

How the age at menopause is related to cigarette smoking in Polish women?

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Background. The aim of the study was to define whether and to what degree cigarette smoking differentiates the age at natural menopause of women in Poland

Materials and methods. The empirical basis for this work was the material obtained from cross-sectional studies carried out in the years 1998 to 2002 among women living in Poland. The material included data on 3793 women aged from 35 to 69 years. The women varied with regard to age, education and socio-economic status. The study was performed in the companies or during check-ups and included healthy women. Women who were treated pharmacologically or on a diet were excluded from the study. The menopausal status and median age at menopause were estimated using the retrospective and status-quo methods (ANOVA and probit analysis).

Results. The median age at natural menopause, estimated by probit analysis, was 50.33 years. The main aim of this work was to define whether and to what extent cigarette smoking influences the age at natural menopause. To state whether and to what degree cigarette smoking influences the age of women undergoing natural menopause, we have done analysis of variations and survival analysis. Cigarette smoking was found to increase the risk of earlier menopause (test value $F = 138.8$, $p < 0.0001$, Fig. 2). Non-smoking women experience menopause on average two years later than the women that are habitual smokers. Moreover, the number of cigarettes smoked per day influenced the age of menopause, accelerating its occurrence in women who smoked more than five cigarettes per day (test value $F = 50.81$, $p < 0.0001$).

Conclusions. The average age at natural menopause was 50.33 years. Cigarette smoking accelerated the risk of earlier menopause. Non-smoking women on average underwent menopause two years later than those who smoked habitually. The number of cigarettes smoked per day influenced the age at natural menopause, accelerating the process in women who smoked more than 5 cigarettes per day.

Key words: tobacco smoking, menopause

INTRODUCTION

Smoking cigarettes is one of the factors accelerating the process of human senescence.

Several studies (1–4) have suggested that smoking women are at an increased risk of vascular and heart diseases, cancer and osteoporosis. Moreover, the overall mortality rate among smokers is twice as high as that of non-smokers (5–13). The probable mechanisms of these associations include

direct toxic effects on the ovaries, an interference with gonadotropin release, and alterations in the metabolism of sex steroids (4, 10). The Polish population makes a group of inveterate smokers. Investigations within the WHO MONICA Project (14) has shown that adult women take a leading part among smokers. In Poland, about 33 percent of women are smokers.

Considering the above data, this work will try to define whether and to what degree smoking cigarettes influences the age at natural menopause of women in Poland.

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MATERIALS AND METHODS

The empirical basis for this work consisted of material collected from the cross-sectional studies conducted in 1998–2002 among women in the Wielkopolska and Silesia regions of Poland.

It comprised a group of 3793 women aged from 35 to 69 years. The women varied with regard to also, education and social-economic status. The study was performed in the companies or during check-ups and included healthy women. The women who were treated pharmacologically or on a diet were excluded from the study. The investigation instrument was a questionnaire including a certain range of questions, which helped to establish the status of menopause in women and their smoking habits (see the Questionnaire). For further analysis only two groups of women, smokers and non-smokers, were distinguished.

The data obtained were examined by a detailed statistical analysis. To estimate the age at menopause of the examined women we applied two different methods: retrospective and “status quo”. Using the retrospective method, we figured out the average and median age of natural menopause from the exact date of the last menstruation and the exact date of birth. Then we figured out the average age at natural menopause, using probit analysis, just to eliminate a mistake which results inevitable in retrospective calculations. To state whether and to what degree cigarette smoking differentiates the age of women undergoing natural menopause, we have done the analysis of variations and survival. The analysis of variations was extended by a posteriori tests to compare particular groups. The estimation of the “survival” function was conducted by the Kaplan–Meier method. To determine the relationship between cigarette smoking and the age at menopause, the Cox proportional hazard model was applied. All the analyses were conducted according to their assumptions, as we have applied the Statistica 6.0 programme package [StatSoft, Inc 2004 Statistica for Windows].

