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# Changes in cardiovascular risk profile in women after menopause (Prague Pre and Post Menopausal Female study)

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ABSTRACT

*Introduction:* Atherosclerosis is the main cause of mortality in the Czech Republic. In our previous cross-sectional studies, we detected a high prevalence of metabolic cardiovascular risk factors in women before and after menopause and found menopausal transition to be critical period for atherosclerosis acceleration. In the present longitudinal study, we studied changes of main cardiovascular risk factors in women after transition to menopause.
*Methods:* We analyzed data of 195 women who became menopausal and 292 women who stayed in menopause during 6-year period. The cardiovascular risk factors under study were as follows: smoking, body mass index, waist circumference, blood pressure, plasma lipids including apolipoprotein B and A1 and fasting glycemia.
*Results:* The most striking differences between newly and steadily menopausal women were found in changes of plasma lipids. With the exception of HDL cholesterol all changes were less favorable in newly menopausal women and were not associated with treatment with statins. No significant differences between both groups were found for changes in body mass index, waist circumference, blood pressure and fasting glycemia.
*Conclusions:* In longitudinal study we confirmed that time around menopausal transition is one of the most dynamic periods regarding changes of cardiovascular risk factors, mainly plasma lipids.

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## Introduction

Cardiovascular disease caused by atherosclerosis is the main cause of mortality among men and women in developed countries including the Czech Republic [1]. Although cardiovascular disease caused by atherosclerosis is rare in premenopausal women, the incidence steeply increases after menopause. Unresolved issue remains if these changes are caused rather by chronological aging or by menopause accompanied by decrease in the estrogen concentration. If the latter is correct, the change of cardiovascular risk factors around menopause could be critical for the development of atherosclerosis and its complications [2,3]. Despite increasing interest in menopausal transition and evidence that it is really atherogenic [4,5], only general recommendations were recently published focused on this period in woman's life [6,7] and only sparse data from reliable longitudinal studies are available [2,3].

In our previous work, we detected a high prevalence of metabolic cardiovascular risk factors in women before and after menopause [8,9]. In addition, we found menopausal status as a risk factor for the development of hypertension, though potentially mediated through increased body mass index [10]. We also found that menopausal transition could be a critical period for atherosclerosis acceleration under certain conditions, namely smoking [11]. The impact of menopausal transition could be mediated through several mechanisms including impaired vascular protection, impaired reverse cholesterol transport, and impaired balance of sex hormones [11]. In a recent longitudinal study, we studied changes of main cardiovascular risk factors after transition to menopause.

## Materials and methods

### *Population*

The study was already described in detail elsewhere [8–11]. In short, the Prague Pre and Post Menopausal Female (3PMFs) study is based on a 5% representative and random sample of women aged 45–54 years living in Prague recruited in 2003. In 2004–2006, 908 women underwent baseline examination. All women throughout the study reported their final menstrual period (FMP) on a monthly basis. For definition of reproductive status, we used criteria proposed by the ''Stages of Reproductive Aging Workshop'' (STRAW) [12] together with levels of follicle stimulating hormone (FSH). According to this, women were divided into 3 groups: premenopausal, when the FMP was reported in within 61 days before the interview; perimenopausal, if the FMP was reported 61–365 days before the interview; and postmenopausal, when the FMP was reported more than 365 days before the interview. The second examination was performed after $5.7 \pm 0.8$ years. Complete data were obtained in 676 women. In this analysis we focused on 303 newly menopausal women and on 292 steadily menopausal women as controls.

The definition of newly menopausal women was as follows: reported FMP within 61 days before baseline examination with level of FSH lower than 40 IU/L and reported FMP more than 365 days before the second examination with levels of FSH more than 40 IU/L. The definition of steadily menopausal women was as follows: reported FMP more than 365 days before the first and second examination with levels of FSH more than 40 IU/L at both examinations. After exclusion of women after hysterectomy/ovariectomy and of women using hormone replacement therapy the study group comprised 195 newly menopausal women and control group comprised 292 steadily menopausal women. The ethics committee of the Institute a priori approved the whole study, and all participants provided their signed informed consent for the second examination.

### *Anthropometric and laboratory variables*

All participants were interviewed about their medical history and main cardiovascular risk factors. Height, weight, waist circumference and blood pressure were measured according to the WHO MONICA (''monitoring trends and determinants in cardiovascular disease'') protocol [13,14]. Body mass index was calculated as weight in kg divided by squared height in meters. Women with a history of current and past regular smoking were defined as smokers. Systolic and diastolic blood pressures were measured in the right arm with the subject in the sitting position after at least ten minutes at rest. Three blood pressure measurements were obtained, and the mean value of the last two measurements was used for further analyses. Blood samples were drawn after overnight fasting. Serum total cholesterol and triglycerides were measured using the fully automated (HITACHI 911 Auto Analyzer, Japan) enzymatic method (reagents from Hoffmann, La Roche, Basel, Switzerland). HDL-cholesterol was determined using the same method after precipitation of serum lipoproteins with sodium phosphotungstate and magnesium chloride kits. Serum LDL cholesterol was measured using an automated method with direct determination using an LDL-C plus kit from Hoffmann-LaRoche (Basel, Switzerland). FSH was measured using IRMA kits (Immunotech, Prague, Czech Republic). Fasting glycemia was determined enzymatically (Lachema, Brno, Czech Republic).

### *Data analysis*

Data are presented as percentages for categorical variables and means for continuous variables. Between-group comparison of continuous variables was performed using unpaired *t*-test. Paired *t*-test was used for the detection of changes of cardiovascular risk factors in the case of continuous variables. The $\chi^2$ test was applied for discrete variables. Between-group comparisons of mean change of particular covariates were performed using unpaired *t*-test.

## Results

At the baseline examination age and FSH levels were significantly lower in newly menopausal women than in steadily menopausal women; the same was found for waist circumference, LDL cholesterol, and apolipoprotein B. No significant differences were found in body mass index, blood

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