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ORIGINAL ARTICLE

Impact of hypertension on the lifetime risk of coronary heart disease

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The lifetime risk estimate conveys the probability of disease in the remaining lifetime for an index age. These estimates may be useful for general audience-targeted knowledge translation activities against hypertension. There are only a few reports on the impact of hypertension on the lifetime risk of cardiovascular events. The Suita Study, a cohort study of urban residents, was established in 1989. We included all participants who were coronary heart disease (CHD) free at baseline. Age (in years) was used as the timescale. Age-specific incidence rates were calculated with the person-year method within 5-year bands. We estimated the sex- and index-age-specific lifetime risk of first-ever CHD, taking the competing risk of death into account. We followed 5834 participants from 1989 to 2007 for a total of 75 387.5 person-years. At age 45 years, the competing risk of death-adjusted lifetime risk for all CHD for men was 14.12% for normotensive men and 26.95% for hypertensive men. The competing risk of death-adjusted lifetime risk for all CHD at 45 years of age for women was 6.21% for normotensive women and 14.85% for hypertensive women. This increased lifetime risk of CHD for hypertensive patients was observed among both men and women across all index ages. Although the overall lifetime risk of CHD was lower than in the Western population, hypertension showed a significant effect on the residual lifetime risk of CHD among Japanese middle-aged men and women. This easy-to-understand knowledge may be used as an important index to assist public health education and planning.
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INTRODUCTION

Although the incidence and mortality of coronary heart disease (CHD) in Japan are reported to be among the lowest of all industrialized countries,[1–4] in the setting of major dietary changes and worsening cardiovascular risk factors, some recent reports have suggested an increasing trend of CHD in the Japanese population.[5–8] With the aging of the population and the presence of unfavorable cardiovascular risk factors, CHD is likely to be an increasingly important health burden in Japan. Therefore, CHD prevention activities deserve important attention. One major modifiable risk factor that can be targeted for prevention at the population level is high blood pressure (BP) or hypertension.

Effective risk communication is an important component of disease prevention and is increasingly seen as crucial to disease control efforts. Hypertension is a modifiable risk factor of CHD,[9,10] and the effect of hypertension on the burden of CHD needs to be presented in an easy-to-understand way to lay audiences, including at-risk populations, patient populations, health policy makers and health educators. An estimation of the lifetime risk of CHD, which provides an absolute risk assessment, may be an important tool for knowledge translation because lifetime risk is more easily comprehensible by lay audiences who are not numerically savvy enough to understand conventional measures of disease burden. In this study, we estimated the effect of hypertension on the short-term risk, intermediate-term risk and lifetime risk of CHD in an urban population in central Japan.

MATERIALS AND METHODS

Lifetime risk estimates

The lifetime risk is an epidemiological measure that articulates the probability of a disease event in the remaining lifespan for a given index age. The basis of the estimation is the cumulative absolute incidence that indicates the cumulative risk of an event over the residual lifetime. In the context of estimating the lifetime risk using a cohort study, the hypothetical remaining lifetime can be determined based on the duration of survival of the study participants. Participants contribute information for each age attained free of disease during their follow-up. Lifetime risks are conventionally estimated by

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treating death as a competing risk event because competing mortality attenuates the actual cumulative risk of the event of interest.[11,12] Using the incidence and death information from the study cohort, a double-decrement approach is taken to estimate lifetime risk.[11,12]

Study sample

The Suita study, a cohort study for cardiovascular diseases among urban residents, was established in 1989. The details of this study have been described elsewhere.[13–16] In brief, the cohort was formed from randomly sampled Suita city residents aged 30–79 years, stratified by sex and age (10-year increments). From this sample pool, 6483 men and women participated in a baseline survey (participant rate 53.2%) at the National Cardiovascular Center between September 1989 and March 1994. After excluding participants who lacked baseline information or were lost to follow-up ($n=602$) and participants who had a previous history of CHD ($n=47$), data from the remaining 5834 participants (2759 men and 3075 women) were included in the analysis (Figure 1). The Institutional Review Board of the National Cardiovascular Center approved this cohort study.

Measurement of BP and categories

The measurement of BP has been described elsewhere.[17] In brief, well-trained physicians measured the BP of each individual three times in a seated position using a mercury column sphygmomanometer, an appropriately sized cuff and a standard protocol. Before the initial BP reading was obtained, the participants were seated at rest for at least 5 min. Systolic and diastolic were recorded as the average of the second and third measurements, which were taken >1 min apart. Hypertension was defined as a systolic BP $\geqslant$ 140 mm Hg, a diastolic BP $\geqslant$ 90 mm Hg and/or the use of antihypertensive medication. Participants with a systolic BP $<$ 140 mm Hg and a diastolic BP $<$ 90 mm Hg were defined as normotensive. When the systolic and diastolic pressures fell into different categories, the higher category was selected for the purposes of classification.

End point ascertainment

The end points of the present study were as follows: (a) the first CHD event, (b) death, or (c) 31 December 2007. The first step in the survey for CHD involved checking the health status of all participants by repeated clinical visits every 2 years and by yearly questionnaires sent by mail or conducted over telephone. The second step involved reviewing the in-hospital medical records of participants who were suspected of having CHD. Registered hospital physicians or research physicians who were blinded to the baseline information performed the reviews. The criteria for definite and probable acute myocardial infarction were defined according to the criteria of the MONICA (Monitoring Trends and Determinants of Cardiovascular Disease) project.[18–20] To complete the surveillance for fatal myocardial infarction, a systematic examination of death certificates was conducted. In addition to acute myocardial infarction, the criteria for the diagnosis of CHD included sudden cardiac death within 24 h after onset of acute symptoms or CHD followed by coronary bypass or angioplasty.[15] Identifying all other deaths during the follow-up involved regular periodic searches of death certificates for Suita city residents by accessing the National Vital Statistics database with the permission of the Management and Coordination Agency of Japan. It is mandatory to register any death in the Japanese family registry through the local authority, which compiles such records encompassing all Japanese citizens within their jurisdiction. The underlying causes of death were coded according to the Ninth International Classification of Diseases to the end of 1994 and according to the Tenth International Classification of Diseases from the beginning of 1995.

Statistical analysis

Age (in years) was used as the timescale.[11,12] Follow-up began at each patient's baseline age. Participants who were aged <40 years at the beginning of the study period entered the sample upon reaching 40 years. The age categories began at the age of 40 years, and the highest age category was set at age $\geqslant 90$ years. The likelihood of death from a particular cause at a given time is simply the product of overall survival until that time. The follow-up ended at CHD occurrence, death or 31 December 2007, depending on which event occurred first.

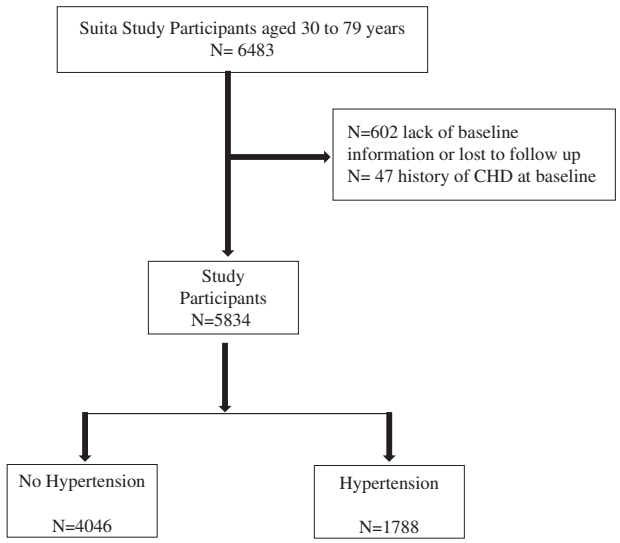

Figure 1 Cohort formation.

We estimated cumulative CHD incidence based on survival to ages 45, 55, 65 and 75 years. The estimation of the cumulative incidence (the outcome of interest) is affected by the competing risk of death owing to other causes. Participants who die of other causes of death during the observation period are treated as censored in the traditional survival analysis, and their potential contribution to the outcome of interest is distributed among subjects who are still at risk. Cause-specific survival is traditionally a net survival measure representing the survival of a specified cause of event in the absence of other causes of death. However, the potential contribution of a participant who has died should not be zero because, to be at risk for an event occurring at a particular time, one must first survive from all causes of death until that time. Treating such participants as censored inflates the estimates of the cumulative incidence. Therefore, to examine the actual risk during one's lifetime, we also estimated the cumulative CHD incidence based on survival to ages 45, 55, 65 and 75 years by using a double-decrement approach, taking into consideration the occurrence of the outcome of interest and all-cause death.[11,12,21–23]

Sex-specific 10-, 20-, 30- and 40-year risks and the lifetime risk for CHD were estimated for CHD-free participants at different index ages. The estimates were calculated using a modified survival analysis technique,[12] as in prior reported analyses.[24,25] All statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA).

RESULTS

We included a total of 75 387.5 person-years of observation in this study. During the follow-up period, 204 (137 men and 67 women) participants had incident CHD. Table 1 shows the basic characteristics of the participants with different hypertension statuses at baseline. In the baseline survey, 33.89% of men and 27.74% of women had hypertension. Among men, 59.57% of participants had stage 1 hypertension and 33.90% had stage 2 hypertension. Among women, 56.98% of participants had stage 1 hypertension and 32.83% had stage 2 hypertension. Hypertensive patients were generally older and had higher mean plasma glucose and higher total blood cholesterol levels. These differences were observed in both men and women.

Table 2 presents the 10-, 20-, 30- and 40-year risks and the lifetime risk of CHD according to the presence of hypertension in men and women of various index ages. The lifetime risk of CHD, accounting for the competing risk of death, at 45 years of age for men without hypertension was 14.12%, whereas the lifetime risk of CHD for hypertensive men of 45 years age was 26.95%. We observed a graded

Table 1 Baseline characteristics of Suita study participants with different hypertension status

		Blood pressure categories	
Gender	*Variables*	*No hypertension*	*Hypertension*
Men	Age, years (s.d.)	53.2 (13.3)	61.2 (11.5)
	BMI, kg m^{-2} (s.d.)	22.5 (2.8)	23.4 (3.1)
	Height, cm (s.d.)	165.8 (6.3)	163.9 (6.0)
	Weight, kg (s.d.)	62.1 (9.0)	63.0 (10.1)
	Plasma glucose, mg dl^{-1} (s.d.)	99.6 (18.6)	103.5 (20.7)
	Total cholesterol, mg dl^{-1} (s.d.)	199.5 (33.3)	204.7 (35.1)
	Serum creatinine, mg dl^{-1} (s.d.)	0.9 (0.2)	0.9 (0.2)
	Smoking, *n* (%)		
	Never smoker	340 (18.6)	171 (18.3)
	Current smoker	978 (53.6)	403 (43.1)
	Ex-smoker	485 (26.6)	341 (36.5)
	Unknown	21 (1.2)	20 (2.1)
	Drinking, *n* (%)		
	Never drinker	395 (21.7)	175 (18.7)
	Current drinker	1340 (73.5)	699 (74.8)
	Ex-drinker	69 (3.8)	44 (4.7)
	Unknown	20 (1.1)	17 (1.8)
Women	Age, years (s.d.)	51.3 (12.6)	62.6 (9.6)
	BMI, kg m^{-2} (s.d.)	21.8 (3.0)	23.5 (3.5)
	Height, cm (s.d.)	153.4 (5.8)	150.5 (5.7)
	Weight, kg (s.d.)	51.2 (7.6)	53.3 (8.9)
	Plasma glucose, mg dl^{-1} (s.d.)	94.5 (14.9)	101.7 (20.7)
	Total cholesterol, mg dl^{-1} (s.d.)	208.3 (37.5)	225.0 (36.9)
	Serum creatinine, mg dl^{-1} (s.d.)	0.7 (0.2)	0.7 (0.3)
	Smoking, *n* (%)		
	Never smoker	1801 (81.1)	712 (83.5)
	Current smoker	295 (13.3)	68 (8.0)
	Ex-smoker	78 (3.5)	34 (4.0)
	Unknown	48 (2.2)	39 (4.6)
	Drinking, *n* (%)		
	Never drinker	1398 (62.9)	578 (67.8)
	Current drinker	740 (33.3)	231 (27.1)
	Ex-drinker	38 (1.7)	14 (1.6)
	Unknown	46 (2.1)	30 (3.5)

Abbreviation: BMI, body mass index.

Table 2 Age- and sex-specific 10-, 20-, 30- and 40-year and lifetime risk estimates for coronary heart disease by the presence of hypertension (adjusted for competing risk of death)

Sex	*Index age (years)*	*Short- and intermediate-term risk*	*No hypertension (%)*	*Hypertension (%)*
Men	45	10-year risk	0.83 (0.11–1.56)	1.08 (0.00–2.56)
		20-year risk	2.37 (1.18–3.55)	6.39 (3.46–9.32)
		30-year risk	4.94 (3.24–6.63)	11.65 (8.20–15.10)
		40-year risk	8.98 (6.53–11.42)	18.77 (14.70–22.84)
		Lifetime risk	14.12 (9.57–18.67)	26.95 (18.10–35.88)
	55	10-year risk	1.56 (0.60–2.52)	5.48 (2.83–8.12)
		20-year risk	4.17 (2.60–5.74)	10.90 (7.63–14.17)
		30-year risk	8.27 (5.88–10.66)	18.25 (14.27–22.22)
		Lifetime risk	13.49 (8.91–18.07)	26.67 (17.56–35.78)
	65	10-year risk	2.72 (1.41–4.04)	5.75 (3.50–8.00)
		20-year risk	7.01 (4.70–9.32)	13.54 (10.07–17.00)
		Lifetime risk	12.46 (7.76–17.15)	22.47 (13.04–31.89)
	75	10-year risk	5.05 (2.77–7.33)	9.59 (6.20–12.98)
		Lifetime risk	11.47 (6.12–16.81)	20.59 (9.25–31.94)
Women	45	10-year risk	0.23 (0.00–0.56)	1.97 (0.00–4.78)
		20-year risk	0.47 (0.01–0.93)	2.78 (0.00–5.77)
		30-year risk	1.01 (0.31–1.70)	5.89 (2.58–9.19)
		40-year risk	4.89 (2.75–7.02)	10.25 (6.48–14.03)
		Lifetime risk	6.21 (3.39–9.04)	14.85 (9.88–19.82)
	55	10-year risk	0.24 (0.00–0.57)	0.81 (0.00–1.92)
		20-year risk	0.78 (0.16–1.41)	3.94 (1.99–5.88)
		30-year risk	4.72 (2.57–6.87)	8.33 (5.53–11.13)
		Lifetime risk	6.07 (3.22–8.92)	12.95 (8.57–17.33)
	65	10-year risk	0.56 (0.01–1.11)	3.24 (1.57–4.91)
		20-year risk	4.63 (2.43–6.82)	7.79 (5.10–10.48)
		Lifetime risk	6.01 (3.09–8.94)	12.58 (8.17–16.99)
	75	10-year risk	4.28 (2.04–6.52)	4.93 (2.57–7.28)
		Lifetime risk	5.74 (2.71–8.77)	10.11 (5.62–14.60)

NB: The short-term and lifetime risk are presented in percentages (%).

increase in CHD risk with increasing age cutoffs. For CHD, the competing risk of death-adjusted 10-year risk at the age of 45 years for normotensive individuals was 0.83%, and this value increased across the 20-, 30- and 40-year risk categories to 2.37, 4.94 and 8.98%, respectively. This phenomenon was observed in both genders and at all index ages.

DISCUSSION

In this urban community-based population, we observed that the residual lifetime risk of CHD is significantly affected by hypertension in men and women of middle age. Individuals with normal BP have a lower lifetime risk of CHD than individuals with hypertension. For all index ages, among both men and women, the lifetime risk of CHD was nearly twice as high for hypertensive individuals than for normotensive individuals.

Overall, our estimated lifetime risk of developing CHD in Japanese population was lower than the estimates reported from Western populations. The authors of the Framingham study reported the lifetime risk of CHD to be 46.9% for men and 31.1% for women at the age of 50 years.[26] The lifetime risk of CHD in men was 34.5% in the Physicians' Health study.[25] Although there are a number of reports regarding the lifetime risks of stroke, CHD, heart failure and atrial fibrillation,[22,23,26–29] only a few prior reports have presented the effect of hypertension on the lifetime risk of CVD; but those reports were mostly on stroke.[30–33] A recent publication from the United Kingdom based on an analysis of the electronic records of 1.25 million people from 1997 to 2010 reported that people aged $\geqslant 30$ years with hypertension have a higher lifetime risk of angina, myocardial infarction, heart disease death and cardiac arrest/sudden cardiac death than people with normal BP.[30] Another study of seven US cohorts pooled together estimated that increases or decreases in BP in middle age were associated with higher and lower remaining lifetime risks of CHD.[31] Studying 61 585 men and women for 700 000 person-years, it was reported that the lifetime risk of CHD increased with increasing baseline BP categories for men and women. The lifetime risks of CHD for men aged 55 years were 29.0% for normal BP, 35.4% for prehypertension and 39.6% for hypertension. For women, the corresponding lifetime risks for normal BP, prehypertension and hypertension were 18.3, 23.4 and 28.8%, respectively.[31]

The strengths of our study include the use of a population-based cohort, the prospective ascertainment of end points using rigorous standardized and previously validated clinical diagnostic criteria and the completeness of CHD event and mortality ascertainment. A limitation of our study is the small sample size with regard to outcomes. Because of the small number of outcomes, we could not further explore the effect of stage 1 and stage 2 hypertension on the lifetime risk of CHD.

Some things should be considered while interpreting our observed estimates. The Suita cohort is based on an urban population; therefore, the estimates may not represent the overall Japanese population. However, Japan has a high urbanization rate, and in an urban environment, changes in lifestyle factors associated with the risk with CHD are more prominent. Therefore, we believe that our findings of high lifetime risk of CHD in an urban population represents the setting in which a large part of the Japanese population lives. Furthermore, the time period and birth cohort effects may limit the external validity of our results. Temporal trends in life expectancy, risk factor prevalence and control among the study population, disease awareness and the sensitivity of diagnostic tests may alter the lifetime risk of CHD.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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