Association of risk factors for atherosclerosis, including high-sensitivity C-reactive protein, with carotid intima-media thickness, plaque score, and pulse wave velocity in a male population

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Abstract

Intima-media thickness (IMT), plaque score (PS) and brachial-ankle pulse wave velocity (baPWV) are non-invasive parameters for evaluation of atherosclerosis. There have been no reports investigating the associations between IMT, PS, or baPWV and known risk factors for atherosclerosis in the same participants. This study aimed to compare the contributed risk factors among IMT, PS, and baPWV. We enrolled 3,128 male participants who underwent health checkups. Carotid ultrasonography was used to measure IMT and PS, and baPWV was measured using an automatic device. We analyzed the association between these parameters and risk factors for atherosclerosis including obesity, smoking, alcohol, high blood pressure (BP), impaired fasting glucose (IFG), dyslipidemia (DL), and high-sensitivity C-reactive protein (hs-CRP). Multivariate logistic regression analysis revealed high IMT (>0.9 mm) to be independently associated with high BP. The presence of atherosclerosis (PS≥1.1 mm) was independently associated with high BP, IFG, and DL. In addition, advanced atherosclerosis (PS≥5.1 mm) showed a significant association with high BP, IFG, DL, log hs-CRP, and smoking. High baPWV (≥1,600 cm/sec) was significantly correlated with high BP, IFG, and log hs-CRP. IMT, PS and baPWV are all associated with different risk factors among Japanese male participants. Only high BP was a common risk factor for all three parameters. Furthermore, hs-CRP was associated with advanced atherosclerosis, not but with the presence of atherosclerosis.

Key words: intima-media thickness, plaque score, brachial-ankle pulse wave velocity, high blood pressure, high-sensitivity C-reactive protein

Introduction

Atherosclerosis is an important pathological condition which is associated with various diseases such as coronary artery disease and stroke. To prevent these diseases, early evaluation of the degree of atherosclerosis and development of an appropriate treatment plan is essential. Measurement of the intima-media thickness (IMT) and plaque score (PS) provides information on the extent of structural vascular damage, and both are measured using carotid ultrasonography. The arterial wall thickness is represented by the IMT; thickening of the IMT can indicate the presence of early-stage atherosclerosis and IMT is a strong predictor for incident stroke[1] and cardiovascular events[2] independent of traditional risk factors. The PS relates to the severity of plaque formation and can be used to assess the presence of advanced atherosclerosis.[3,4] This parameter has been reported to be an independent predictor of stroke[5] and coronary heart disease.[6,7] On the other hand, brachial-ankle pulse wave velocity (baPWV) measured using non-invasive equipment, has conventionally been used as a measurement of arterial stiffness. In a meta-analysis, baPWV has a significant association with cardiovascular events as well as all-cause mortality, independent of traditional risk factors.[8]

Inflammation is involved in the pathogenesis of atherosclerosis and progress atherosclerosis. Recently, atherosclerosis is considered a chronic inflammatory disease.[9]

High-sensitivity C-reactive protein (hs-CRP) is a parameter which is used to assess inflammation, and high hs-CRP is a risk factor for cardiovascular events[10] and elevated arterial stiffness.[11] Moreover, several reports have described an association between carotid atherosclerosis and hs-CRP.[12,13] Because it is significantly correlated with IMT[14], high hs-CRP is frequently accompanied by high IMT.[15]

It is important to elucidate the relationship between the risk factors for atherosclerosis including inflammation and atherosclerotic parameters such as IMT, PS and baPWV in order to prevent cardiovascular diseases.[8,14,15] Furthermore, in previous studies, it is revealed that the higher IMT or PWV was associated with risk factors. Thickening of IMT was associated with systolic blood pressure (BP) elevation.[16] The percentage of diabetes mellitus in IMT>0.9 mm group was higher than that in IMT≤0.9 mm group in older black participants.[17] In addition, even if children, IMT was related to 24-hour and night-time BP when they were overweight or obese.[18] On the other hand, although PWV was associated with systolic BP and insulin resistance syndrome in elderly participants,[19] PWV was not independently associated with systolic BP dipping percent.[20] baPWV was related to the level of triglycerides in older men and women.[21] There are not many reports on the relationship PS and risk factors. It is reported that carotid plaque evaluated using magnetic resonance imaging was associated with middle and high tertiles of total cholesterol.[22] Although the previous epidemiological studies have demonstrated the relationship between IMT, PWV or cardiac plaque and risk factors, there are no reports on data that simultaneously analyze and compare the association between IMT, PS and baPWV and risk factors for atherosclerosis within the same participants. So, we cannot compare the clinical significance of risk factors for each atherosclerotic parameter directly because the participants' background is different in each study.

