Risk Factors for the Incidence of Aortic Stiffness by Serial Aortic Pulse Wave Velocity Measurement in Middle-aged Japanese men

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Abstract

To examine the risk factors related to the incidence of aortic stiffness, 1,045 Japanese men aged 40 to 54 years with aortic pulse wave velocity (PWV) of less than 8.0 m/sec were followed up for seven years with annual examinations, with an average period of observation of 6.3 years with standard deviation of 1.56 years. Subjects who showed 8.0 m/sec and over of PWV during follow-up surveys were defined as incidental cases of aortic stiffness. Kaplan-Meier analysis showed that the incidence of aortic stiffness increased significantly with increases in age, body mass index, and total cholesterol and low-density lipoprotein (LDL) cholesterol levels. The incidence of aortic stiffness was significantly higher among those who had or currently smoked than among those who never smoked. From multivariate analysis using Cox proportional hazards model, the incidence of aortic stiffness showed a significant dose-response relationship for age, PWV, total cholesterol and LDL cholesterol levels and smoking habits. These results indicate that increased levels of total cholesterol and LDL cholesterol and smoking habits may constitute contributing factors for the development of aortic stiffness in middle-aged Japanese men.

Key words: pulse wave velocity, aortic stiffness, risk factors, follow-up study

Introduction

Previous studies¹⁻⁴ have reported that increased aortic stiffness or decreased aortic compliance is associated with a higher propensity for cardiovascular diseases. It has also been demonstrated that the human aorta gradually becomes stiffer with age, with the process of arteriosclerosis occurring even in the absence of any concurrent disease⁴⁻⁹. Therefore, the detection of early arteriosclerotic changes in the aorta and a better knowledge of the risk factors involved may have major clinical significance for the prediction of cardiovascular diseases¹⁰.

Non-invasive measurement of aortic pulse wave velocity (PWV) as an aortic distensibility index represents a potentially useful approach, since aortic PWV is reported to be a reliable index of aortic stiffness¹¹⁻¹⁷. Several studies^{9, 14, 17-19} suggest that an

increase in aortic PWV could be an early indicator of arteriosclerotic in the aorta. Although there have been many cross-sectional investigations confirming the deleterious effects of advancing age and other determinants such as blood pressure and serum lipid levels on aortic stiffness^{4-9, 18, 20-28}, few follow-up studies have been completed.

In this follow-up study, we attempted to identify the risk factors related to early alterations in aortic stiffness on the basis of the measurement of aortic PWV in middle-aged Japanese male office workers.

Methods

Subjects and baseline data

A systematic surveillance to evaluate the risk factors related to the development of aortic stiffness was conducted between 1990 and 1997 among employees of T Corporation, which is one of the biggest building contractors in Osaka, Japan. All male employees aged 40 to 54 years in May 1990 were invited to attend a survey (N=1,173), and the participation rate was 99.8% (n=1,171).

The health examination at entry included a questionnaire,

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physical examination, blood pressure measurement, collection of blood samples for laboratory analysis, and the measurement of PWV. Data on alcohol intake and smoking habit were obtained by interview. The subjects were asked to quantify their consumption of alcohol in terms of how much sake (Japanese rice wine) they drank per day. Alcohol intake was then converted into the equivalent number of *go*, a traditional Japanese unit of volume for sake (1 *go* = 180 mL and contains 23 g of ethanol). Weight and height were measured with the subjects in typical indoor clothing but without shoes. Body mass index (BMI) was calculated as weight/height² (kg/m²). Blood pressure was measured to the nearest 2 mmHg with a standard sphygmomanometer on the right arm of the subjects sitting after 5 min rest, and Korotkoff phases I and V were taken as representing systolic (SBP) and diastolic (DBP) blood pressure, respectively. Following the blood pressure measurement, fasting blood samples were drawn from an antecubital vein. Total cholesterol, triglyceride, high-density lipoprotein (HDL) cholesterol and hemoglobin A_{1c} (HbA_{1c}) were analyzed with an Olympus AU-5000 (Olympus Japan Co, Ltd., Tokyo, Japan) by the Nihon Clinical Laboratories Inc. (Tokyo, Japan). Low-density lipoprotein (LDL) cholesterol was calculated with the formula of Friedewald et al²⁹, for those with triglyceride levels of less than 400 mg/dL because LDL cholesterol estimation becomes less accurate if the triglyceride value is 400 mg/dL or more³⁰.

