A study of the association between the aortic pulse wave velocity and atherosclerotic risk factors among Japanese Americans in Seattle, U.S.A.

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Abstract

Cardiovascular disease prevention screening was conducted among 1389 Japanese Americans in Seattle, Washington, U.S.A. from 1989 to 1994. The association between atherosclerotic risk factors and the aortic pulse wave velocity (PWV), an indicator of atherosclerosis, was examined by using multiple logistic regression method. Based on a study in 1996 by Suzuki et al. on the association between PWV and atherosclerotic indicators, abnormally high PWV was defined as 8.0 m/sec. and over for those less than 60 years of age and 9.0 m/sec. and over for those 60 years of age and older. Significant odds ratios to estimate the risk for the presence of abnormally high PWV were found in age >or= 60 years (4.31, $p < 0.001$), hypertension (2.00, $p < 0.001$), diabetes (5.65, $p < 0.001$), current drinker (0.44, $p < 0.001$), ex-drinker (0.49, $p < 0.05$), and ex-smoker (1.82, $p < 0.01$) among men. Women showed a similar association: age > or = 60 years (3.03, $p < 0.001$), hypertension (1.94, $p < 0.01$), diabetes (2.47, $p < 0.05$), TC/HDL-C >or= 4.5 (1.98, $p < 0.001$), current drinker (0.47, $p < 0.001$), and ex-drinker (0.45, $p < 0.05$). Our findings are almost identical to those from other studies showing the association between coronary heart disease and its risk factors. The question of whether PWV can be a predictor of atherosclerotic diseases, particularly coronary heart disease, remains to be answered by additional studies. However, PWV may serve as a simple and valuable indicator to estimate the extent and severity of asymptomatic atherosclerosis in the large artery.

I. Introduction

Some researchers have pointed out for a long time that pulse wave velocity (PWV) is closely related to modulus of elasticity of arterial wall[1,2)]. Hasegawa and Otsuka established the experimental and theoretical rationale for aortic pulse wave velocity as a non-invasive and quantitative index reflecting atherosclerosis[3,4)]. Morishita followed up the examinees of PWV measurement for one year and reported that the average PWV measurement of those who developed cerebrovascular and/or cardiovascular diseases (angina, AMI, cerebral infarction, cerebral hemorrhage, subarachnoid hemorrhage and transient ischemic attacks (TIA)) was significantly higher than that of those who did not[5)]. Others reported that an average PWV measurement is significantly higher in patients under treatment of hypertension, diabetes and hypercholesterolemia (60 years old and over) than in healthy normal controls[6~8)]. If PWV serves as an index of atherosclerosis, it can be hypothesized that PWV is also significantly related to risk factors of atherosclerosis. In this study, we tested this hypothesis by applying it to health screening data of Japanese Americans in Seattle, U.S.A.

II. Methods

Participants were recruited by way of informal channels such as advertisements in local community newspapers, billboards in shopping centers and direct mails utilizing directories of the Japanese community compiled by NDPC (Nikkei Disease Prevention Center) soliciting participation in health examinations, because the U.S. has no official resident registry records like Japan. The study subjects thus recruited were 1,389 Japanese Americans aged 20 years old and older who voluntarily participated in preventive cardiovascular disease screening conducted by NDPC in Seattle, Washington, U.S.A. (Prior to 1992, subjects were voluntary participants (about 10%), but after 1993 subjects were randomly selected, about 90% of entire samples). Breakdowns of generation were, 12% for the first generation, 49% for the second generation, 37% for the third generation and 2% for the fourth and above.

Health examinations included PWV, electrocardiogram (EKG), observation of small artery changes in retina, serum lipid and lipoproteins, height, weight, pulmonary function tests and urinalysis. Participants were asked to fill out the self-administered questionnaire including occupation, past medical history, lifestyle and nutrition.

