[Environmental Health and Preventive Medicine 1, 206-210, January, 1997]

Original Article

Risk Estimation for Hypertension Based on Follow-up Health Examination Data in a Small Village in Kumamoto Prefecture, Japan

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Abstract

The estimation of risk for incidence of hypertension was carried out by follow-up study in a small village in Kumamoto Prefecture, Japan (N=750, 48.2±15.2months). The most significant risk in both sexes was blood pressure at entry. As for other risks, age, total cholesterol, and BMI in females were significant risks for systolic and diastolic blood pressure changes to greater than the borderline level. These factors in males were not significant. From the results of analysis using Cox's proportional hazards model, drinking in males was shown to be a significant risk for diastolic change, and in females for systolic change. It was concluded that excessive drinking in both sexes and obesity in females led to important health problems associated with hypertension among the subjects of the study.

Key words: Risk estimation, Health examination data, Hypertension, Alcohol consumption, Obesity

Introduction

Annual medical examinations have been performed in Japan since 1982 based on the Health and Medical Service Law for the Aged. This law has contributed to the active promotion of regional primary health care. Stroke prevention is one of the main purposes of these examinations, because stroke is a major health problem associated with mortality and disability, especially in areas with aging populations [1, 2]. There is a general consensus among reserchers that hypertension is a strong risk factor for stroke [3-8]. As a result, many strategies to reduce hypertension have been developed, such as limitation of salt intake or use of antihypertensive drugs. This has resulted in some reports of a decrease in the incidence and mortality of stroke, especially cerebral hemorrhage [3, 4, 9, 10], due to the control of hypertension in various areas in Japan.

From the viewpoint of regional health promotion and disease prevention, we decided to apply that the health examination data not only to the identification of health problems in a specific area but also to estimation of risk and prediction of incidence of diseases. The present study is unique in that we focused mainly on hypertensive changes of blood pressure. This is an important regional health problem for stroke prevention. The purpose of this investigation was to identify risk factors by estimating the risk of incidence of hypertension as the most probable risk factor for stroke in a community using a follow-up study.

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Materials and Method

Study cohort

Subjects were older than 40 years of age and participated in this annual examination at least once betwen 1989 and 1992 (N=1698), in a small village of Kumamoto Prefecture, located in the southern part of Japan. The main industries in this village are small-scale fishery and agriculture. The percentage of residents who participated (≥40years) in the health examinations was nearly 50%. Mean age of the subjects was 60.0±10.4 at entry. All subjects were followed up to analyze the incidence of hypertension or mortality due to other associated diseases, including stroke. The follow-up was from entry (1989-92) up to Aug 31, 1994. A total of 410 subjects (24.1%) were identified as borderline (WHO criteria), and 317 subjects (38.6%) were identified as hypertensive at entry examination. One hundred subjects (5.8%) had had medical care for or a past history of hypertension, and they had normotensive blood pressure at entry examination. Among the subjects, we defined a hypertension-free cohort, which included the subjects who had had no medical treatment

for hypertension and who were identified as normotensive at the entry examination. The number of hypertension-free subjects was 871 (368 males, 503 females). Of them, 121 subjects (67 males, 54 females) participated only once, and therefore could not be followed-up in this study. As a result, 750 subjects were used for analysis. The mean observation period of this cohort was 48.6±15.2 months, and the mean number of times of participation was 4.3±1.4. Subjects who began to use an antihypertensive drug during the observation period were considered to be hypertensive.

Study items

The examination included a questionnaire, physical examination, and collection of blood samples for laboratory analysis. The questionnaire was accomplished by interview with regard to past medical history, present medical care, smoking habits (cigarettes/day × years), alcohol consumption (g/week), and general health status. Systolic and diastolic blood pressure were measured once with an automatic sphygmomanometer (A & D Com. Ltd TM-2510) after rest. Body mass index was calculated as weight [kg]/height [m]^2. Regarding the blood samples, total cholesterol, high density lipoprotein cholesterol, glutamic oxaloacetic transaminase, γ -glutamyl transpeptidase, and blood urea nitrogen were determined according to standard laboratory procedures by the same institute every year. Individual blood sample data were classified into two or three groups (normal, high or low) based on normal limit values defined by the laboratory as shown in Table 2. Diagnosis of hypertension was based on WHO criteria[11].