PWV of the aorta of each participant was measured using a PWV Adapter (PWV-100, Fukuda Denshi Corporation, Tokyo, Japan) as follows: two pulse waves detected as displacement by transducers were recorded from the spots where pulses of the right (left) carotid and the left (right) femoral arteries were felt. A phonocardiogram was recorded at the right sternal border in the second or third intercostal space at the same time on the same recorder. As soon as the recording was completed, blood pressure was measured with the subject in the supine position. The time required for a pulse to be transmitted from the aortic valve to the pulsing point of the femoral artery was estimated from the recording chart by adding the time difference between the starting points of pulse waves of the carotid and femoral arteries to the time difference between the start of the second heart sound and the dicrotic notch in the carotid pulse wave. The length of the artery from the aortic valve to the pulsing point of the femoral artery was calculated by multiplying by a factor of 1.3 the distance measured along a straight line from the right (left) sternal border in the second intercostal space to the pulsing point of the left (right) femoral artery. The velocity was obtained by dividing the length of the artery by the time needed for transmission. Since velocity measured in this way was known to be strongly dependent on diastolic blood pressure intra-individually¹², it was standardized to diastolic blood pressure of 80 mmHg using a standardization table for different diastolic blood pressures.

Follow-up survey

Of the 1,171 subjects participated in the survey, 126 (10.8%) showed 8.0 m/sec and over of PWV at the initial examination in May 1990 (Table 1) and were excluded from this study as those who had abnormally high PWV values or increased aortic stiffness^{13, 14, 19}. The remaining 1,045 subjects constituted the study cohort and were followed up for seven years with annual examinations up to May 1997. Subjects who showed 8.0 m/sec and over of PWV during the follow-up surveys were defined as incidental cases of aortic stiffness. Only 901 subjects (86.2%) completed the follow-up till May 1997 because 144 (13.8%) had either been transferred to another locality or had retired during the follow-up study. Of these 144 subjects who could not be followed up till May 1997, 17 (11.8%) showed 8.0 m/sec and over of PWV during the follow-up period. Among 212 subjects who had not abnormally high PWV values at the initial examination and showed 8.0 m/sec and over of PWV during the follow-up period, 17 (8.0%) could not be followed up until the end of the follow-up.

The observation times were calculated by using the date of the initial examination and the date of the incidence of aortic stiffness or the date of follow-up (the eighth examination), or the date of last registration in T Corporation, Osaka. Those who had been transferred to another locality or had retired during the follow-up period have censored observation times as do those members of the cohort who were still in T Corporation, Osaka, at the end of the follow-up. The mean observation period of this cohort was 6.3 years with standard deviation (SD) of 1.56 years, and the mean (SD) number of times of PWV measurement, including the initial examination, was 7.3 (1.52).

With respect to age, BMI, blood pressures, serum lipid levels, HbA_{1c} levels, treatments for hypertension, hyperlipidemia, and diabetes mellitus, alcohol intakes, and smoking habits at entry, the 144 cases which could not be followed up till May 1997 did not differ significantly from the 901 cases which could.

Statistical methods

Differences in the prevalence of potential confounding factors among the age groups were tested by the chi-square test. The method of Kaplan-Meier³¹ was used to estimate the cumulative incidence of aortic stiffness according to the characteristics identified from baseline data, and the log-rank test was used to assess the significance of the unadjusted difference among the incidence curves. Proportional hazards models³² were used to evaluate the multivariate relations between the characteristics at entry and the development of aortic stiffness. Estimates of hazard ratios (HRs) compared to the reference level of each subclass were calculated by creating two dummy variables for each variable: x1=0, x2=0 for the reference level; x1=1, x2=0 for the second level, and x1=0, x2=1 for the third level. The HR estimates were also

Table 1 Distribution of aortic pulse wave velocity according to age group at baseline.

Pulse wave velocity (m/sec)	Age group (years)							
	40-44		45-49		50-54		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
<7.2	171	(30.3)	69	(19.3)	35	(14.1)	275	(23.5)
7.2-7.5	262	(46.4)	161	(45.1)	67	(26.9)	490	(41.8)
7.6-7.9	123	(21.8)	101	(28.3)	56	(22.5)	280	(23.9)
≥8.0	9	(1.6)	26	(7.3)	91	(36.5)	126	(10.8)
Total	565	(100.0)	357	(100.0)	249	(100.0)	1,171	(100.0)

Table 2 Characteristics of aortic stiffness-free subjects for selected variables at baseline by age group.

Characteristics	Subclass	Age group (years)			Significance by χ^2 <i>p</i> value
		40-44 (n=556)	45-49 (n=331)	50-54 (n=158)	
Body mass index (kg/m ²)	< 22.0	28.8	31.7	24.1	0.535
	22.0-24.1	37.6	35.6	39.2	
	≥ 24.2	33.6	32.6	36.7	
Systolic blood pressure (mmHg)	< 140	72.8	74.6	70.9	0.585
	140-159	21.4	21.8	24.7	
	≥ 160	5.8	3.6	4.4	
Diastolic blood pressure (mmHg)	< 90	75.7	77.0	70.3	0.097
	90-94	12.9	10.6	19.6	
	≥ 95	11.3	12.4	10.1	
Treatment for hypertension	No	95.3	93.4	94.3	0.453
	Yes	4.7	6.6	5.7	
Total cholesterol (mg/dL)	< 180	28.2	26.3	20.3	0.212
	180-219	41.2	46.2	48.1	
	≥ 220	30.6	27.5	31.6	
Low-density lipoprotein cholesterol* (mg/dL)	< 100	26.3	26.7	25.5	0.388
	100-139	48.5	52.8	46.4	
	≥ 140	25.2	20.6	28.1	
High-density lipoprotein cholesterol (mg/dL)	< 50	32.6	29.3	34.8	0.186
	50-69	53.6	51.1	48.7	
	≥ 70	13.8	19.6	16.5	
Triglyceride (mg/dL)	< 80	29.0	28.4	29.1	0.305
	80-159	44.8	49.2	40.5	
	≥ 160	26.3	22.4	30.4	
Treatment for hyperlipidemia	No	90.3	94.9	92.4	0.505
	Yes	9.7	5.1	7.6	
Hemoglobin A _{1c} (%)	< 5.5	27.9	26.0	27.2	0.595
	5.5-6.4	64.0	62.8	62.0	
	≥ 6.5	8.1	11.2	10.8	
Treatment for diabetes mellitus	No	97.1	96.4	94.3	0.238
	Yes	2.9	3.6	5.7	
Alcohol intake (go /day)	0	36.9	38.7	44.9	0.140
	0.1-1.9	42.3	38.1	40.5	
	≥ 2.0	20.9	23.3	14.6	
Smoking habit	Non-smoker	29.9	28.4	31.6	0.560
	Ex-smoker	17.4	18.7	22.2	
	Current-smoker	52.7	52.9	46.2	

*For the calculation of low-density lipoprotein cholesterol, 12 subjects aged 40-44, 5 subjects aged 45-49, and 5 subjects aged 50-54 were excluded because the levels of triglyceride were 400 mg/dL or over.

tested for heterogeneity tendency.

Data analysis was performed with the SPSS/PC statistical package (Marija J. Norusis/ SPSS Inc., Chicago, IL, USA). All reported *p*-values were two-tailed and the level of significance was set at *p*<0.05.

Results

Characteristics of aortic stiffness-free (less than 8.0 m/sec of PWV) subjects at baseline according to age group are shown in Table 2. BMI, blood pressures, serum lipid levels, HbA_{1c} level, treatment for hypertension, hyperlipidemia, and diabetes mellitus, alcohol intake, and smoking habits did not differ significantly among the three age groups.

Table 3 shows the estimated incidence rates of aortic stiffness over seven years as determined with the Kaplan-Meier method. The estimated incidence increased with increases in age, PWV, BMI, total cholesterol level, and LDL cholesterol level. The incidence curves for the three subclasses of each variable achieved statistical significance on the basis of the log-rank test. The estimated incidence rate was higher among those who were ex-smokers or current smokers than among those who were non-smokers, and the incidence curves for the three subclasses were statistically significant by the log-rank test. On the other hand, there was no significant correlation between SBP, DBP, HDL cholesterol, triglyceride, HbA_{1c}, treatment for hypertension,

hyperlipidemia, and diabetes mellitus, and alcohol intake and the incidence of aortic stiffness.