PWVs were measured by medical technicians (who were trained in Japan) using a PWV-200 device (Fukuda Denshi Co., Tokyo, Japan). As illustrated in Figure 1, the time difference between the upstarts of carotid and femoral pulse wave propagation(t) and the time difference between the upstart of the first component of the heart sound II and the notch on propagation of carotid pulse wave (tc) are measured. If the distance between the aortic valve and the pulsation point on femoral artery is denoted as D, then PWV is calculated as $[D \times 1.3/(t+tc)]_p$. Here, D x 1.3 reflects a correction factor considering anatomical structure. PWV values are adjusted at 80 mmHg of diastolic blood pressure (DBP) which is denoted as p because PWV values are highly correlated to DBP.

Lipids and lipoproteins were measured by the Northwest Lipid Research Laboratories of the University of Washington whose quality control is under strict surveillance by CDC. Total cholesterol was measured by the enzymic Abbot spectrum method, and high density lipoprotein cholesterol (HDL) was measured by the dextran sulfate-magnesium precipitation method.

Suzuki, et al. studied the relationship between PWV values and age-specific prevalence of atherosclerotic diseases based on the data involving more than 220,000 subjects[9)]. According to his findings, prevalence of abnormal systolic blood pressure (SBP), arteriolar sclerotic changes of retinal artery and ischemic changes of EKG among those younger than 60 years old with PWV $\geq$8 m/sec and among those 60 years of age and over with $\geq$9 m/sec became significantly elevated than that among all persons of the corresponding age groups with <8 m/sec for and <9 m/sec, respectively. Accordingly, the PWV value was used as a dependent variable and an abnormal PWV value was defined as the one >8 m/sec for those younger than 60 years of age and as the one >9 m/sec for those 60 years of age and older: coded "1" for abnormality and "0" for no abnormality. The following explanatory variables were also dichotomized as follows:

age (≥60:1, <60:0)

sex (male:1, female:0)

hypertension (present:1, not present:0): Hypertension is defined as either SBP≥160 mmHg or DBP≥95 mmHg plus anybody who is taking antihypertensive drugs.

diabetes (present:1, not present:0): History of diabetes is based on responses in self-administered questionnaires.

total cholesterol/HDL cholesterol (≥4.5:1, <4.5:0): Because an average ratio in American men is 4.5, we assumed that the ratio above this signifies an elevated risk of coronary heart disease[10)].

Body Mass Index (BMI) (>27:1, ≤27:0): BMI=body weight (kg)/height(m)^2 and above 27 is defined as obesity.

Drinking habit was classified into three categories: non-drinkers, current drinkers, ex-drinkers, and an odds ratio was calculated with non-drinkers as controls. Likewise, smoking habit was classified into three categories and an odds ratio was calculated with non-smokers as controls.

The relationship between PWV and atherosclerotic risk factors was examined using multiple logistic regression analysis[11)]. We did not adopt linear multiple regression analysis because the relationship between PWV values and atherosclerotic risk factors (e.g., hypertension and diabetes) is not linear and hence inappropriate for linear multiple regression analysis. Multiple logistic regression analysis is preferable for quantitatively estimating the magnitudes of individual risk factors regarding the abnormal PWV findings. All statistical analysis was conducted by using IBM/AT, SPSSPC+V3.0[12)].

III Results

Table 1 shows characteristics of screening participants of Japanese Americans in Seattle. Their average age was 56 years old for both men and women. Average PWV values were 8.0 m/sec for men and 8.1 m/sec for women. Averages of BMI were 25.6 for men and 23.9 for women, indicating that men were slightly heavier than women. Average SBP was higher in men (133 mmHg) than in women (128 mmHg). Although average total cholesterol levels were almost the same for women and for men (226 vs 224 mg/dl), the average HDL cholesterol level for women was higher by 12 mg/dl than for men, making the average of TC:HDL ratios 4.7 for men and 3.8 for women. The TC:HDL ratio for men was greater than 4.5, a threshold above which a risk of myocardial infarction becomes significantly elevated. The sex difference in drinking was large: while men consume 6.0 g of pure alcohol per day, women consume only 1.4 g. Proportion of current drinkers was 65% in men and 46% in women. Proportion of current smokers was 15% in men and 9% in women.

