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Original article

Association between earlier age at natural menopause and risk of diabetes in middle-aged and older Chinese women: The Dongfeng–Tongji cohort study

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ABSTRACT

Aim. – Age at menopause is associated with cardiovascular disease, but little is known of its relationship with diabetes, and previous findings are controversial. The objective of this study was to evaluate the association between earlier menopause (at age ≤ 45 years) and the prevalence of diabetes in the Chinese population.

Methods. – A total of 16,299 postmenopausal women, aged 42.0–94.3 years, who completed the study questionnaires, underwent medical examinations and provided blood samples, were included in our analysis. Participants self-reported their age at menopause and were then divided into three age groups (≤ 45 , 46–52, ≥ 53 years). Logistic regression models were used to estimate odds ratios (ORs) and 95% confidence intervals (CIs).

Results. – Of the study participants, 2811 (17.2%) had diabetes. The average age at menopause was 49.5 ± 3.3 years. For each 1-year delay in menopausal age, the presence of diabetes was reduced by 2% (OR: 0.98, 95% CI: 0.97–0.99) after adjusting for potential confounding factors. Compared with those whose menopausal age was 46–52 years, the OR for diabetes was 1.20 (95% CI: 1.03–1.39) for those with an earlier menopausal age (≤ 45 years).

Conclusion. – Our findings suggest that earlier menopause may be independently associated with an increased prevalence of diabetes. Future prospective studies are needed to verify this relationship.

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Introduction

Diabetes is a major public-health problem throughout the world. According to the International Diabetes Federation, 415 million people were living with diabetes in 2015, and it is expected that the number will increase to 642 million by 2040 [1]. In China, the prevalence of diabetes among adults was estimated to be 11.6% in 2010, which increased with age in both men and women. Within the Chinese population, women aged < 60 years have been shown to have a lower prevalence of diabetes than men, while women aged > 60 years have a higher prevalence [2,3].

Menopause, which marks the end of a women's reproductive life, is a midlife milestone in women. Numerous studies have demonstrated that menopause was associated with unfavourable changes in, for example, body composition and lipid metabolism [4,5]. These changes may increase the risk of diabetes. In addition, endogenous sex hormones have been reported to modulate glycaemic status and diabetes risk in men and women differently. For example, high testosterone levels increase the risk of diabetes in women, but decrease the risk in men, while sex hormone-binding globulin (SHBG) is more protective in women than in men [6]. Therefore, it may be that menopause itself, which is characterized by hormonal changes, can account for the pronounced increase in diabetes risk in midlife women.

Many studies have focused on the question of whether menopausal status is associated with the risk of diabetes [7,8], but the issue of whether age at menopause influences diabetes risk

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remains unclear. The few epidemiology studies that examined the association of menopausal age and diabetes have reported mixed results [9–14]. Two cross-sectional studies, from Italy and Japan, could find no association between age at menopause and risk of diabetes [9,11]. A study conducted in China also failed to find any significant relationship between age at menopause and diabetes [12]. In fact, only two studies to date, conducted in Europe and the US, have reported a positive association between early age at menopause and risk of type 2 diabetes (T2D) [10,14]. For this reason, the present study has examined the association of age at menopause and the prevalence of diabetes in a large sample population of middle-aged and older women in China.

Methods

Study population

This study was based on data from the first follow-up of the Dongfeng–Tongji cohort study performed in 2013. The method and study design have been previously described [15]. A total of 38,295 participants were recruited, including 17,108 men and 21,187 women who responded to the questionnaires and underwent medical examinations. Of these 21,187 women, 4888 were excluded because information on menopausal status and age at menopause were missing, they were premenopausal, they reported menopause due to disease or they had been diagnosed with diabetes before menopause. Ultimately, 16,299 participants were included in the analysis. Fig. 1 illustrates the recruiting process for these women. The study was approved by the medical ethics committee of the School of Public Health, Tongji Medical College and Dongfeng General Hospital. Informed consent forms were obtained from all participants.

