



Hypertension and age at onset of natural menopause in Korean postmenopausal women: Results from the Korea National Health and Nutrition Examination Survey (2008–2013)

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ABSTRACT

Objectives: Menopause is a natural phenomenon of aging, although the timing and management of menopause can significantly affect a woman's quality of life. It is therefore important to identify measures to ensure a healthy menopause. We set out to investigate the association between hypertension and early menopause in Korean women.

Study design: This cross-sectional study was based on 2008–2013 data from the Korea National Health and Nutrition Examination Survey (KNHANES). Of the 53,829 participants surveyed, 13,584 women were selected. We analyzed the contents of the health interview, health examination, and nutrition survey.

Main outcome measure: The main outcome was defined based on hazard ratios (HR) to identify the effects of hypertension on age at onset of menopause.

Results: Among postmenopausal women ($n = 6650$), the mean age at onset of menopause was 50.4 years. Premenopausal hypertension was statistically significantly associated with age at menopause, oral contraceptive usage, household income, education level, occupation, marital status and smoking and drinking habits. With lower age at diagnosis of hypertension, HRs for menopause tended to be higher, and hypertension diagnosed before age 40 years conferred a statistically significantly higher HR (Model 1, HR = 2.32, 95% CI = 1.87–2.88; Model 2, HR = 2.31, 95% CI = 1.86–2.86; Model 3, HR = 2.23, 95% CI = 1.80–2.77; Model 4, HR = 2.00, 95% CI = 1.52–2.63).

Conclusion: Premature menopause is strongly associated with lifestyle factors, in combination with incomplete management of chronic diseases. Our findings support the hypothesis that younger age at diagnosis of hypertension is associated with younger age at onset of menopause in Korean women.

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1. Introduction

Menopause is characterized by a gradual decrease in estrogen secretion, with significant implications on overall health and well-being [1]. Menopausal symptoms become evident upon initiation of the menopausal transition, which is characterized by

changes in menstruation and musculoskeletal function, as well as other physiological and psychological symptoms [2]. The subsequent transition into the post-menopausal phase is associated with a sharp rise in the incidence of diabetes mellitus [3], cardiovascular disease [4], and osteoporosis [5], with significant impacts on quality of life. According to the World Health Organization (WHO), by 2030 there are expected to be some 1.2 billion postmenopausal women worldwide, with 47 million women becoming postmenopausal per year [6]. Among Korean women, the average age at onset of natural menopause was 49.7 years in 2014; given that their average life expectancy is 84.6 years, around 40% of their life span will be spent in the postmenopausal state [7].

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A wide range of lifestyle choices and environmental influences have been shown to lower the age at onset of menopause, among which smoking [8,9], occupation [10], education [11], obesity [12], alcohol consumption [13], and nutrition [14] are the most important. Of these, smoking is the only factor associated with premature ovarian insufficiency and early menopause. Co-morbidities, such as diabetes mellitus [15], hypercholesterolemia [16], and myocardial ischemia [17], have also been associated with premature menopause; however, the results of studies are inconsistent. A decrease in total serum cholesterol levels during premenopause was statistically significantly associated with later age at onset of menopause. Decreasing blood pressure was associated with a later menopausal age in one study, but this association was not statistically significant [18].

In Korea, hypertension is the most significant risk factor for cardio- and cerebrovascular disease. Not only does the prevalence of hypertension increase drastically after the age of 50 years, but also the incidence of hypertension in women surpasses that of men in their 60s [19]. Although the age at diagnosis of hypertension has been trending downwards for years, general awareness and overall cure rates remain low, and so a larger, multifaceted approach is required to the prevention of this chronic disease.

Studies examining the frequency of diabetes mellitus and metabolic syndrome after menopause have been performed, although these studies have not directly addressed the association between chronic disease and menopause in Korea. Here, we used population-based public health data to identify risk factors, such as socioeconomic status and lifestyle, associated with age at onset of menopause and analyzed the effect of hypertension on the timing of menopause. Through this study we sought to develop a model of menopause onset in Korean women and to identify steps that could be taken at a national level to improve health outcomes for millions of premenopausal women.