This study, therefore, aimed to investigate and compare the associations between non-invasive and simple parameter such as IMT, PS or PWV and common risk factors for cardiovascular diseases including obesity, smoking, alcohol, high BP, impaired fasting glucose (IFG), dyslipidemia (DL) and hs-CRP in the same general participants. Furthermore, our study aimed to clarify the clinical relationship between the atherosclerotic parameters and hs-CRP.

Methods

Study Population

We recruited 10,035 individuals who underwent a voluntary routine health checkups at the JA Kagoshima Kouseiren Medical Health Care Center between April 2001and March 2015. Exclusion criteria were: individuals who received health checkups more than once; atrial fibrillation on electrocardiogram (ECG); right or left ankle-brachial pressure index (ABI) of <0.9 or >1.4, because this may affect the reliability of baPWV measurements due to peripheral artery disease [23]; missing data of ABI, PS, or hs-CRP; missing data of direct measurement low-density lipoprotein cholesterol (LDL-C) with TG levels of >400 mg/dL. Moreover, we excluded female individuals because females represented 23% of individuals who were recruited, meaning the number of females was small compared with the number of males in the recruited population.

This study and its protocols conformed to the Declaration of Helsinki and was approved by the Institutional Ethic Committees of the Graduate School of Medical and Dental Sciences, Kagoshima University (No.170130 (520)).

Data Collection

Medical history including information on hypertension, diabetes mellitus, dyslipidemia, medications, smoking and alcohol were obtained through self-administered questionnaires.

Blood samples, which were collected after overnight fasting, were obtained from participants on the health checkups day. Serum concentrations of triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), LDL-C, fasting blood sugar (FBS), and hs-CRP were measured by standard laboratory procedures. Although LDL-C was usually analyzed by direct measurement; where direct measurement data was not available, we calculated LDL-C using Friedewald's equation if only TG<400 mg/dL; [LDL-C = total cholesterol - (TG/5) - HDL-C].

Assessment of Cardiovascular Risk Factors

We calculated BMI for each participant from body weight (kg) and height (m), and obesity was defined as BMI ≥25.0 kg/m^2. Pack-years of cigarette smoking was calculated using the following formula: average number of packs of cigarettes smoked per day × years of smoking. Smoking history included current or previous smoking behavior. Alcohol history included current or previous drinking behavior. High BP was defined as systolic BP (SBP) of ≥130 mmHg, diastolic BP (DBP) of ≥85 mmHg, or use of antihypertensive drugs. Definition of DL was taken as LDL-C ≥140 mg/dL, TG ≥150 mg/dL or HDL-C <40 mg/dL, according to the Japan Atherosclerosis Society guideline, [24] or use of lipid-lowering medications. IFG was defined as FBS ≥110 mg/dL or treatment with hypoglycemic agents.

Measurement of Intima-Media Thickness, Plaque Score and brachial-ankle Pulse

Wave Velocity

Measurements of IMT and PS were taken from carotid ultrasonograms (LOGIQ 400 PRO; GE Healthcare, Korea, Vivid 7 PRO; GE Healthcare, Norway, HD 15; Philips, USA, 9-12 MHz) based on previous reports.[25,26] The former was measured at three points of the segmentation of the internal carotid artery, carotid bulb and common carotid artery (CCA). The mean overall IMT, which is the mean of the values of right and left IMT, was used for analysis. High IMT was defined as >0.9 mm because this is an independent variable for risk stratification using an appropriate estimation of the known cardiovascular risk factor.[27]

We screened the longitudinal image for plaque at the three points of segmentation, and measured the thickest point of the segment from the short-axis image. We defined a plaque as IMT of ≥1.1 mm, and calculated the PS by summing the thickness of plaques in the right and left carotid arteries.[25,28,29] We then divided PS into the presence of atherosclerosis or advanced atherosclerosis by PS ≥ 1.1 mm or PS ≥ 5.1 mm, respectively. The measurements of IMT and PS were examined by the well-trained sonographers and checked by cardiologists.

The baPWV was measured as previously reported.[30] