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Progression from prehypertension to hypertension and risk of cardiovascular disease

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ABSTRACT

Background: Subjects with prehypertension (pre-HT; 120/80 to 139/89 mm Hg) have an increased risk of cardiovascular disease (CVD); however, whether the risk of pre-HT can be seen at the pre-HT status or only after progression to a hypertensive (HT; ≥140/90 mm Hg) state during the follow-up period is unknown.

Methods: The Jichi Medical Cohort study enrolled 12,490 subjects recruited from a Japanese general population. Of those, 2227 subjects whose BP data at baseline and at the middle of follow-up and tracking of CVD events were available (median follow-up period: 11.8 years). We evaluated the risk of HT in those with normal BP or pre-HT at baseline whose BP progressed to HT at the middle of follow-up compared with those whose BP remained at normal or pre-HT levels.

Results: Among the 707 normotensive patients at baseline, 34.1% and 6.6% of subjects progressed to pre-HT and HT, respectively, by the middle of follow-up. Among 702 subjects with pre-HT at baseline, 26.1% progressed to HT. During the follow-up period, there were 11 CVD events in normotensive patients and 16 CVD events in pre-HT patients at baseline. The subjects who progressed from pre-HT to HT had 2.95 times higher risk of CVD than those who remained at normal BP or pre-HT in a multivariable-adjusted Cox hazard model.

Conclusion: This relatively long-term prospective cohort study indicated that the CVD risk with pre-HT might increase after progression to HT; however, the number of CVD events was small. Therefore, the results need to be confirmed in a larger cohort.

1. Introduction

Prehypertension (pre-HT), defined as a blood pressure (BP) of 120–139/80–89 mm Hg, has been considered to be associated with risk of cardiovascular disease (CVD).[1–3] Therefore, lifestyle modification interventions in subjects with pre-HT have been performed. Additionally, the results of the Trial of Preventing Hypertension (TROPHY) study,[4] in which candesartan was administered to subjects with pre-HT, have raised the question of whether or not antihypertensive treatment for pre-HT is necessary.

We previously reported that pre-HT at baseline was associated with a 45% higher risk of CVD events than normal BP after adjusting for traditional CVD risk factors. In the population evaluated in this study, the risk of CVD among pre-HT patients was increased, especially among non-elderly subjects, after more than 5 years of follow-up,[5] suggesting that the risk of pre-HT might be seen after their BP progressed to HT. However, it was not clear how their BP had changed by the middle of the follow-up period.

Therefore, the purpose of this study is to clarify whether the CVD risk of pre-HT can be seen in subjects with or without progression to HT among study subjects for whom BP data were available in the middle of the follow-up period.

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2. Methods

2.1. Subjects

The Jichi Medical School (JMS) Cohort Study has been conducted in 12 rural areas across Japan since 1992. The study subjects were enrolled from the medical checkup system for CVD in accordance with the Health and Medical Service Law for the Aged. A municipal government office in each community sent invitations to all dwelling adults.

The present study, a population-based prospective cohort study, enrolled 12,490 subjects at baseline between April 1992 and July 1995 to investigate risk factors for CVD, including myocardial infarction (MI) and stroke. After the exclusion of 442 subjects with insufficient BP information, 746 subjects with a history of receiving medication for HT, 159 with a history of CVD, 52 subjects with atrial fibrillation by ECG at baseline, and 91 who could not be completely tracked for CVD events were excluded at follow-up. Therefore, the total number of baseline subjects whose CVD risk was able to be evaluated was 11,000. Although we need BP data at the middle of follow-up to evaluate the risk of BP progression in this study, the middle BP data could be obtained from only seven areas (Iwaizumi, Kuze, Takasu, Wara, Sakugi, Ainoshima, and Akaike). Therefore, we additionally excluded subjects for whom no information had been collected in 1999 (8127), those who were unable to provide sufficient information about BP in 1999 (613), and those in whom CVD had already occurred before 1999 (33). After applying these exclusions, the eligible sample for the current study consisted of 2227 subjects.

This study was approved by the Institutional Review Board of Jichi Medical University School of Medicine and written informed consent was obtained from all subjects.

