal n=554	Overweight n=425	Obesity n= 101	p	Normal n=405	Overweight n=230	Obesity n=61	p	Normal n=149	Overweight n=195	Obesity n=40	p
Body weight [kg]	62±8.3	77±9.9	91±10.5	<0.001	59±6.2	71±6.3	85±7.1	<0.001	70±8.0	85±7.8	100±7.0	<0.001
Body height [cm]	166±8.5	169±9.4	169±9.1	<0.001	162±6.0	162±5.7	163±5.3	0.512	175±7.1	176±6.4	178±5.8	0.123
BMI [kg/m^2]	22.5±1.8	27.0±1.4	31.8±1.3	<0.001	22.4±1.7	26.9±1.3	32.0±1.3	<0.001	23±1.8	27±1.4	32±1.2	<0.001
Systolic blood pressure [mmHg]	119±15.0	124±14.3	127±13.7	<0.001	117±13.8	121±13.4	125±13.2	<0.001	124±16.9	127±14.7	130±14.0	0.031
Diastolic blood pressure [mmHg]	77±10.0	79.5±9.4	81.5±9.3	<0.001	75±9.2	78±9.2	80±8.8	0.001	82±10.4	82±9.2	84±9.7	0.220
Glucose [mg/dl]	81±16.8	83±16.7	89±18.0	<0.001	80±13.1	82±19.5	90±19.6	<0.001	85±23.7	84±12.6	87±15.3	0.035
Cholesterol [mg/dl]	210±37.8	221±42.7	225±41.5	0.003	209±38.1	217±41.1	227±42.4	0.001	213±36.9	226±44.1	222±40.5	0.025
Triglycerides [mg/dl]	92±57.9	133±80.0	165±109.9	<0.001	83±46.4	116±67.6	153±119.7	<0.001	115±76.9	154±88.2	185±91.1	<0.001
HDL cholesterol [mg/dl]	72±16.7	63.7±15.0	59.3±13.5	<0.001	74±16.1	68±14.9	63±13.0	<0.001	68±17.6	59±13.5	54±12.7	<0.001

Table III. Mean values of analysed variables in males and females by BMI. Standard deviations are shown in brackets

Variables	Normal			Overweight			Obesity		
	Females n=405	Males n=149	p	Females n=230	Males n=195	p	Females n=61	Males n=40	p
Body weight [kg]	59±6.2	70±8.0	<0.001	71±6.3	85±7.8	<0.001	85±7.1	100±7.0	<0.001
Body height [cm]	162±6.0	175±7.1	<0.001	162±5.7	176±6.4	<0.001	163±5.3	178±5.8	<0.001
BMI [kg/m^2]	22.4±1.7	22.8±1.8	0.009	26.9±1.3	27±1.4	0.030	32.0±1.3	32±1.2	0.992
Systolic blood pressure [mmHg]	117±13.8	124±16.9	<0.001	121±13.4	127±14.7	0.001	125±13.2	130±14.0	0.085
Diastolic blood pressure [mmHg]	75±9.2	82±10.4	<0.001	78±9.2	82±9.2	<0.001	80±8.8	84±9.7	0.036
Glucose [mg/dl]	80±13.1	85±23.7	0.054	82±19.5	84±12.6	0.018	90±19.6	87±15.3	0.639
Cholesterol [mg/dl]	209±38.1	213±36.9	0.127	217±41.1	226±44.1	0.037	227±42.4	222±40.5	0.967
Triglycerides [mg/dl]	83±46.4	115±76.9	<0.001	116±67.6	154±88.2	<0.001	153±119.7	185±91.1	0.003
HDL cholesterol [mg/dl]	74±16.1	68±17.6	<0.001	68±14.9	59±13.5	<0.001	63±13.0	54±12.7	<0.001

Table IV. Mean values of analysed variables in males and females by age

Variables	Females			Males		
	<45 years n=215	≥45 years n=481	p	<45 years n=124	≥45 years n=260	p
Body weight [kg]	64±10.4	66±10.1	0.042	82±12.1	80±12.5	0.082
Body height [cm]	163±6.1	162±5.7	0.022	177±6.9	176±6.5	0.040
BMI [kg/m^2]	24.1±3.4	25.0±3.4	0.001	26.2±3.1	25.9±3.3	0.365
Systolic blood pressure [mmHg]	117±12.3	120±14.3	0.004	125±15.0	126±15.9	0.447
Diastolic blood pressure [mmHg]	75±9.0	77±9.3	0.014	81±8.6	82±10.2	0.396
Glucose [mg/dl]	79±9.9	83±18.5	0.041	83±11.4	86±20.3	0.356
Cholesterol [mg/dl]	198±33.9	219±40.6	<0.001	215±39.3	223±42.3	0.192
Triglycerides [mg/dl]	89±50.2	105±72.7	<0.001	153±106.5	137±76.2	0.481
HDL cholesterol [mg/dl]	71±14.3	71±16.6	0.440	60±15.1	63±16.2	0.090

including hypertensive ones, mean blood pressure was higher than in our study population, with similar trends for females and males [16].

Our previous observations showed that increase in body weight was associated with higher blood pressure in obese or overweight males and females. Moreover, characteristics and obvious blood pressure differences in females with normal body weight compared to the corresponding group of males were less clear in obese and overweight females.

Older females aged above 45 years had significantly higher systolic and diastolic blood pressure than younger ones. In a recently published Italian study the investigators revealed similarly increased blood pressure in perimenopausal females [17]. They also established additional factors contributing to blood pressure increase in females, including poorer education and decreased physical activity as well as overweight.