2. Methods

2.1. Data sources and oversight

The Korea National Health and Nutrition Examination Survey (KNHANES) was initiated in 1998 by the Korea Centers for Disease Control and Prevention as a yearly survey of patient health. KNHANES is a cross-sectional, representative, and reliable study providing a basic overview of the health of the Korean population, which can be used to inform health policy. Every year, around 4000 stable households (>1 year in duration) are selected randomly using a pre-defined sampling method that accurately records age, gender, and other factors nationwide. All participants provide informed, written consent authorizing use of their data for the duration of the study. The survey is made up of three parts: a health interview, a health examination, and a nutrition survey. All surveys are performed using self-administered structured questionnaires. Statistical overviews are considered representative of the Korean population and are provided to the WHO and the Organization for Economic Cooperation and Development. The data are also used for domestic health policy development and epidemiological studies [20]. This study was approved by the Korea Centers for Disease Control and Prevention. Additional oversight in terms of study design was provided by the Institutional Review Board.

2.2. Study population

We used KNHANES data collected between 2008 and 2013. Initial screening revealed 53,829 potential subjects who provided health-related information between 2008 and 2013, of whom 23,161 were over 18 years of age. Among them, 5801 were

excluded from the analysis due to surgical menopause, along with 318 women with oophorectomy, 255 diagnosed with cancer of the uterine cervix, and 1056 receiving estrogen therapy. Surgical menopause was defined as bilateral oophorectomy, failure of the ovaries due to surgical trauma, and failure of the ovaries due to radiation or chemotherapy. An additional 1407 subjects with incomplete data regarding socioeconomic and other lifestyle factors and 740 patients with incomplete data regarding the diagnosis of hypertension were also excluded, resulting in a final study population of 13,584 for analysis. The flow diagram of the study process is shown in Fig. 1.

2.3. Variables

Clinical covariates were categorized as reproductive, physical, socioeconomic, and lifestyle factors, along with hypertension status. Reproductive and physical factors included menopause status, age at onset of menopause, number of pregnancies, breastfeeding status, and premenopausal oral contraceptive use. We used only the baseline information from the survey in these analyses. Women were characterized as underweight (<18 kg/m²), normal (18–24 kg/m²), or obese (≥25 kg/m²) according to the standard body mass index (BMI) scale. Socioeconomic and lifestyle factors included household income (low, middle-low, middle-high, high), education level (≤elementary school, middle school, high school, ≥undergraduate), occupation (supervisor/manager, official, service/sales, agricultural/fishery, skilled operator, labor, homemaker/student), and marital status (single, married, separated, widowed, divorced). Smoking status (non-smoking, smoking after menopause, smoking before menopause), alcohol consumption, and physical activity (none, moderate, intense) were also included in this analysis.

2.4. Definition of hypertension before menopause

Hypertension was defined based on the results of a hypertension health survey, with the final diagnosis determined by the attending physician. Age at diagnosis of hypertension was also considered in relation to menopausal age. Premenopausal hypertension was defined as an initial diagnosis of hypertension before the onset of menopause, with patients classified based on the decade of life in which they were first diagnosed (30s, 40s, or 50s). In this study it was divided into two groups depending on whether hypertension was diagnosed before or after menopause.

2.5. Endpoints

The primary goal of this study was to examine the effect of premenopausal hypertension on age at onset of menopause. These data were used to calculate the hazard ratio (HR) for hypertension on age at menopause onset.

2.6. Statistical analysis

There were no missing values for reproductive, physical, socioeconomic, and lifestyle factors and hypertension factors among the 13,584 subjects included in the analyzed dataset. All characteristics of the study groups categorized by premenopausal hypertension status were summarized as counts and percentages for qualitative variables and as means and standard deviations (SD) for quantitative variables. Group comparisons were performed using the chi-square test for qualitative variables and the independent *t*-test or non-parametric equivalents for quantitative variables as appropriate, following the normality test and equivalent variance test using the Kolmogorov-Smirnov test and Levene's test.

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