RESULTS

On performing preliminary analysis, we found that 1326 women were still menstruating, whereas 2467 women were in the post-menstrual period. In the latter group, 2117 women claimed to have natural menopause which means that it occurred either without any surgical interference or without applying supplementary hormonal therapy, while the other 156 women had hormonal therapy in their perimenopausal period. Women who started their supplementary hormonal therapy before the onset of menopause, as well as the women whose menopause was not a result of surgical interference were included into this group. However, in 194 women menopause was a

consequence of some surgical interference, such as extirpation of ovaries or uterus.

It is known that the age of menopause varies depending on its character. Artificial menopause usually occurs about four years earlier, while women who underwent hormonal replacement therapy in their perimenopausal period experience menopause two years later than the natural menopause appears. For this reason all the analyses were performed on women whose menopause was of natural character.

As we applied the retrospective method, we were able to calculate the median age of natural menopause based on the date of the last menstruation and the date of birth. The mean age at menopause was 49.81, $SD = 2.27$, while the menopause occurrence ranged from 37.72 to 56 years. Next, in order to eliminate the error with which the retrospective method is unavoidably burdened (many women may not remember exactly the date of their last menstruation), we have estimated the median age at natural menopause applying probit analysis which enabled us to determine in each age group the percentage of women who had their menstruation at least 12 months before they were examined. That median age at natural menopause, estimated by probit analysis, was found to be 50.33 years (variation estimator was 0.02). The median age of menopause was estimated also by the Kaplan–Meier method. The 50th percentile in the study group of women was assessed at 50 years. These percentages reflect the nature of the distribution of the functions examined.

In Fig. 1, the Kaplan–Meier “survival” curve applied to the age at menopause is shown. In the study women, a curve with a distinct slope was observed. The decline of the curve falls on the period between the 48th and 53rd years of life. The slope was most distinct in the 50th year of life.

We have studied if and how cigarette smoking influences the age at natural menopause. The analysis included only women who had never smoked cigarettes (they made 68.38%) and those who smoked

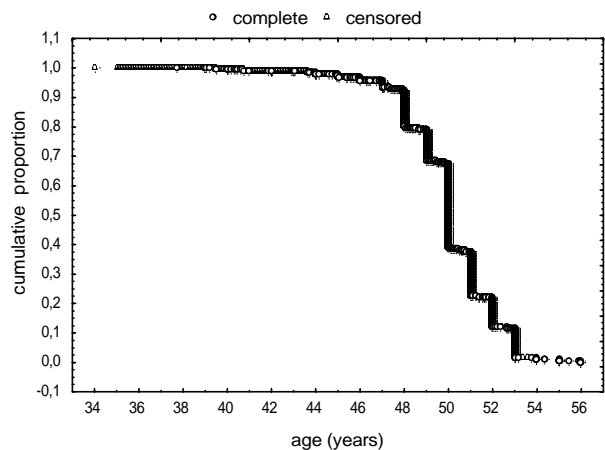


Fig. 1. The Kaplan–Meier “survival” curve applied to age at menopause

habitually both during their menopause period and before (31.62%). We have taken no account of the females who gave up smoking in their perimenopausal period, because they made a very small group of 24 women. Besides, they did not say how long and how many cigarettes per day they had smoked. The one-factor analysis of variations showed a highly significant statistical dependence of cigarette smoking on the age at natural menopause (value of test $F = 138.8$; $p < 0.0001$). Women who had never smoked experienced their menopause much later – their mean age was 50.05 years ($SD = 2.04$), whereas women who smoked habitually before and during menopause experienced menopause much earlier, at the mean age of 48.38 years ($SD = 2.96$). The results are presented in Table 1.

Table 1. Cigarette smoking and the age at natural menopause

Variable	N	\bar{X}	SD
Women who never smoked cigarettes	1332	50.05	2.04
Women smoking habitually	616	48.38	2.96

N – number of women, \bar{X} – average, SD – standard deviation.

In the further statistical procedure the Cox's proportional hazard model was applied. According to the obtained results (F Cox test: $T1 = 619.83$, $T2 = 1342.17$; $F(584, 33) = 2.64$; $p < 0.001$) it was found that cigarette smoking was a significant predictor of the time of menopause occurrence. Next, the Kaplan-Meier survival functions were estimated (Fig. 2). The curves plotted for the women according to their smoking habits showed that cigarette smoking influenced the age at menopause. The women who had never smoked experienced their menopause later, whereas those who smoked habitually experienced menopause much earlier.