Table 2 indicates distribution patterns of PWV values by age. The distribution of PWV values becomes skewed toward higher age brackets with a wider variation particularly after 50 years old, indicating the increasing individual difference in PWV values as age advances.

Table 3 presents odds ratios (ORs)of abnormal PWV values calculated for each explanatory variable by multiple logistic regression analysis for both sexes combined. An odds ratio (OR) of each variable is adjusted for effects of other variables. ORs for all explanatory variables except BMI and current smokers were significant. The OR of abnormal PWV values for those over 60 years of age was three times that for those younger than 60. The OR for men was 35% less than that for women. OR for hypertension was 2 times that for non-hypertension and OR for diabetics became 3.7 times that for non-diabetics. The OR for those with high (>=4.5) TC/HDL ratios was 1.6 times that for those with low TC/HDL ratios. However, current drinkers had a 50% smaller OR than non-drinkers, and also the OR for former drinkers was almost 50% smaller than that for non-drinkers. On the other hand, the OR for former smokers was elevated by 1.6 times that for nonsmokers.

Table 4 displays ORs for men. The results are similar to the results for both sexes combined in Table 3 except that the risk of elevated TC/HDL was reduced from 1.61 to 1.32 making it insignificant. Table 5 displays ORs for women. It differs from those for men in that the OR for elevated TC/HDL ratios became 1.98 making it significant at $p<0.001$. The reduced risk observed in current and ex-drinkers was held good for women too, with ORs being 0.47 for current drinkers ($p<0.001$) and 0.45 for ex-drinkers ($p<0.05$). However, the slightly elevated ORs observed in current and ex-smokers of women failed to reach statistical significance.

IV. Discussion

Since Japanese Americans are an ethnic minority and there is no resident registry as seen in Japan, it was impossible to conduct a random sampling (based on the census). Study subjects were partially voluntary participants (about 10%) and mostly random-sampled participants in health examinations casting doubt on whether the sample actually represents the Japanese American population residing in and around the Seattle area (King County).In the United States the National Census has been conducted every ten years and its results are published 2-3 years later, which include a distribution of annual household income levels of Japanese Americans in King county. To verify the representativeness of the study sample, we conducted a survey using household income as a proxy variable. We mailed out anonymous questionnaires asking their annual household income in 1994 to be compared with the income reported in the census. A total of 1,117 households (80% of study participants) responded.

Figure 2 compares the distribution of annual household income levels of the study participants with those of the Japanese American population in King county[13]. Although the distribution of the study participants is slightly skewed to higher income brackets, both distribution patterns resemble each other. Considering 5.4% of an annual growth rate in household income during the five-year interval between the census year (1989) and our survey year(1994)[14], the mean household income, $49,000, of the study participants corresponds well to $50,000 of the estimated household income of the Japanese American population in 1994. With these findings, the study participants may well be deemed to represent the Japanese American population at least in terms of their income.

Participants during 1989-92 and those in 1994 did not differ significantly in terms of their characteristics (% of current drinkers: male 63% (1989-1992) vs. 65% (1989-94), female 42% vs. 46%, percent of current smokers: male15% vs.15%, female 10% vs. 9%). Hence it was considered that combining the data from the two periods is appropriate to increase statistical power. For 60 participants who participated in the health examinations in both periods, the first data were included for analysis.

Since the study participants in this study were recruited from volunteers, it might be questioned whether the study participants differ from non-participants in terms of their health status. Unfortunately, we are unable to provide an answer. In this respect, the Honolulu Heart Study conducted in Hawaii investigated the difference between participants and non-participants and revealed that total mortality and CHD incidence were higher in non-participants than in participants[15]. If this finding is also applicable to our study, one may well assume that nonparticipants would be less healthy than participants.

What characterizes Japanese Americans in Seattle can be examined in comparison with the American general population and the Japanese general population. With regards to BMI, the average BMI of Japanese American males (25.6) is close to American men and that of females is close to Japanese women (23.9). The average BMI of American general population (20-74 years old) was 26.3 for men and 26.3 for women[16], and the age-specific average BMI of Japanese general population (20-80 years or over) ranges from 21.0 to 23.2 for men and 21 to 23.4 for women[17]. In this study, obesity was dichotomized as above or below 27[16] to be used as an explanatory variable but failed to demonstrate any significant association with PVW abnormalities in men and demonstrated 1.28, only a slightly elevated non-significant odds ratio in women.

The second characteristics of Japanese Americans in Seattle is that they have a higher average total cholesterol level than American and Japanese general populations: 224.3 mg/dl for men and 226.0 mg/dl for women as compared to the averages of 202 mg/dl for American men and 200 mg/dl for American women[18], 198.6 mg/dl for Japanese men and 207.1 mg/dl for Japanese women[19]. In this study, TC/HDL-C ratio was dichotomized as above or below 4.5 to be used as an explanatory variable and demonstrated a significantly elevated odds ratio of 1.61 for both sexes combined and 1.98 for women but proved to be non-significant in men (1.32) suggesting a gender discriminatory effect of cholesterol on PWV.

Morishita reported that average PWV values in the hypertensives were higher than in controls in every age group[6)]. Also, our results showed that the association between hypertension and prevalence of PWV abnormalities as shown by significant odds ratios of 2.0 for men and 1.94 for women, suggesting strong effects of hypertension on development of atherosclerosis.

Diabetes is a known atherosclerotic risk factor[20,21)] and our study shows highly elevated odds ratios in men (5.7) and women (2.5) of the prevalence of abnormal PWV values for diabetics as compared to non-diabetics. This finding is consistent with the findings by Hasegawa and Morishita that PWV for diabetics is more accelerated than PWV for non-diabetics[22,23)].

Smoking is another known atherosclerotic risk factor[24,25)] but the odds ratios of abnormal PWV values for current smokers were not significant: 1.56 for men and 1.32 for women. As for ex-smokers, the odds ratios were 1.82 ($p<0.01$) for men and 1.38 (NS) for women. It is possible, however, that an extremely low rate of smokers among Japanese Americans in Seattle (15.3% for men and 8.9% for women), in comparison to rates in American general population (27.7% for men and 22.5% for women[26)]) and in native Japanese (59.8% for men and 13.8% for women[27)]), might have weakened the statistical power to reach significance in an odds ratio of abnormally high PWV values for current smokers.

Alcohol consumption among Japanese Americans in Seattle (3.7 g/day/person in pure alcohol in Table 1) was also extremely lower (only one-fifth of) than among Americans and among native Japanese living in Japan (19.9g and 17.9g/day/person, respectively, calculated from published reports[27,28)] in both countries).

Moore and Pearson reported that they had identified studies demonstrating the negative relationship between alcohol consumption and atherosclerosis but no studies showing the positive association after their careful review of pathological studies[29)]. Barboriak[30)], Gruchow[31)] and Pearson[32)] also reported that alcohol consumption and coronary occlusions were inversely correlated. We found that the odds ratio of abnormal PWV values for current drinkers was 50% smaller than that for non-drinkers in both sexes, and such findings are consistent with findings of other previous studies suggesting protective effects of drinking on atherosclerosis. Furthermore, the negative odds ratio observed for ex-drinkers suggests anti-atherosclerotic effects of drinking persists even after drinking cessation. The inverse relationship between coronary heart disease （CHD） and alcohol consumption has been reiterated by numerous studies[29, 33-37)] warranting further investigation in Japanese Americans in Seattle.