To determine the independent risk factors related to the incidence of aortic stiffness, the variables shown as statistically significant in the univariate analysis were included in a multivariate model. The analysis was carried out separately once using total cholesterol as an index of serum lipid and repeated using LDL cholesterol, because total cholesterol had a strong association with LDL cholesterol ($r=0.870$, $p<0.001$). The incidence of aortic stiffness showed a significant dose-response relationship for age, PWV, total cholesterol level and smoking habit (Table 4). The adjusted HRs were 3.29 (95% confidence interval [CI]: 2.34-4.64) for 45-49 years and 5.55 (95% CI: 3.83-8.04) for 50-54 years in comparison with 40-44 years. The adjusted HR for 7.6 to 7.9 m/sec of PWV compared to that for less than 7.2 m/sec of PWV was 2.11 (95% CI: 1.42-3.14). Furthermore, the adjusted HR for 220 mg/dL or more of total cholesterol was 1.67 (95% CI: 1.13-2.47), compared to less than 180 mg/dL of total cholesterol. The adjusted HR for current smokers to non-smokers was 1.54 (95% CI: 1.14-2.07). In contrast, no significant association was observed for BMI. In the multivariate analysis using LDL cholesterol instead of total cholesterol, a significant dose-response relationship was also observed for age, PWV, LDL cholesterol and smoking habits. The relevant values for 100-139 mg/dL and 140 mg/dL or more of LDL cholesterol

Table 3 Cumulative incidence of aortic stiffness over a 6.3-year period in average for selected variables.

Variable	Subclass	n=1,045	Incidence of aortic stiffness		p value*
			%	95% confidence interval	
Age group (years)	40-44	556	9.2	6.8 - 11.6	<0.001
	45-49	331	28.7	23.8 - 33.6	
	50-54	158	41.8	34.1 - 49.5	
Pulse wave velocity (m/sec)	<7.2	275	12.7	8.8 - 16.7	<0.001
	7.2-7.5	490	18.0	14.6 - 21.4	
	7.6-7.9	280	31.8	26.3 - 37.2	
Body mass index (kg/m ²)	<22.0	303	17.8	13.5 - 22.1	0.041
	22.0-24.1	389	18.3	14.4 - 22.1	
	≥24.2	353	24.7	20.2 - 29.1	
Systolic blood pressure (mmHg)	<140	764	19.5	16.7 - 22.3	0.362
	140-159	230	21.3	16.0 - 26.6	
	≥160	51	37.5	15.2 - 39.7	
Diastolic blood pressure (mmHg)	<90	787	19.7	16.9 - 22.5	0.685
	90-94	138	22.5	15.5 - 29.4	
	≥95	120	21.7	14.3 - 29.0	
Treatment for hypertension	No	988	19.8	17.4 - 22.3	0.114
	Yes	57	28.1	16.4 - 39.7	
Total cholesterol (mg/dL)	<180	276	14.5	10.3 - 18.6	0.003
	180-219	458	20.1	16.4 - 23.8	
	≥220	311	25.7	20.9 - 30.6	
Low-density lipoprotein cholesterol †(mg/dL)	<100	269	16.4	11.9 - 20.8	0.010
	100-139	507	18.9	15.5 - 22.3	
	≥140	247	26.3	20.8 - 31.8	
High-density lipoprotein cholesterol (mg/dL)	<50	333	19.8	15.5 - 24.1	0.960
	50-69	544	20.4	17.0 - 23.8	
	≥70	168	20.8	14.7 - 27.0	
Triglyceride (mg/dL)	<80	301	17.9	13.6 - 22.3	0.199
	80-159	476	20.0	16.4 - 23.5	
	≥160	268	23.5	18.4 - 28.6	
Treatment for hyperlipidemia	No	962	19.7	17.1 - 22.2	0.061
	Yes	83	27.7	18.1 - 37.3	
Hemoglobin A _{1c} (%)	<5.5	284	20.4	15.7 - 25.1	0.965
	5.5-6.4	662	20.1	17.0 - 23.1	
	≥6.5	99	21.2	13.2 - 29.3	
Treatment for diabetes mellitus	No	1,008	20.0	17.6 - 22.5	0.217
	Yes	37	27.0	12.7 - 41.3	
Alcohol intake (go /day)	0	404	17.8	14.1 - 21.5	0.260
	0.1-1.9	425	21.2	17.3 - 25.1	
	≥2.0	216	23.2	17.5 - 28.8	
Smoking habit	Non-smoker	310	16.5	13.2 - 19.8	0.017
	Ex-smoker	194	23.2	16.8 - 29.6	
	Current-smoker	541	23.7	19.5 - 27.9	

* The difference between the curves was established with the log-rank test.

† For the calculation of low-density lipoprotein cholesterol, 22 subjects were excluded because the levels of triglyceride were 400 mg/dL or over.

Table 4 Multivariate hazard ratios for incidence of aortic stiffness over a 6.3-year period in average.*

Variable	Subjects	Hazard ratio	95% confidence interval	p value
Age group (years)	40-44	1.00 (reference)		
	45-49	3.29	2.34 - 4.64	<0.001
	50-54	5.55	3.83 - 8.04	<0.001
	Test for trend			<0.001
Pulse wave velocity (m/sec)	<7.2	1.00 (reference)		
	7.2-7.5	1.30	0.87 - 1.92	0.196
	7.6-7.9	2.11	1.42 - 3.14	<0.001
	Test for trend			<0.001
Body mass index (kg/m ²)	<22.0	1.00 (reference)		
	22.0-24.1	0.98	0.69 - 1.41	0.934
	≥24.2	1.21	0.85 - 1.72	0.296
	Test for trend			0.273
Total cholesterol (mg/dL)	<180	1.00 (reference)		
	180-219	1.27	0.87 - 1.84	0.216
	≥220	1.67	1.13 - 2.47	0.010
	Test for trend			0.007
Smoking habit	Non-smoker	1.00 (reference)		
	Ex-smoker	1.37	0.93 - 2.02	0.109
	Current-smoker	1.54	1.14 - 2.07	0.005
	Test for trend			0.003

* Data for 1,023 subjects with triglyceride levels of less than 400 mg/dL were analyzed.

relative to less than 80 mg/dL of LDL cholesterol were 1.22 (95% CI: 0.85-1.75, $p=0.280$) and 1.71 (95% CI: 1.16-2.53, $p=0.007$), respectively.

Discussion

The clinical and epidemiological application of the pulse wave propagation procedure has shown that increased PWV is associated with age^{4,9, 16}. In the present study, the incidence of aortic stiffness over 7 years increased with age, and a strong dose-response relationship for age was maintained in the multivariate analysis. These results indicate that age is a powerful determinant of the incidence of aortic stiffness in middle-aged Japanese men. Studies by several investigators have shown an apparent decrease in the concentration of elastin in the entire vessel with advancing age, largely due to an increase in the concentration of collagen³³⁻³⁵. The frayed appearance of elastin with age has also been reported as evidence of its degeneration³⁶, while elastic fibers in the wall are stiffened by calcium deposits³⁷. The strong correlation between age and the incidence of aortic stiffness observed in our study appears to be consistent with the age-related reduction in arterial elastin and increase in collagen content in human artery^{33, 38}.

The effects of serum lipids and lipid fractions on aortic distensibility have been controversial. Hopkins et al.³⁹ have recently shown a positive association of aortic stiffness with LDL cholesterol and LDL-HDL cholesterol ratio in healthy adults. However, after adjusting for age, LDL cholesterol lost its significance, and the positive relation of aortic stiffness to LDL-HDL cholesterol ratio remained significant in men only. Some epidemiological studies of Japanese and Japanese-Americans^{6, 7} also showed a weak but positive simple association of aortic stiffness with total cholesterol and triglyceride levels. However, other studies of Chinese and German populations have failed to demonstrate any association between aortic stiffness and total cholesterol level^{8, 9, 20}. Furthermore, Kupari et al.²⁷ showed that aortic stiffness was inversely associated with LDL cholesterol, which accorded with the finding of Dart et al.⁴ showing an inverse association of aortic stiffness with total cholesterol. In familial hypercholesterolemia, a reduction of aortic stiffness has been reported in youths (aged less than 24)²⁴ but an increase in adults²⁵. Experimental studies⁴⁰⁻⁴³ show that in the early stages of diet-induced atheromatosis in animals, when cholesterol accumulation and foam cells predominate in the intimal lesions, the aorta becomes more distensible than normal, but stiffens later when the lesions acquire an increased amount of collagen and calcification. As for HDL cholesterol, which, in contrast to LDL cholesterol, is involved in reverse cholesterol transport and is recognized to be anti-atherogenic⁴⁴, several studies^{6, 7, 21, 23} found a weak negative correlation between HDL cholesterol and aortic PWV. However, the association of HDL cholesterol with PWV was reported to be either non-existent^{16, 22, 26} or positive^{24, 27}. In the present follow-up study, the incidence rate of aortic stiffness increased with increases in total cholesterol and LDL cholesterol levels, and total cholesterol and LDL cholesterol were maintained as independent factors after adjustment for other potential factors. On the other hand, we observed no significant relationship between HDL cholesterol and triglyceride levels and treatment for hyperlipidemia and the incidence of aortic stiffness. These results indicate that increased levels of total cholesterol and LDL cholesterol are likely to be responsible for the subsequent aortic stiffness observed in middle-aged Japanese men.