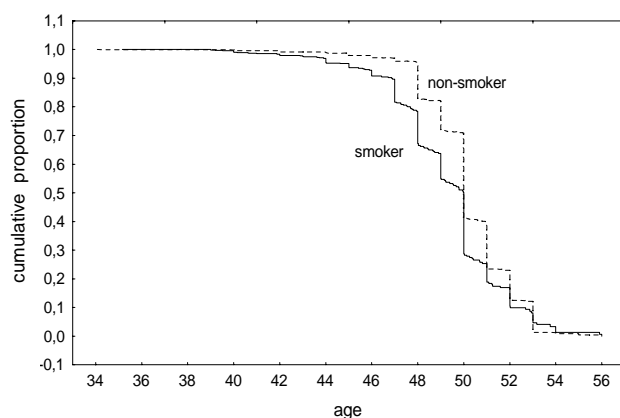


Fig. 2. Kaplan-Meier "survival" curves for groups of women depending on cigarette smoking

Then, we have investigated whether the number of cigarettes smoked per day influenced the age at natural menopause onset. The results showed a highly significant statistical difference (value of test $F = 50.81$; $p < 0.0001$). Females who smoked more than 5 cigarettes per day underwent their menopause on average two years earlier.

The results are presented in Table 2. Table 3 presents results of the T Tukey test for irregular numerical, showing a varied influence of cigarette smoking on the natural menopause age of the women. The Tukey test implies the lack of differences between the age at menopause onset in non-smoking females and those who smoked up to 5 cigarettes per day.

DISCUSSION

The analyses we have carried out show that cigarette smoking accelerates the risk of an earlier onset of natural menopause.

Habitual smokers had their menopause about two years earlier than the women who have never smoked. The number of cigarettes smoked per day also influenced the age at menopause onset. However, women who smoked more than 5 cigarettes per day had menopause earlier than those women who smoked occasionally or did not smoke at all.

Our results support the data presented in the literature (5–13; 15–19). Nevertheless, not all the studies point out a correlation between the number of cigarettes smoked per day and the age at menopause.

Willet et al. (12) demonstrated in a prospective study that current smokers were more likely to undergo an earlier menopause than non-smokers. The median age at menopause was 52.4 for never-smokers and 51.9, 51.7 and 50.4 years for women who currently smoked 1–14, 15–24, 25–34 and 35 or more cigarettes per day. In Harlow and Signorello's (19)

Table 2. Mean age of natural menopause with regard to the number of cigarettes smoked per day

Variable	N	\bar{X}	SD
Women who never smoke cigarettes	1332	50.05	2.04
Those smoking up to 5 cigarettes per day	214	49.77	2.07
5–10 cigarettes per day	211	47.70	3.10
10–20 cigarettes per day	154	47.79	3.19
More than 20 cigarettes per day	37	46.98	3.02

N – number of women, \bar{X} – average, SD – standard deviation.

Table 3. Influence of cigarette smoking on the age at natural menopause

	Never smoked	Up to 5/day	5-10/day	10-20/day	More than 20/day
Never smoked		0.896	0.000	0.000	0.000
up to 5/day	0.896		0.000	0.000	0.002
5-10/day	0.000	0.000		0.999	0.872
10-20/day	0.000	0.000	0.999		0.813
More than 20/day	0.000	0.002	0.872	0.813	

study, cigarette smoking was found to hasten the onset of menopause by as much as one year. Cramer et al. [6] found that women who ever smoked had a significantly earlier mean age at menopause – 50.1 *versus* 50.7 years to women who never smoked.

Kaufman et al. (8) showed that female smokers had a significantly earlier menopause than women who had never smoked. The mean age at menopause declined with increasing the number of cigarettes smoked, although the trend was not significant. Women who smoked at least 15 cigarettes per day had their menopause on average 1.8 years sooner than women who had never smoked.

Di Prospero et al. (7) found that female smokers experienced menopause significantly earlier (mean age 47.1 ± 3.3 SD) than non-smokers (49.4 ± 3.6 years) and the prevalence of cigarette smoking was more frequent in females with ovarian failure before 46 years of age.

Mattison and Thorgeirsson (20) presented a very probable mechanism that could be responsible for the earlier age at natural menopause in women who had smoked habitually. They discovered that in mice benzopyrene, a polycyclic aromatic hydrocarbon which is one of the components of cigarette smoke, damages the primary ovary vesicles. If we assume that the same mechanism occurs in women, then, according to the concept that menopause appears when the ovaries knock out a certain number of oocytes, we may expect earlier menopause even in those females who stopped smoking long before the menopausal period. According to the mechanism suggested by Mattison and Thorgeirsson, the more cigarettes women smoked and the longer they had done it, the more oocytes they had damaged. That is why they undergo earlier menopause in comparison to the women who had smoked occasionally or not at all. Cigarette smoking may not only accelerate the reduction of oocytes in the ovaries, but it may also influence the ovaries and the whole organism, because this is the factor that increases cellular membrane oxidation caused by combustion products such as nitrogen dioxide (12). Baron et al. (5) have also pointed out that cigarette smoking reduces the level of estrogens and thus may endanger an earlier occurrence of natural menopause in female. It is known that postmenopausal women who smoke and take oral estrogens have serum estron and estradiol le-

vels lower than women who never smoke cigarettes (21). These data prove irrefutably that smoking cigarettes has an influence on the diverse metabolism of hormones. Women who smoke cigarettes develop more 2-hydroxyestradiol, which has virtually no estrogenic activity, and less estrinol, potentially leaving them with less circulating active estrogens than those who never smoke cigarettes (22).

The obtained results encourage further studies in this field so that we could publicise harmful results of cigarette smoking and popularise the healthy lifestyle among women who smoke in their reproduction period.

CONCLUSIONS

1. The average age of natural menopause is 50.33 years.
2. Cigarette smoking accelerates the risk of earlier menopause occurrence.
3. Non-smoking women on average undergo menopause two years later than those who smoke habitually.
4. The number of smoked cigarettes per day influences the age of natural menopause occurrence, accelerating the process in women who smoke more than 5 cigarettes per day.

Received 1 February 2005

Accepted 18 October 2005

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The Questionnaire

This questionnaire is anonymous and includes a number of questions we would like you to answer honestly (tick the proper answer in a square). The questionnaire is made only for research study and will not be publicized in any form. The results will be used for the evaluation of the health condition of Polish middle-aged women and to indicate preventing procedures in the public health care. We are grateful for your cooperation.

1. **Date of birth:** _____
2. **Are you** before _____ in the middle of _____ after _____ **menopause**
3. **The date of the first period (age)** (approximately): _____
4. **Do did you have periods:** regularly _____ irregularly _____ If irregularly, please state _____
5. when it was: _____
6. **Define the length of menstruation cycle:** shorter than 28 days _____ 28–32 days _____ longer than 32 days _____
7. **State the day of the last period (age):** _____
8. **What do you think about the course of menopause:** natural: yes _____ no _____ during the menopause I applied hormonal therapy: yes _____ no _____ it you remember, indicate what kind of therapy: _____ was surgical intervention necessary?: yes _____ no _____ It yes, give the details (for example. Curettage, ovariectomy or hysterectomy): _____
9. **Marital status:** married _____ how many times: _____ spinster _____ widow _____ others: _____
10. **Do you smoke cigarettes:** _____ yes _____ sometimes _____ no _____ How much do you smoke: only sometimes _____ up to 5 cigarettes per day _____ 5–10 cigarettes per day _____ 20 cigarettes per day _____ more _____
11. **Do you consider yourself habitual smoker:** yes _____ rather yes _____ no _____
12. **How old were you when you started smoking:** _____
13. **If you gave up smoking, when:** _____ and state how long you smoked before that: _____
14. **Where do you live:** provincial city _____ big city _____ small city _____ village _____
15. **Education:** not accomplished primary _____ primary vocational _____ secondary _____ high school _____ university degree _____