Original article

Risk factors of atherosclerosis in premenopausal women with a sense of well-being. A pilot study

Rafał Łukaszewicz[1], Magdalena Łukaszewicz[2], Leszek Ceremużyński[1]

[1]Medical Centre of Postgraduate Education, Department of Cardiology, Grochowski Hospital, Warsaw, Poland
[2]Primate Stefan Wyszyński University, Warsaw, Poland

Abstract

Introduction: Women before menopause are thought to be relatively safe from cardiovascular disease due to the protective effects of oestrogens, although one may question this opinion with regards to women with many typical risk factors. However, because of the shortage of data concerning prevalence of risk factors in young women, it is not known whether this phenomenon is confined to a limited group or affects many women.

Aim: The purpose of this study was to determine the prevalence of either typical risk factors of atherosclerosis or emotional disturbances that might increase the probability of coronary artery disease in young women.

Methods: The study group involved 62 premenopausal women with a sense of well-being (regular menstruations, activity of serum follicle stimulating hormone < 15 IU/L). Mean age of women was 43.5 years. Total cholesterol, LDL and HDL fractions, triglyceride, lipoprotein (a) and homocysteine concentrations were examined and body mass index was calculated. A psychological examination assessing depression and neuroticism intensity was also performed.

Results: Total cholesterol concentration (mean values ± SD, expressed as mg%, percentage of abnormal results are given in brackets) was 206.3±35.8 (67.2), LDL cholesterol 124.3±30.2 (55.1), HDL cholesterol HDL 62.5±14.8 (6.9), triglyceride 101±60.1 (13.8), lipoprotein (a) 18.9±17.5 (44.8). Body mass index was 25.2±4.1 (41.3). History of smoking was positive in 27.4% and 6.5% of examined women had arterial hypertension. Coexistence of 4 to 5 aforementioned risk factors was noted in 27.4% of studied subjects. Mean homocysteine concentration was 10.7±2.1 μmol/L, while 41.3% of subjects had levels above the threshold of 11 μmol/l, commonly considered pathological. Symptoms of depression and neuroticism were seen in 30.5% and 22.5% of women, respectively.

Conclusions: This pilot study of young women demonstrated that, in contrary to popular belief, this population is vulnerable to cardiovascular disease due to high prevalence of many risk factors.

Epidemiological data indicate that the prevalence of atherosclerotic vascular disease in women at childbearing age is relatively low [1].

The differences in the prevalence of cardiovascular (CV) disease are less clear in females who have undergone bilateral ovariectomy or are after natural menopause [2, 3]. Thus, it was hypothesised that oestrogens acted as protective agents on the vascular wall [4]. This opinion has gained wide pathophysiological justification.

Moreover, it was documented that oestrogens decreased LDL-cholesterol, increased HDL-cholesterol

concentrations [5] and decreased lipoprotein A content. Lipoprotein A is also considered an independent risk factor of coronary artery disease (CAD). These hormones increase endothelial secretory activity, resulting in improved organ perfusion and inhibition of prothrombotic processes [6].

According to current knowledge women at childbearing age are considered a population with low risk of CV disease. Thus, they are exceptionally referred to prophylactic examinations in order to reveal risk factors of atherosclerosis. Additionally, large epidemiological studies evaluating prevalence of risk

Address for correspondence:

Rafał Łukaszewicz, Centrum Medyczne Kształcenia Podyplomowego, Oddział Kardiologii, Szpital Grochowski, ul. Grenadierów 51/59, 04-073 Warszawa, Poland, tel./fax: +48 22 810 17 38, e-mail: rlukasz@kkcmkp.pl

factors have involved mainly populations of a wide age spectrum, including only a small percentage of women of childbearing age who were not analysed separately [7].

Thus, we decided to establish the community prevalence of typical risk factors of atherosclerosis in premenopausal females with a sense of well-being. Because it has been shown earlier that emotional status has an impact on pathogenesis of CV disease, some psychological parameters were also assessed.

We were encouraged to perform this study by reports indicating that despite the relatively low incidence of CV disorders in women at childbearing age the diseases usually featured more severe course in the involved subjects (9). Still it needs to be clarified whether it is a result of accumulation of many risk factors.

The study presented herein is a pilot one. Results will be helpful in working out the protocol of a similar study involving a larger population in order to reach more definite conclusions.

The aim of this study was to establish the prevalence of both typical risk factors of atherosclerosis and potential emotional disturbances (depression, neuroticism) in a group of women with a sense of well-being at childbearing age.

Methods

Patients

The studied group involved 62 women with a sense of well-being at the age of 33 to 49 years, mean 43.5 years. They were employed in an insurance agency (clerks) or in a hospital in a large city (doctors, nurses and ward attendants). All subjects gave written informed consent to participate in the study.

Premenopausal criteria were as follows: regular menstruations, activity of serum follicle stimulating hormone (FSH) <15 IU/L without any hormonal contraceptives (mean FSH concentration in the group of women enrolled in the study was 6.5±2.4 IU/L).

Exclusion criteria

Pregnancy, natural or artificial menopause, irregular menstrual cycles (independently of reason), use of hormonal substitutive therapy or hormonal contraception during the period three months before enrolment, polycystic ovarian syndrome.

FSH assessment

Follicle stimulating hormone activity was assessed between day 7 and day 9 of the cycle utilizing MEIA macromolecular immunoenzymatic assay method (AxSYM FSH).

Serum biochemical examinations

Fasting glucose, total cholesterol, LDL fraction, HDL fraction and triglyceride concentrations were evaluated. These examinations were performed using biochemical analyser (DIMENSION) and Dade Behring kits with ISO international quality certification. Blood lipoprotein (Lp (a)) and homocysteine concentrations were also assessed.

Lipoprotein (a) - concentration was measured by means of immunoturbidimetric method using antisera, standard solutions and control materials of DAKO (Denmark). In order to eliminate error related to the examined material self-turbidity, during all measurements dilutions of examined samples in reactive buffer as reference (baseline) tests were used. Lp(a) concentration in the studied samples was calculated using the standard curve. Variability index for calculations within series was 4.1% and between series 5.6%.

Homocysteine concentration was assessed using the enzymatic method employing Abbott reagent kits compatible with an IMAX device. Measurements were performed according to instructions provided by the manufacturer. Variability index for calculations within series was 2.1% and between series 4.2%.

Psychological tests

Examined women were requested to fill in two psychological questionnaires. Degree of depression was evaluated by means of the Depression Inventory proposed by Beck et al [10].

Table I. General risk factors

CAD in parents	Diabetes	Hypertension (at any time)	Smoking	BMI		Waist/lHip factor (W/H)	
n/%	n/%	n/%	n/%	Median ± SD	BMI >25n/%	Median ± SD	W/H >0.8 n/%
6/9.7	0/0	4/6.5	17/27.4	25.2±4.1	19/41.3	0.8±0.1	15/32.6

n - number of patients, CAD - coronary artery disease, BMI - body mass index

Table II. Lipid risk factors

		Cholesterol	LDL	HDL	TG	Lp (a)
Median* ± SD		206.3	124.3	62.5	101	18.9
		35.8	30.2	14.8	60.1	17.5
Abnormal	n	39	32	4	8	13
values	%	67.2	55.1	6.9	13.8	44.8

* values in mg%

Neuroticism was evaluated using one of the scales of the NEO-FFI personality questionnaire described by Costa and McCrae [11].

Results

General risk factors of cardiovascular diseases

These are presented in Table I.

Overweight or obesity was noted in more than 41% of women, while one in every four females smoked cigarettes. Distribution of BMI values is shown in Figure 1.

Lipid risk factors

These are outlined in Table II.

Mean concentrations of total cholesterol and LDL fraction as well as Lp(a) exceeded the normal range. Percentage of individual with abnormal results was high, 67.2%, 55.1% and 44.8%, respectively.

Lipid concentrations in individual subjects are illustrated in Figure 2.

Importantly, most female subjects presented abnormal concentrations of total cholesterol and its LDL fraction. Moreover, many of them had elevated values of Lp (a).

Analysis of individual burden of risk factors was performed for each participant and is presented in Figure 3.

Four or five typical CAD risk factors were found in 17 (27.4%) subjects. Only 16 (25.8%) examined women had one or no risk factors. It should be emphasized that these figures are probably underestimated because not all participants underwent the complete set of examinations.

Homocysteine

Homocysteine is an independent risk factor. Homocysteine level should be kept below 11 μmol/l [11]. The results of measurements are presented in Figure 4.
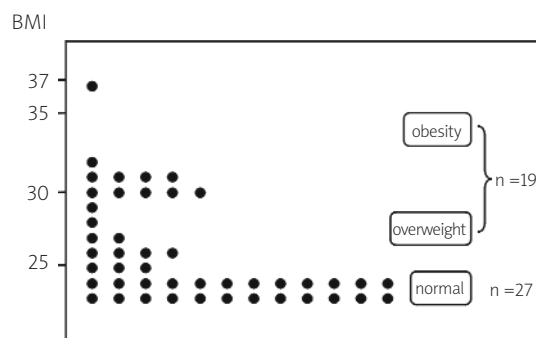
Figure 1. Body Mass Index (BMI). Individual values distribution

The mean concentration was 10.7±2.1. Values exceeding the normal range were noted in 41.3% of subjects.

Psychological risk factors

Results of depression evaluation are shown in Figure 5.

According to Beck et al. [10], values equal to or higher than 10 indicate depression. Such values were found in 30.5% of examined women, i.e. in almost one in every three of them.

Results of neuroticism evaluations are presented in Figure 6.

According to Costa and McCrae [12] features of neuroticism are present in women with 23 or more points. 22.5% of study participants had such a result.

Discussion

This pilot study demonstrated that numerous risk factors of CD were present in a large number of women with a sense of well-being at childbearing age. Elevated total cholesterol (in 67.2%), LDL cholesterol (in 55.1%) as well as Lp(a) (in 44.8%) concentrations were noted particularly often. Such lipid conformation drives a particularly high risk of CAD development in women
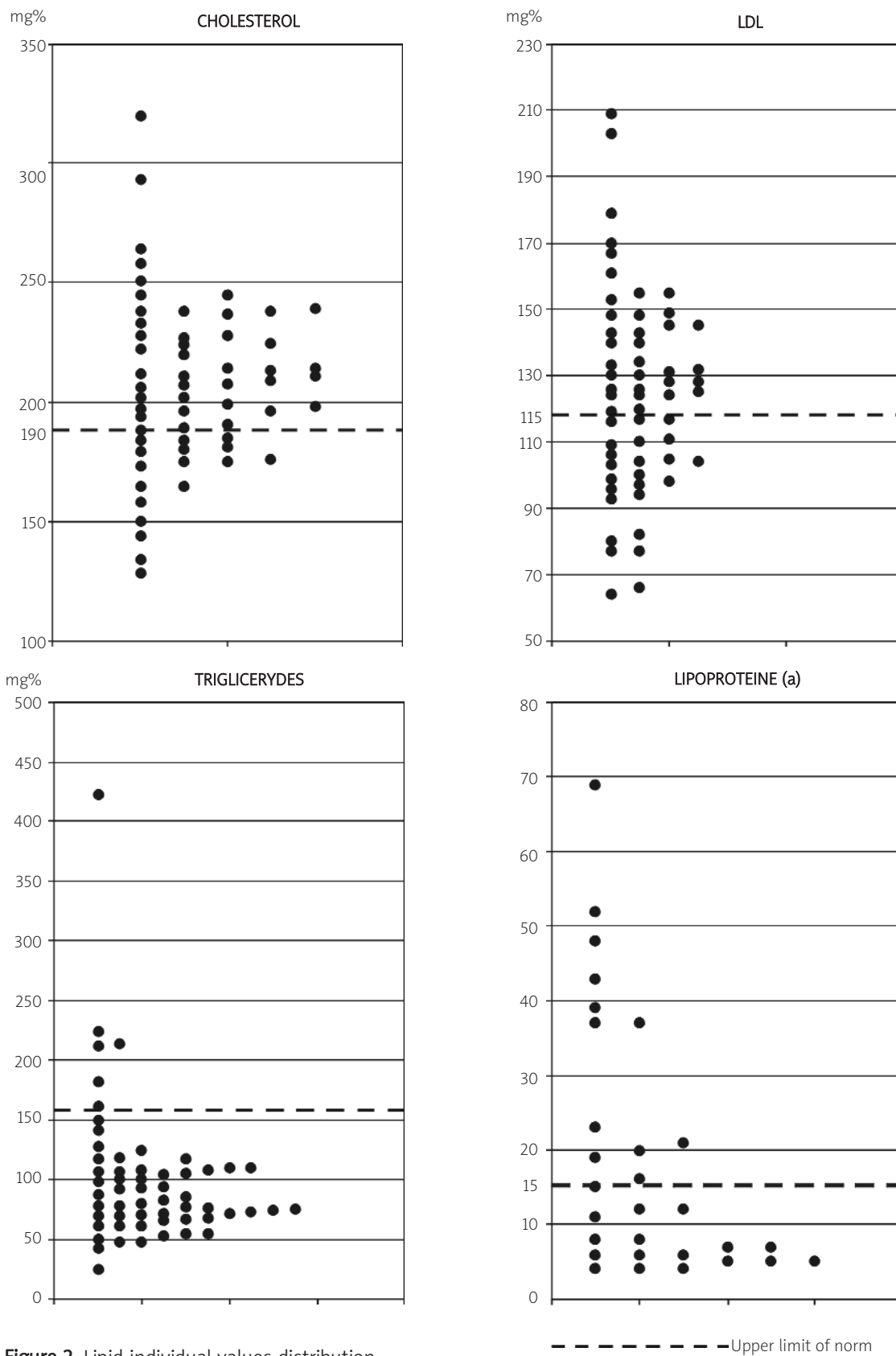
Figure 2. Lipid individual values distribution