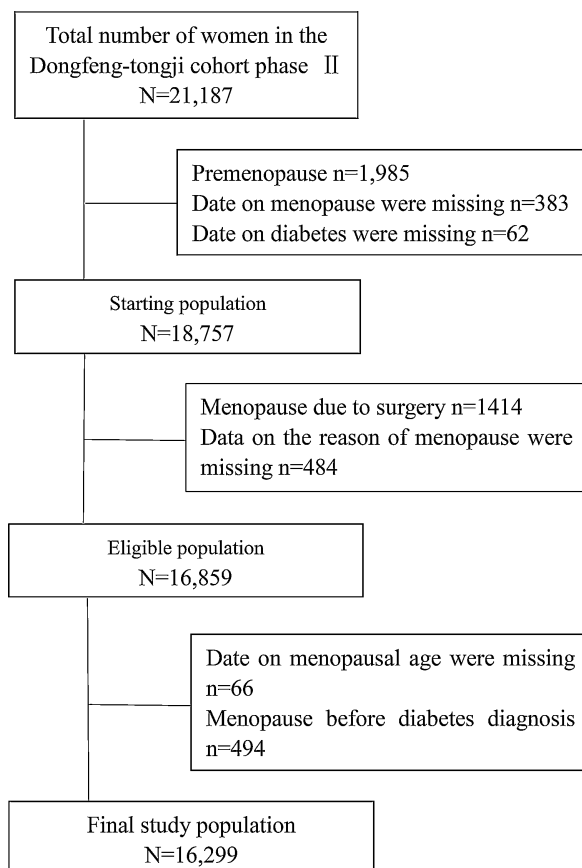


Fig. 1. Flow chart of women ultimately included in the study.

Diagnosis of diabetes

T2D was defined according to American Diabetes Association criteria [16] as a fasting plasma glucose (FPG) level ≥ 7.0 mmol/L, a self-reported history of physician-diagnosed diabetes, or self-reported use of hypoglycaemic agents or insulin.

Age at menopause

Women were asked whether their menstrual periods had stopped for more than 1 year. If the answer was 'yes', they were then further asked their age at menopause and the cause of the menopause (natural, disease). Women were described as post-menopausal if they had ceased menstruation for at least 1 year, and age at menopause was defined as the self-reported age at the last menstrual period.

Assessment of covariates

Age, marital status (married, single, divorced/windowed), educational level (primary school or below, junior high school, high school, college or above), family history of diabetes, smoking status (never, current, past), alcohol intake (never, current, past), physical activity, parity, and history of the use of oral contraceptives and/or hormone replacement therapy (HRT) were obtained by self-reporting via questionnaire. Smoking was defined as having at least 1 cigarette per day for >6 months, and drinking was defined as the consumption of alcohol at least once a week for >6 months, while physical activity was defined as doing physical exercise at least three times a week.

Standing height, weight, waist circumference and blood pressure were obtained by physical examination. Body mass index (BMI) was calculated by weight (kg)/height squared (m^2). Waist-to-hip ratio (WHR) was calculated by waist circumference (cm)/hip circumference (cm). Hypertension was defined as systolic blood pressure (SBP) ≥ 140 mmHg or diastolic blood pressure (DBP) ≥ 90 mmHg, or a self-reported history of physician-diagnosed hypertension or antihypertensive drug use [17]. Triglyceride (TG), high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, total cholesterol and fasting glucose levels were obtained by laboratory examinations.

Statistical analysis

Continuous variables were described as means \pm SD and compared by analysis of variance (ANOVA). Categorical variables were described as percentages (%) and compared using the χ^2 test. A series of logistic regression analyses were performed to calculate odds ratios (ORs) and 95% confidence intervals (95% CIs) to estimate the relationship between menopausal age and T2D. Age at menopause was divided into three categories (≤ 45 years, 46–52 years, ≥ 53 years) according to the 10th, 10–90th and 90th percentile, with menopausal age at 46–52 years as the reference.

Multiple linear regression models were used to obtain marginal mean values and 95% CIs for glucose. Logistic regression was performed in three consecutive models adjusted for potential confounders, which was age at enrolment in model 1. In model 2, educational level, marital status, smoking, drinking, physical activity, family history of diabetes, parity, and history of oral contraceptive and/or HRT use were added. Finally, anthropometric and biochemical factors, including BMI, WHR, hypertension, HDL and LDL cholesterol, total cholesterol and TG levels were further added in model 3. The median of each group for age at menopause was also included as a continuous variable for computing the P value for linear trend. We took menopausal age as continuous

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