As for the association between obesity and aortic PWV, no

previous positive data on aortic PWV in relation to obesity have been published. However, it is well-known association of other heart disease risk factors with obesity that makes a positive association of obesity with the risk of ischemic heart disease biologically plausible. Overweight persons are more likely to have higher levels of blood pressure, serum total cholesterol, triglyceride, and glucose than leaner persons⁴⁵. Levels of the apparently protective lipoprotein, HDL cholesterol, have been shown to be lower in heavier persons⁴⁶. Further, prospective studies have shown that weight change in adult life is linearly and directly associated with change in the levels of heart disease risk factors⁴⁷. In this study, BMI was significantly associated with the incidence of aortic stiffness in the univariate analysis, but did not remain as statistically significant in the multivariate analysis. Increased BMI could be a potential risk factor for the development of aortic stiffness, but further studies are needed to clarify whether obesity is associated with the development of aortic stiffness or contribute to or is responsible for increased aortic stiffness.

As for the relationship of diabetes mellitus to aortic stiffness, a decreased arterial elasticity in diabetic subjects is well known¹⁸. The independent relation of hyperglycemia and family history of diabetes to increased PWV was already reported²⁰, and a positive association between blood glucose and PWV was also found in non-diabetic hypertensive subjects¹⁹. It has been suggested that glycosylation of bioelastomers inside the arterial media might be involved in the alteration of the arterial wall⁴⁸. However, the incidence of aortic stiffness was unrelated to HbA_{1c} level and treatment for diabetes mellitus in this study. Thus, further studies are needed to clarify whether diabetic status is responsible for increased aortic stiffness in middle-aged Japanese.

Several cross-sectional studies indicate that hypertension contributes more than arteriosclerosis to increased arterial stiffening with age^{7, 15, 16, 21, 26}. Structural medial degeneration subsequent to chronic elevation in blood pressure is reported to participate in the association between hypertension and increased PWV⁴⁹. However, in this follow-up study, the incidence of aortic stiffness was not significantly associated with blood pressure level and treatment for hypertension. When examining the reason for the absence of correlation between blood pressure and the incidence of aortic stiffness, the following factor should be taken into consideration: if the subjects in this study population were detected as hypertensive during any given period, their blood pressure was subsequently checked and controlled by the physicians at the company medical office. In fact, out of 988 subjects without antihypertensive drugs at entry, 59 (6.0%) started to use medical treatment for hypertension during the follow-up period. Among the subjects who could be followed up till 1997 and showed 160 mmHg and over of SBP or 95 mmHg and over of DBP at entry, the respective means (SD) for SBP ($n=44$) and DBP ($n=107$) were 168.8 mmHg (7.5 mmHg) and 101.9 mmHg (6.3 mmHg) at entry and 151.6 mmHg (16.1 mmHg) and 92.0 mmHg (11.6 mmHg) in 1997, respectively (t value = 6.70, $p<0.001$ for SBP and t value = 7.52, $p<0.001$ for DBP). The predictive power of blood pressure for the incidence of aortic stiffness might be wiped out by these blood pressure changes during the follow-up period.

As for alcohol intake and smoking habits, Namekata et al.²⁸ have recently shown a significant association of aortic stiffness with alcohol intake and smoking habits in Japanese Americans. They reported the comparative (non-drinkers) significant low odds ratios for estimating the risk for the presence of abnormally high

PWV to be found in current-drinkers and ex-drinkers in both sexes while the comparative (non-smokers) significant high odds ratio to be found in ex-smokers in men. In this study, the incidence of aortic stiffness was not related to alcohol intake, but showed an independent dose-response relationship for smoking habits. These results indicate that smoking habits are responsible for or contribute to the development of aortic stiffness. Further investigations should be needed to clarify whether alcohol consumption contributes to decreased aortic stiffness in Japanese.

In conclusion, our data suggest that total cholesterol and LDL cholesterol levels and smoking habits are independent risk factors for the development of aortic stiffness in middle-aged Japanese men. Although age is the most powerful determinant for

aortic stiffness, undue aortic stiffness may be preventable or reversible by improving total cholesterol and LDL cholesterol levels or cessation of smoking.

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