Upper limit of norm

just after menopause, as has been shown by Kuller et al. [13]. Many women smoked cigarettes (27.4%) and were overweight /obese (41.3%).

Four or five CV risk factors were found in 27.4% of examined females. Undoubtedly, these persons are especially susceptible to early onset of the disease. Such risk factor accumulation in some women at premeno-pausal age may be a reason for the particularly severe course of CAD in this population, as observed earlier [9].

Elevated homocysteine concentration was seen in more than 40% of examined women. Nygard et al. [14] reported 3.8% mortality during follow-up of 4.6 years in patients with CAD and homocysteine concentration <9 µmol/L, 8.6% with homocysteine level 9-14.9 µmol/L and as high as 24.7% with concentration of >15 µmol/L.

Depression is an established risk factor of CAD [8]. Depressive symptoms were noted in almost one in every three women in the study, including those who had four or five typical CAD risk factors, further increasing the probability of disease. Features of neuroticism were found in one in every four to five subjects.

Prior to study recruitment, examined persons were also asked if they had suffered from depression in the past or at the time of examination. All women gave a negative answer to this question. It was really surprising how many of them had positive results in Beck's questionnaire indicating the presence of depressive symptoms. It appeared that women who reported "a sense of well-being" were not aware that their way of thinking, feeling and somatic symptoms were associated with depression. Because depression is a risk factor of CAD, it can be and should be treated.

Neuroticism is a personality feature that is determined mainly genetically [15], thus changing minimally throughout lifetime and due to stressful life events [16]. As was documented in the earlier prospective studies, persons with higher neuroticism indices were more susceptible to the impact of negative emotions such as anxiety, anger and sense of guilt and were more prone to psychological stress [17]. Thus, they more frequently presented symptoms of depression [17]. They are more likely to respond with depression to all stressful life events including disease as a psychologically difficult situation. This depressive response may negatively influence the course of disease [18]. Therefore, it may be supposed that seriously expressed neuroticism as a personality feature predisposes to depression occurrence then consequently to CAD development and unfavourable outcome. Reviewing the medical literature, no reports on either depressive symptoms or neuroticism indices among premenopausal women were found.
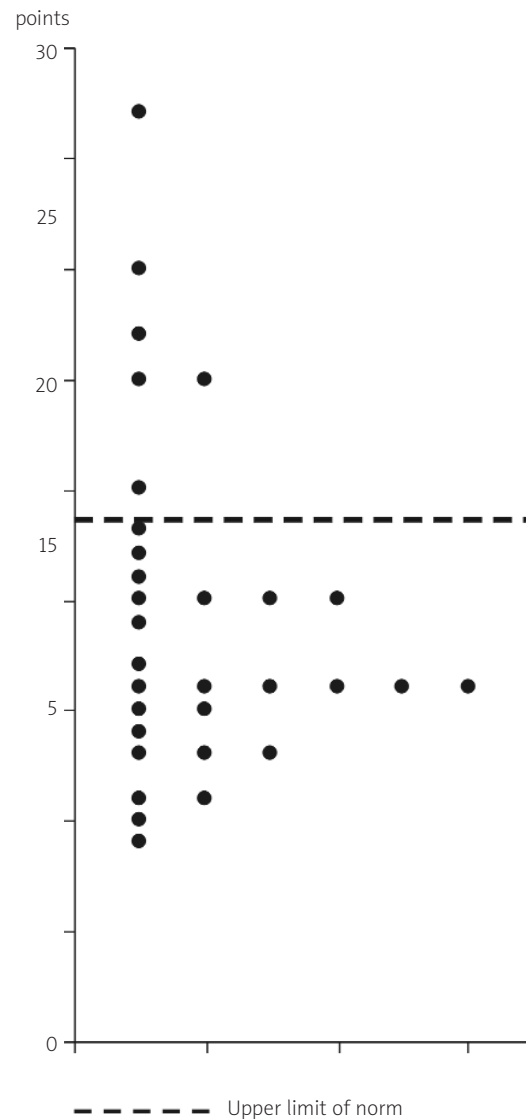
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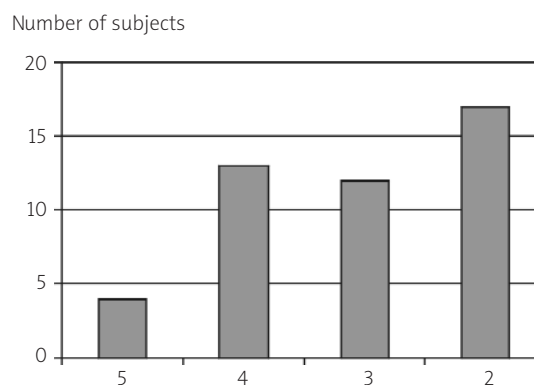
Figure 3. Distribution of the number of CAD risk factors (hypertension, smoking, abnormal LDL, TG, Lp(a) values, BMI >25, incidence of CAD in parents)

Number of subjects

- - - - - Upper limit of norm
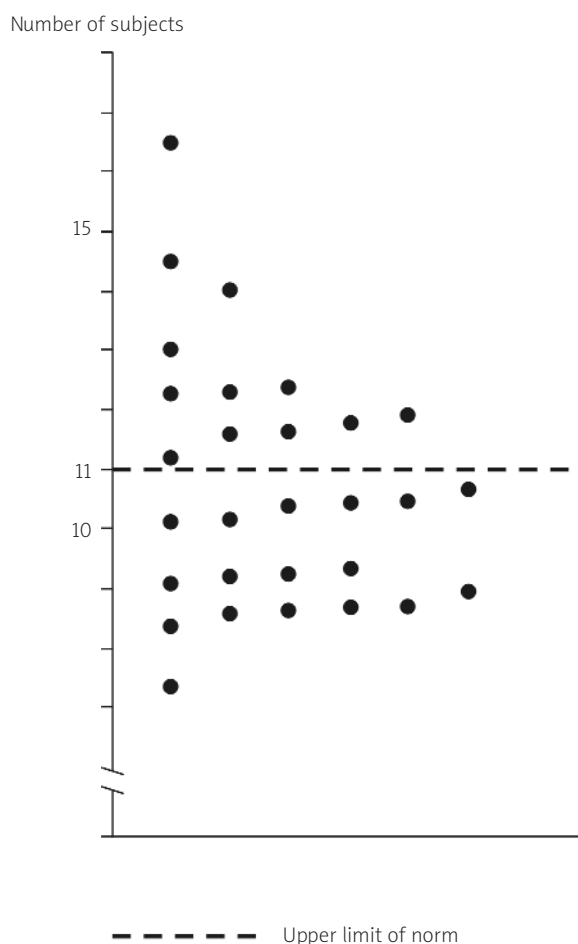
Figure 4. Homocysteine - individual values distribution
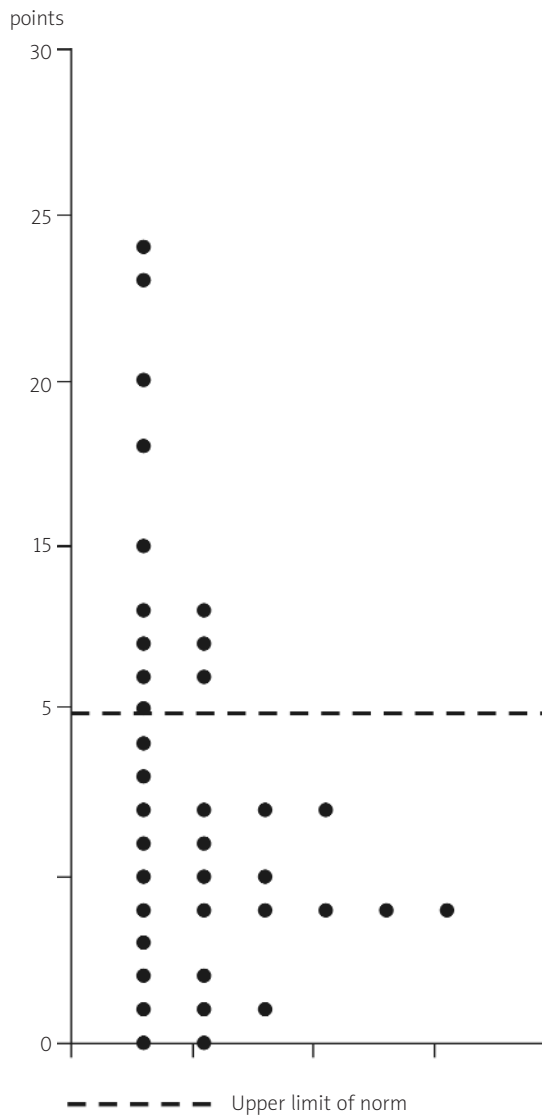
Figure 5. Distribution of individual values of depression parameters

Figure 6. Distribution of individual values of neuroticism parameters

The results of this study indicate that an opinion suggesting that women at childbearing age are a population at relatively low risk of cardiovascular disease may not be true. It seems they are not a homogeneous group with regards to this risk. Dyslipidemia and depression may be present in as many as 30 to 50% of them. A marked percentage of them smoke cigarettes and are overweight/obese. The results presented herein, although preliminary, are alarming and should encourage further investigations involving a large number of participants. If the results of future trials confirmed our findings it would mean that women at premenopausal age should undergo screening in order to identify subjects at particularly high risk. This group of women must be subject to an intensive preventive programme.

Study limitations

Our study is a pilot one, and thus concerns a relatively small although clearly defined population. They are young women who live in the environment of a big city and are employed as intellectual employees. Thus, our results cannot be extrapolated to other social groups, including women who live and work in the countryside.

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Czynniki ryzyka miażdżycy u kobiet w wieku przedmenopauzalnym o poczuciu zdrowia. Badanie pilotowe

Rafał Łukaszewicz[1], Magdalena Łukaszewicz[2], Leszek Ceremużyński[1]

[1]Centrum Medyczne Kształcenia Podyplomowego, Klinika Kardiologii, Szpital Grochowski, Warszawa
[2]Uniwersytet im. Prymasa Stefana Wyszyńskiego, Warszawa

Streszczenie

Wstęp: Uważa się, że z racji ochronnego działania estrogenów kobiety przed menopauzą raczej nie są zagrożone chorobami sercowo-naczyniowymi. Można jednak kwestionować ten pogląd w odniesieniu do kobiet, u których występują liczne, typowe czynniki ryzyka. Nie wiadomo jednak, czy są to przypadki kazuistyczne czy jest to zjawisko szersze, bowiem mało jest danych na temat występowania czynników ryzyka u młodych kobiet.

Cel pracy: Ustalenie częstości występowania typowych czynników ryzyka miażdżycy, a także ewentualnych zaburzeń emocjonalnych zwiększających prawdopodobieństwo choroby wieńcowej u młodych kobiet.

Metodyka: Grupa badana składała się z 62 kobiet o poczuciu pełnego zdrowia, w wieku średnio 43,5 lat, będących w okresie premenopauzalnym (regularne miesiączki, follikulotropina w surowicy <15 IU/l). U badanych oznaczano: cholesterol ogólny, frakcje LDL i HDL, trójglicerydy, lipoproteinę (a), homocysteinę, obliczano indeks masy ciała. Przeprowadzono także badania psychologiczne, oznaczające poziom depresji i neurotyzmu.

Wyniki: Cholesterol ogólny (wartości średnie ± SD, w mg%, w nawiasach podano % nieprawidłowych wyników): 206,3±35,8 (67,2), cholesterol LDL 124,3±30,2 (55,1), cholesterol HDL 62,5±14,8 (6,9), trójglicerydy 101±60,1 (13,8), lipoproteina (a) 18,9±17,5 (44,8). Indeks masy ciała 25,2±4,1 (41,3). Papierosy (kiedykolwiek) paliło 27,4% badanych, a nadciśnienie tętnicze miało 6,5% z nich. U 27,4% badanych stwierdzono jednoczesne wystąpienie 4–5 powyższych czynników ryzyka. Średnie stężenie homocysteiny wyniosło 10,7±2,1 μmol/l, przy czym 41,3% badanych miało wartości powyżej 11 μmol/l, uznawane za nieprawidłowe. Wskaźniki depresji stwierdzono u 30,5%, a neurotyzmu u 22,5% kobiet.

Adres do korespondencji:

Rafał Łukaszewicz, Centrum Medyczne Kształcenia Podyplomowego, Klinika Kardiologii, Szpital Grochowski, ul. Grenadierów 51/59, 04-073 Warszawa, tel./faks: +48 22 810 17 38, e-mail: rlukasz@kkcmkp.pl