Prevalence of abnormal PWV values was 25.8% in men and 28.8% in women. Logistic regression analysis demonstrated that the male-sex factor reduces the risk of abnormal PWV values by 35% (Table 3). Hasegawa reported that the average PWV value was higher in women than in men after 50 years of age based on his age- and sex-specific PWV measurement on healthy Japanese population and attributed such a sex difference to hormonal changes in women passing 50 years of age and healthy survivors' effect (attrition due to atherosclerotic deaths) in men[38]. Such effects may be particularly strong in Japanese Americans in Seattle. The sex ratio (men/women) of Japanese Americans in King county including the City of Seattle over 55 years old was 0.67[39], lower than that of native Japanese of the same age group, 0.8[27]. Although no ready explanation is given to a sharp drop in the male population after 55 years of age in Seattle, the healthy survivors' effects cannot be ruled out as a possible explanation of the low prevalence of PWV abnormalities in men, which may lead to further research.

It is generally accepted that atherosclerotic changes in coronary arteries advance faster in men than in women as evidenced by a sharp sex difference in age-specific CHD mortality below age 70, but our findings suggest that atherosclerotic changes in large arteries differ from coronary atherosclerosis. Current research indicates that atherosclerosis of large arteries precedes that of cerebral and coronary arteries[40~42]. Also, the presence of atherosclerosis in large arteries and coronary arteries does not necessarily translate into the onset of CHD, suggesting that causes of CHD are affected by a complexity of other risk factors. Such complex issues may be partly answered by comparing PWV values with EKG readings[43].

In 1984 Hara, et al. reported that the age-specific means of PWV values in Japanese Americans in Hawaii islands were significantly ($p<0.001$) higher than in native Japanese after age 50s[44]. If the findings in Japanese Americans in Hawaii applies to Japanese Americans in Seattle (i.e., their PWV values are higher than those of native Japanese after their 50s), the relationship between PWV and atherosclerotic risk factors could have been overestimated among Japanese Americans leading to statistical significance. We are planning to pursue this hypothesis by comparing our results in Seattle with native Japanese.

The findings obtained from this study in addition to our other studies are summarized as follows: 1) age-specific averages of total cholesterol, LDL cholesterol and triglycerides in Japanese Americans were significantly higher than those of both American and Japanese general populations[45]; 2) age-adjusted prevalence of high PWV abnormalities in Japanese American men is significantly higher than male urban workers in Japan[46]; 3) age-adjusted prevalence of abnormal changes in retinal arteries in Japanese American men was significantly lower than that in male urban workers in Japan[47]; 4) prevalence of coronary heart disease in Japanese American men and women was significantly higher than that in male urban workers in Japan[48]. These observations reflect differences in progress of atherosclerosis and prevalence of related diseases resulting from differences in eating habits, life style and environmental factors between the United States and Japan. Comparative studies of Japanese Americans and native Japanese continue to play an important role in elucidating how environmental factors affect the onset of diseases.

PWV reflects the anatomical severity of atherosclerotic changes in aorta. However, whether or not PWV predicts the onset of atherosclerotic diseases particularly coronary heart disease warrants further investigation. PWV is an effective tool to measure the severity of atherosclerotic changes in a quick and easy manner and to keep patients well informed of their severity of atherosclerotic changes.