Table 1 Number of hypertension-free subjects by age, and incidence.

Age	N	Incidence (%)	Observation period until incidence (Mean ± SD) (months)
40-49	194	43 (22.2)	34.0 ± 15.3
50-59	231	70 (30.3)	29.5 ± 15.4
60-69	247	94 (38.1)	30.3 ± 14.4
70-79	69	24 (34.8)	30.5 ± 15.0
80-	9	3 (33.3)	20.0 ± 13.9
Total	750	234 (31.2)	30.6 ± 14.9

Analytic procedures

The incidence of hypertension was defined by the year in which hypertension was identified in the annual examination. The relative risk of incidence was calculated using Cox's proportional hazards model. First, to estimate the age adjusted risk of each factor, categorized variables of each factor were put into the model, which included age as the covariate. Next, multivariate analysis was carried out to adjust for any confounding factors, especially between SBP at entry and other factors. Selection of variables was carried out using a backward stepwise procedure

Table 2 Results of age-adjusted risk for incidence of hypertensive change to greater than the borderline level.

Variables (at entry)	SBP HR	SBP 95%CI		DBP HR	DBP 95%CI	
Male (N=301)						
Age (1 year)	1.019	0.999	1.040	1.018	0.997	1.039
SBP	1.059	1.036	1.083	1.050	1.020	1.082
DBP	1.045	1.018	1.072	1.092	1.050	1.136
TC High (≥220mg/dl)	1.686	0.938	3.032	0.955	0.343	2.660
Low (≤160mg/dl)	0.942	0.605	1.466	1.001	0.543	1.847
HDL (≤40mg/dl)	1.295	0.786	2.132	1.615	0.835	3.124
BUN (≥22mg/dl)	0.848	0.422	1.702	1.358	0.569	3.240
rGTP (≥60IU/l)	0.848	0.366	1.965	1.064	0.374	3.025
GOT (≥40IU/l)	0.926	0.515	1.664	1.462	0.706	3.027
BMI low (≤20.0)	1.019	0.587	1.770	0.484	0.186	1.261
over (≥24.0)	1.550	0.989	2.430	1.153	0.623	2.134
Smoking (1 unit)	0.968	0.911	1.028	0.966	0.886	1.054
Drinking (1 unit)	1.048	0.972	1.131	1.129	1.058	1.205
Female (N=449)						
Age (1 year)	1.034	1.015	1.053	1.030	1.011	1.049
SBP	1.069	1.049	1.090	1.101	1.065	1.138
DBP	1.070	1.047	1.093	1.123	1.083	1.164
TC High (≥220mg/dl)	1.509	1.000	2.276	1.922	1.033	3.577
Low (≤160mg/dl)	0.831	0.533	1.293	0.811	0.413	1.593
HDL (≤40mg/dl)	1.174	0.708	1.945	1.676	0.810	3.468
BUN (≥22mg/dl)	0.774	0.314	1.950	0.940	0.225	3.922
rGTP (≥60IU/l)	1.238	0.172	8.892	2.549	0.349	18.585
GOT (≥40IU/l)	0.800	0.458	1.396	0.504	0.181	1.399
BMI low (≤20.0)	0.509	0.291	0.890	0.234	0.071	0.771
over (≥24.0)	1.547	1.062	2.254	1.079	0.603	1.928
Smoking (1 unit)	0.935	0.683	1.281	1.097	0.760	1.581
Drinking (1 unit)	1.325	0.854	2.056	1.385	0.783	2.451

SBP; systolic blood pressure, **DBP**; diastolic blood pressure, **TC**; total cholesterol, **HR**; hazards ratio, **95%CI**; 95% confidence interval, **Smoking**; cigarettes/day × year/100 (unit), **Drinking**; g/week/100 (unit).

(log likelihood). SPSS for Windows (6. 1. 3) was used for statistical analysis in this study. Exclusion by missing values was carried out in each analysis concerned with drinking (13; males, 22; females) and smoking (39; males, 21; females); therefore the number of subjects differed in the analysis.

Results

Among the cohort subjects, we found that blood pressure had increased beyond borderline levels in 234 subjects at follow-up (Table 1). Of these, 133 showed elevated systolic blood pressure, diastolic pressure was increased in 11, and both were elevated in 90. Table 2 shows the detailed results of univariate estimation of the risk of incidence of systolic and diastolic hypertension. Both systolic and diastolic blood pressure at entry were significant for the incidence of both hypertensive changes. The other significant risk factors associated with systolic change were age, total cholesterol (≥220mg/dl) and BMI (≥24.0, ≤20.0) in females. In contrast, age, total cholesterol (≥220mg/dl), and BMI (≥24.0) in males were not significant. The significant risk factor associated with diastolic change was drinking in males; however, drinking in females was not a significant risk for the elevation of systolic or diastolic blood pressure. In females, age, total cholesterol (≥220mg/dl), and low BMI (negative risk) were significant for diastolic change. Table 3 shows the results of multivariate estimation with age, SBP (at entry), total-cholesterol, HDL, BMI, drinking and smoking as the variables. As to systolic change in females, the hazards ratios of total cholesterol and BMI were found not to be significant, and drinking became significant. On the other hand, the hazards ratio of BMI (lower) was also found not to be significant in females, and drinking in males remained significant. Table 4 shows the factors selected in multivariate analysis similar to that in Table 3 after a backward stepwise procedure (log likelihood). Systolic blood pressure at entry was a

Table 3 Results of multivariate estimation of risk for incidence of hypertensive change to greater than the borderline level.

Variables (at entry)		SBP HR	SBP 95%CI		DBP HR	DBP 95%CI	
Male							
Age	(1 year)	1.009	0.987	1.031	0.994	0.962	1.027
TC	(≥220mg/dl)	1.893	0.981	3.653	1.209	0.419	3.490
HDL	(≤40mg/dl)	1.194	0.688	2.070	1.542	0.726	3.276
BMI low	(≤20.0)	1.232	0.675	2.248	0.508	0.174	1.484
over	(≥24.0)	1.154	0.700	1.901	0.734	0.359	1.498
Smoking	(1 unit)	0.991	0.929	1.057	0.978	0.893	1.071
Drinking	(1 unit)	1.042	0.959	1.133	1.132	1.051	1.220
SBP		1.061	1.035	1.087	1.042	1.007	1.078
Female							
Age	(1 year)	1.022	1.001	1.044	0.971	0.938	1.004
TC	(≥220mg/dl)	1.191	0.768	1.848	1.466	0.762	1.024
HDL	(≤40mg/dl)	1.111	0.653	1.891	1.460	0.673	3.166
BMI low	(≤20.0)	0.557	0.301	1.030	0.240	0.057	1.024
over	(≥24.0)	1.394	0.947	2.051	0.907	0.500	1.646
Smoking	(1 unit)	0.911	0.655	1.268	1.035	0.674	1.588
Drinking	(1 unit)	1.649	1.042	2.609	1.713	0.917	3.201
SBP		1.073	1.052	1.095	1.100	1.062	1.140

SBP; systolic blood pressure, **DBP**; diastolic blood pressure, **HR**; hazards ratio, **95%CI**; 95% confidence interval, **TC**; total cholesterol, **Smoking**; cigarettes/day × year/100 (unit), **Drinking**; g/week/100 (unit).

Table 4 Results of multivariate estimation of risk for incidence of hypertensive change to greater than the borderline level after selection by a backward stepwise procedure

Variables (at entry)		SBP HR	SBP 95%CI		DBP HR	DBP 95%CI	
Male							
SBP		1.063	1.038	1.089	1.044	1.010	1.078
TC	(≥220mg/dl)	1.344	0.976	1.849			
Drinking	(1 unit)				1.125	1.048	1.207
Female							
Age	(1 year)	1.025	1.004	1.049			
SBP		1.074	1.053	1.096	1.095	1.059	1.138
BMI low	(≤20.0)	0.589	0.397	0.873	0.343	0.133	0.884
over	(≥24.0)	1.544	1.163	2.051	1.647	0.932	2.910
Drinking	(1 unit)	1.684	1.084	2.618			

SBP; systolic blood pressure, **DBP**; diastolic blood pressure, **HR**; hazards ratio, **95%CI**; 95% confidence interval, **TC**; total cholesterol, **Drinking**; g/week/100 (unit).

common risk factor for systolic and diastolic changes in both sexes. BMI in females was significant for both systolic and diastolic changes. On the other hand, total cholesterol was so for systolic change. Drinking affected systolic changes of females, and diastolic ones of males.

Discussion

In terms of stroke prevention, it is important to estimate the risk of hypertensive change, because both cerebral infarction and hemorrhage have a common risk associated with elevated blood pressure[9,10,12]. Many studies have documented the association between hypertension and some factors such as obesity and drinking. However, most of them were based on cross-sectional study. The studies of Leitshuh et al.[13], and Miura[14] are among the few cohort studies on the incidence of hypertension using a Cox's hazards model. As for the incidence of hypertension, it is hard to compare our results with other studies, because there have been few studies using the same definition of incidence for hypertension. However, Reed et al.[15] reported an incidence of 32% for a 6-year follow-up, which was similar the 31.2% for 5-years follow-up in our study.

This study was based on annual health examination data, which might have resulted in some problems in estimation. The first problem concerns censoring of cases, because it was possible that subjects who became hypertensive might not have participated in follow-up examinations. In this study, the mean observation period was 48.6 months, and the mean number of times of participation was 4.3. These results suggested that most subjects participated once every 1-2 years, and that there was not a very strong influence on estimation by this problem.

As shown in Table 3 and Table 4, both systolic and diastolic blood pressure were significant, which suggested that blood pressure remained a risk even under the borderline level. SBP was included as a covariate in multivariate analysis, because the most incidences of diastolic change followed systolic change or occurred at the same time (91.0%).

The present study showed that drinking in males was a significant risk factor for diastolic hypertension and might also influence systolic hypertension. On the other hand, in females, drinking was not a significant factor either in systolic or diastolic hypertension in univariate analysis. This was probably due to differences in alcohol consumption between males and females; in fact, the mean alcohol consumption in males was 213g/week, but it was only 39.5g/week in females in this cohort. However, multivariate analysis indicated that drinking in females was a significant factor for systolic change just as in males. Many studies have documented the relation between alcohol intake and blood pressure, and the effect of decreasing blood pressure by reduction of alcohol intake[16-21]. Considiering that diastolic blood pressure was a strong risk factor for the incidence and mortality of stroke in the Oslo study[6], excessive drinking appends to be an important health problem in this study area.

Since that BMI in females was found not to be significant by multivariate analysis, there were some confounding factors similar to drinking. It is conceivable that the most probable factors concerned were total cholesterol, BMI, SBP, and drinking. In females, only BMI (≥24.0) was a significant risk for systolic change, and a low BMI (≤20.0) was negatively significant for both systolic and diastolic changes. These results suggested that hypertensive change in females might be mainly due to an overload of the circulation system caused by obesity. There are many studies showing association of blood pressure with hypercholesterolemia and obesity. These results suggest that obesity must be taken into account when considering measures for prevention for hypertension. There was no relation of smoking to hypertension in our study. Recent investigations on the effects on blood pressure of smoking have variously found that it is unrelated[14, 22] to hypertension, related[23], or inversely related[24]. Therefore the effect of smoking remains unclear at present.

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(Received Jun. 4, 1996/Accepted Nov. 22, 1996)