Mean body weight in our group of older females was by 2 kg higher than in younger females; this may suggest that both perimenopausal period and body weight increase might influence the higher blood pressure in the analysed group.

Hypercholesterolaemia occurred more often in our subjects compared to the WOBASZ population [8]. In the female population a linear correlation was found between increasing body weight, age and hypercholesterolaemia. Gostyński et al. observed such a correlation for both genders [18]. However, in females blood cholesterol level increased significantly faster with aging. As a consequence, females aged 50-64 years had significantly higher cholesterol levels than the respective male group [18]. The analysis showed that perimenopausal period was associated with significant increase of body weight as well as statistically significant increase of serum cholesterol.

In the WOBASZ study, blood glucose ≥100 mg/dl was almost 2 times more prevalent than in our study population, both in males and females. This seems to be a result of selection of a study population comprising healthy subjects without prior knowledge of existing abnormalities. Despite these differences there is a noticeable association between increasing body weight and higher glucose levels, particularly in analysed females. A similar correlation was observed by Toumilehto et al., who additionally showed that modification of lifestyle and reduction of body weight by mean 4.2±5.1 kg reduced the risk of diabetes by 58% in patients with overweight and glucose intolerance [6].

It was also confirmed that overweight affects long--term prognosis in patients with clinically apparent diabetes. Williamson et al. reported that decrease in body weight in overweight patients with type 2 diabetes resulted in a 25% reduction of total mortality [19]. Yan et al. showed that overweight and obesity in middle--aged subjects were associated with increased number of hospital admissions and higher mortality rate due to coronary artery disease, other cardiovascular diseases and diabetes mellitus independently from recognised risk factors such as high blood cholesterol or hypertension [20].

The increased body weight observed in our study in females aged above 45 years is unfavourable, in particular when associated with increased values of other analysed risk factors.

The demonstrated correlation between overweight and obesity and analysed risk factors in apparently healthy, cardiovascular treatment – naive individuals confirms the significant role of prophylactic examinations and usefulness of lifestyle modification leading to reduction of body weight prior to potential diagnosis of cardiovascular disease or diabetes.

Conclusions

1. The healthy male population aged 35-55 years had significantly higher blood pressure, fasting serum glucose, total cholesterol and triglycerides and significantly lower HDL cholesterol levels as compared to age-matched healthy females.

2. A highly significant correlation was found between BMI increase and levels of analysed risk factors in females. There were no significant differences in systolic blood pressure, serum glucose and total cholesterol in obese males and females.
3. Perimenopausal age was associated with a significant increase of body weight and prevalence of all analysed risk factors, which should result in active counselling leading to lifestyle modifications and, as a consequence, loss of body weight.

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Analiza wybranych czynników ryzyka choroby wieńcowej w populacji osób zdrowych w wieku 35–55 lat

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Streszczenie

Wstęp: Praca stanowi analizę wyników badań uzyskanych w ramach programu profilaktyki chorób układu krążenia finansowanego przez Narodowy Fundusz Zdrowia.

Cel: Określenie zależności między wskaźnikiem masy ciała (ang. *body mass index*, BMI) a wartościami ciśnienia tętniczego krwi, glikemią i zaburzeniami lipidowymi występującymi w jednolitej etnicznie populacji kobiet i mężczyzn od 35. do 55. roku życia, z poczuciem pełnego zdrowia, u których dotychczas nie rozpoznano chorób układu krążenia i cukrzycy.

Metodyka: Badanie przeprowadzono w populacji 175-tysięcznego miasta w ciągu 9 mies., obejmując analizą 1080 osób (696 kobiet i 384 mężczyzn) w wieku 35–55 lat (średnia wieku 47,2±5,4). Oceniono pomiary wartości skurczowej i rozkurczowej ciśnienia tętniczego krwi, masę i wysokość ciała, BMI, stężenie glukozy na czczo, cholesterolu całkowitego, trójglicerydów i frakcji HDL cholesterolu.

Wyniki: W badanej populacji mężczyzn stwierdzono znamiennie wyższe wartości ciśnienia tętniczego, stężenia glukozy, cholesterolu całkowitego, trójglicerydów i niższe stężenia frakcji HDL cholesterolu w porównaniu z populacją kobiet w tym samym przedziale wiekowym. W populacji kobiet obserwowano bardziej wyraźną niż w grupie mężczyzn zależność między wzrostem wskaźnika BMI a wartościami ciśnienia tętniczego krwi, stężeniem glukozy i cholesterolu w surowicy. Znamienne, korzystne dla płci żeńskiej, różnice w wartościach skurczowego ciśnienia tętniczego krwi, stężenia glukozy i cholesterolu w surowicy krwi nie były widoczne w podgrupie kobiet otyłych (brak istotnych statystycznie różnic w porównaniu z podgrupą otyłych mężczyzn). Wśród kobiet w wieku 45–55 lat obserwowano znamiennie wyższe wartości masy ciała, ciśnienia tętniczego krwi oraz stężenia glukozy, cholesterolu i trójglicerydów w porównaniu z kobietami młodszymi (35–45 lat).

Wnioski: Nadwaga i otyłość łączą się ze wzrostem wartości ciśnienia tętniczego krwi, z zaburzeniami lipidowymi i wzrostem stężenia glukozy w surowicy krwi. Związek między wskaźnikiem BMI a badanymi czynnikami ryzyka zależy od wieku i płci badanych osób. Okres menopauzy wiąże się ze wzrostem masy ciała i niekorzystnymi zmianami ocenianych czynników ryzyka.

Słowa kluczowe: otyłość, profil lipidowy, nadciśnienie tętnicze, glukoza, płeć

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