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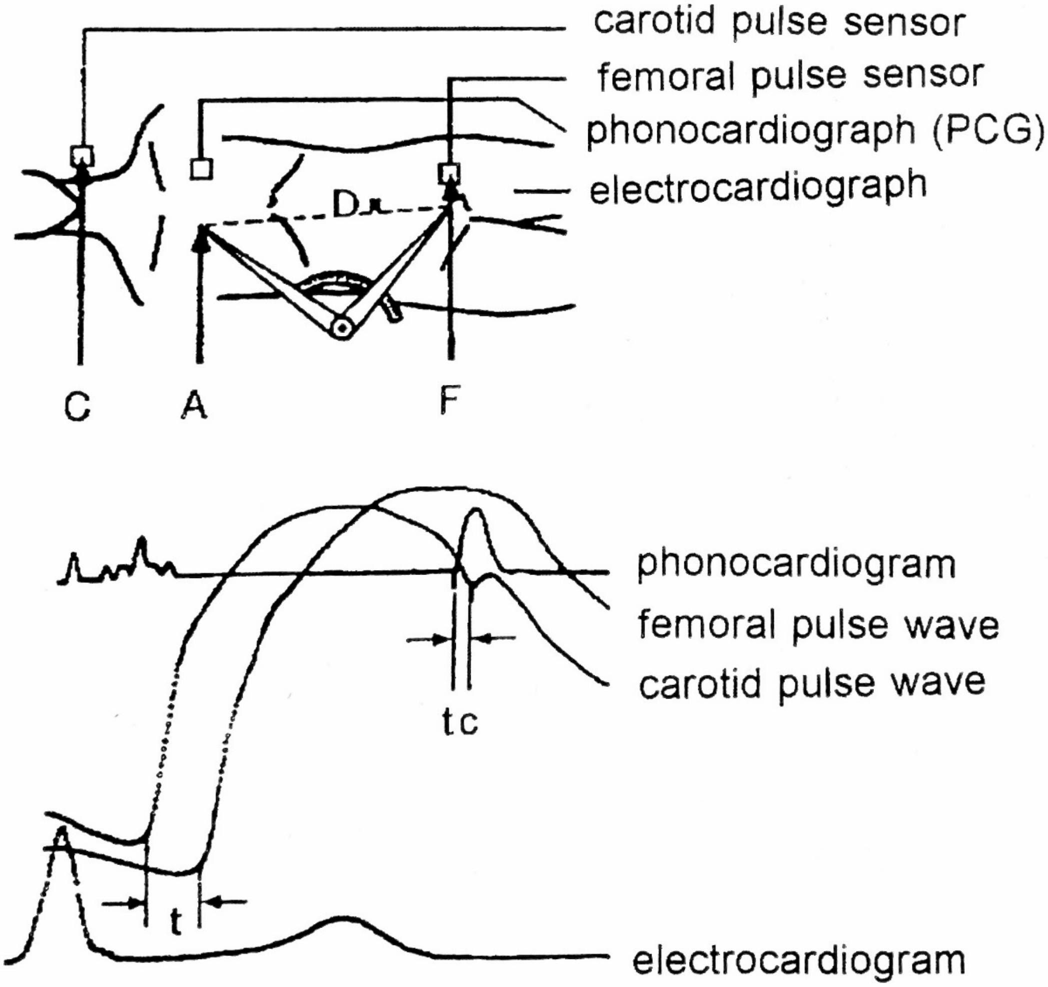
(Translated by Tsukasa Namekata)

Figure 1 Method for measuring the aortic pulse wave velocity (PWV)



$$PWV = \left[\frac{D \times 1.3}{t + tc}\right]_p \ \text{m/sec}$$

Figure 2 Comparison between 1994 household income of Japanese American (JA) screening participants and 1989 household income of JA population in King County, Washington, U.S.A.