2.2. Blood pressure

BP was measured once using a fully automated device (BP203RV-II; Nippon Colin, Komaki, Japan)[6] placed on the right arm of the subject after a seated 5-min rest period. Subjects were classified as having normal BP (systolic BP [SBP]/diastolic BP [DBP] <120/80 mm Hg), pre-HT (SBP 120–139 mm Hg and/or DBP 80–89 mm Hg), or HT (SPB/DPB ≥140/90 mm Hg or medicated for HT) according to the definitions of the Joint National Committee 7 (JNC7). Subjects who used antihypertensive medications at baseline were classified as having HT.

BP data at follow-up were obtained in 1999 from seven areas. The subjects were residents aged 40–69 years in five areas, those aged >35 years in one area, and those aged 20–90 years in another area. We could not obtain information about medications for HT in 1999, so we applied the information about the administration of antihypertensive medications at baseline to categorize the BP group in 1999.

2.3. Variables

Obesity was defined as body mass index (BMI) ≥25 kg/m^2. Total cholesterol levels were measured using an enzymatic method (Wako, Osaka, Japan; interassay coefficient of variability [CV]: 1.5%). We defined hyperlipidemia as total cholesterol ≥240 mg/dL or being medicated for hyperlipidemia. Blood glucose was measured using an enzymatic method (Kanto Chemistry, Tokyo, Japan; interassay CV: 1.9%). We defined impaired glucose tolerance (IGT) as fasting blood glucose levels between 100 and 125 mg/dL or postprandial glucose levels between 140 and 199 mg/dL. We defined diabetes mellitus (DM) as fasting blood glucose levels ≥126 mg/dL or a postprandial glucose levels ≥200 mg/dL.

Trained interviewers obtained medical history and lifestyle by using a standardized questionnaire. Subjects whose father or mother had HT were defined as having a family history of HT. Smoking status was classified as current smoker or not. An alcohol habit was defined as drinking more than 20 g of alcohol per day for ≥4 days per week.

2.4. Follow-up

The annual medical checkup system was also used to follow the subjects. At each follow-up, medical records were checked to determine whether the subjects had stroke or MI events. We contacted those who did not come to the health checkup by mail or phone. Public health nurses also visited them to obtain additional information. If the subjects were suspected to have developed stroke, duplicate computer tomography scans was performed, while electrocardiograms were performed for those suspected to have developed MI.

2.5. Diagnostic criteria

Stroke was defined as the onset of a focal and nonconvulsive neurological deficit lasting more than 24 h.[7] MI was defined based on the World Health Organization Multinational Monitoring of Trends and Determinants in the Cardiovascular Disease (MONICA) Project criteria.[8] A diagnosis committee consisting of one radiologist, one neurologist, and two cardiologists diagnosed stroke and MI independently.

2.6. Statistical analysis

Differences in mean values among the normal BP, pre-HT, and HT groups were tested using analysis of variance. Tukey's honestly significant difference test was used for intergroup differences. Differences in percentages among these groups were estimated using a chi-square test. The Kaplan-Meier method was applied for each BP group, and comparisons were made using the log-rank test. P values were calculated using the log-rank test. We used the multivariable adjusted Cox hazard model as a tool to assess the risk of CVD. Statistical analysis was performed using SPSS ver. 16.0 (SPSS Inc., Chicago, IL, USA). P values < 0.05 were considered to indicate statistical significance.

3. Results

3.1. Subjects

The characteristics of the subjects in the whole JMS study population have been reported previously.[9] Of these, BP data were available for 2227 subjects during the middle of the follow-up period for this study. The prevalence rates of subjects with normal BP, pre-HT, and HT by the classifications of JNC7 were 31.7% (n = 707), 31.5% (n = 702), and 36.7% (n = 818), respectively. Of the 2227 subjects included in the present analysis, 37.5% (n = 836) were males. The mean (standard deviation) for age was 56.0 (10.1) years. Subjects aged 65 years or older (n = 486) constituted 21.8% of the sample. The percentage of subjects with obesity was 23.8% (n = 529). The prevalence rates of hyperlipidemia, IGT, and diabetes were 9.6% (n = 214), 15.5% (n = 346), and 3.5% (n = 79), respectively. The percentage of subjects with an alcohol drinking habit was 19.8% (n = 441), and the percentage of subjects who currently smoked was 18.9% (n = 442). The percentage of subjects using hypertensive drugs was 13.1% (n = 291). The number of area dwellings were 688 (30.9%) for Wara, 576 (25.9%) for Takasu, 291 (13.0%) for Iwaizumi,