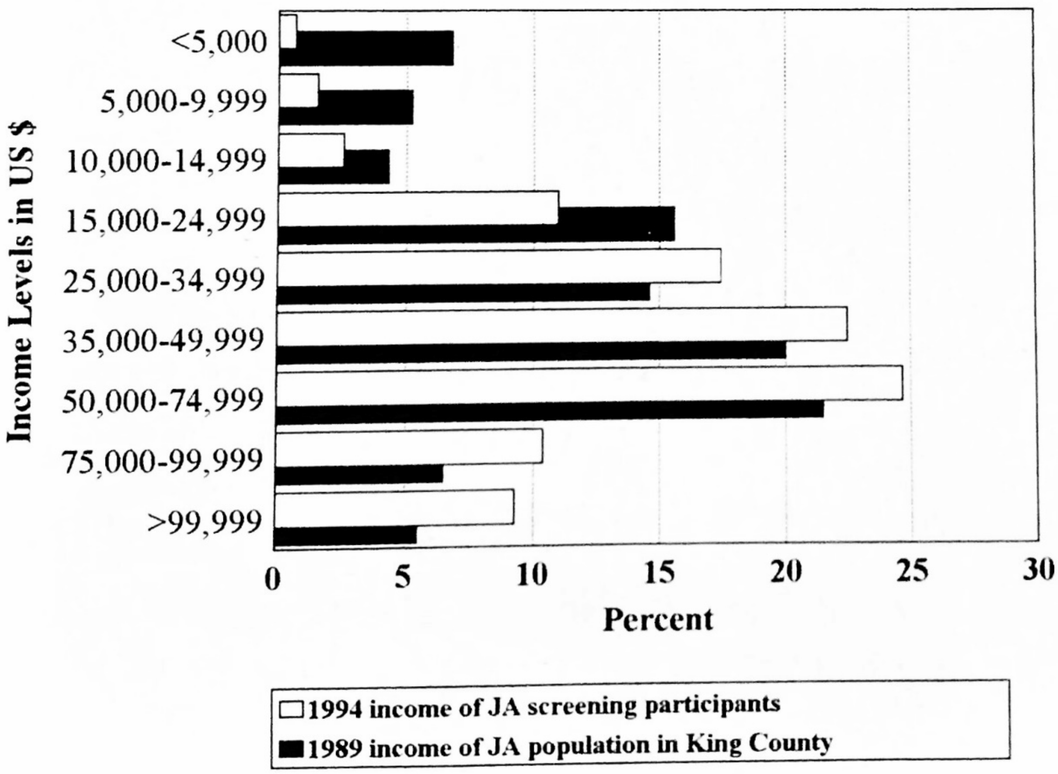


Table 1 Characteristics of study participants in Seattle, U.S.A.

Variables	Total (n=1,389)		Males (n=681)		Females (n=708)	
	Mean	SD	Mean	SD	Mean	SD
Age	56.0	13.7	56.1	13.7	55.9	13.7
PWV (m/sec)	8.0	1.5	8.0	1.5	8.1	1.5
Body mass index	24.8	3.6	25.6	3.3	23.9	3.7
Systolic BP (mmHg)	130.5	18.5	133.1	17.5	128.0	19.1
Total cholesterol (mg/d*l*)	225.6	40.0	224.3	38.0	226.0	41.8
HDL cholesterol (mg/d*l*)	57.4	16.6	51.2	14.0	63.4	16.7
TC/HDL ratio	4.2	1.4	4.7	1.5	3.8	1.3
Daily alcohol consumption (grams)	3.7	10.1	6.0	12.7	1.4	6.0
	Number	Percent	Number	Percent	Number	Percent
Current drinkers	767	55.2	441	64.8	326	46.0
Ex-drinkers	189	13.6	115	16.9	74	10.5
Non-drinkers	433	31.2	125	18.3	308	43.5
Current smokers	167	12.0	104	15.3	63	8.9
Ex-smokers	468	33.7	319	46.8	149	21.0
Non-smokers	754	54.3	258	37.9	496	70.1

Table 2 Distribution of persons by age and aortic pulse wave velocity among Japanese Americans in Seattle, U.S.A.: males and females combined

PWV (m/sec)	Age in Years					
	<40	40–49	50–59	60–69	≥70	all ages
<6.0	48(22.9%)	15(5.7%)	4(1.4%)			67(4.8%)
6.0– 6.9	116(55.2%)	121(46.4%)	50(17.4%)	17(4.2%)	1(0.4%)	305(22.0%)
7.0– 7.9	40(19.0%)	106(40.6%)	129(44.8%)	84(20.8%)	14(6.2%)	373(26.9%)
8.0– 8.9	6(2.9%)	19(7.3%)	77(26.7%)	142(35.2%)	45(19.8%)	289(20.8%)
9.0– 9.9			26(9.0%)	96(23.8%)	80(35.2%)	202(14.5%)
10.0–10.9			2(0.7%)	41(10.2%)	54(23.8%)	97(7.0%)
11.0–11.9				18(4.5%)	19(8.4%)	37(2.7%)
≥12.0				5(1.2%)	14(6.2%)	19(1.3%)
total	210(100%)	261(100%)	288(100%)	403(100%)	227(100%)	1,389(100%)

Table 3 Adjusted odds ratio for presence of abnormally high PWV values among Japanese Americans in Seattle, U.S.A.: males and females combined

Variable		Persons at risk	Adjusted odds ratio†	Significance
Sex:	females	708	1.00	
	males	681	0.65	<0.01
Age:	<60 years	759	1.00	
	≥60 years	630	3.60	<0.001
Hypertension:	no	1,093	1.00	
	yes	296	2.01	<0.001
Diabetes:	no	1,311	1.00	
	yes	78	3.66	<0.001
TC/HDL–C:	<4.5	857	1.00	
	≥4.5	532	1.61	<0.001
BMI:	≤27	1,053	1.00	
	>27	336	1.08	NS‡
Alcohol:	non–drinkers	433	1.00	
	current drinkers	767	0.45	<0.001
	ex–drinkers	189	0.47	<0.001
Smoking:	non–smokers	754	1.00	
	current smokers	167	1.47	<0.10
	ex–smokers	468	1.65	<0.01

† Odds ratios were simultaneously adjusted for all variables included in the model.
‡ NS=not significant

Table 4 Adjusted odds ratio for presence of abnormally high PWV values among Japanese Americans in Seattle, U.S.A.: males

Variable		Persons at risk	Adjusted odds ratio†	Significance
Age:	<60 years	369	1.00	
	≥60 years	312	4.31	<0.001
Hypertension:	no	524	1.00	
	yes	157	2.00	<0.001
Diabetes:	no	639	1.00	
	yes	42	5.65	<0.001
TC/HDL–C:	<4.5	329	1.00	
	≥4.5	352	1.32	NS‡
BMI:	≤27	474	1.00	
	>27	207	0.93	NS‡
Alcohol:	non–drinkers	125	1.00	
	current drinkers	441	0.44	<0.001
	ex–drinkers	115	0.49	<0.05
Smoking:	non–smokers	258	1.00	
	current smokers	104	1.56	NS‡
	ex–smokers	319	1.82	<0.01

† Odds ratios were simultaneously adjusted for all variables included in the model.
‡ NS=not significant

Table 5 Adjusted odds ratio for presence of abnormally high PWV values among Japanese Americans in Seattle, U.S.A.: females

Variable		Persons at risk	Adjusted odds ratio[†]	Significance
Age:	<60 years	390	1.00	
	≥ 60 years	318	3.03	<0.001
Hypertension:	no	563	1.00	
	yes	139	1.94	<0.01
Diabetes:	no	672	1.00	
	yes	36	2.47	<0.05
TC/HDL-C:	<4.5	528	1.00	
	≥ 4.5	180	1.98	<0.001
BMI:	≤ 27	579	1.00	
	>27	129	1.28	NS[‡]
Alcohol:	non drinkers	308	1.00	
	current drinkers	326	0.47	<0.001
	ex-drinkers	74	0.45	<0.05
Smoking:	non-smokers	496	1.00	
	current smokers	63	1.32	NS[‡]
	ex-smokers	149	1.38	NS[‡]

† Odds ratios were simultaneously adjusted for all variables included in the model.

‡ NS=not significant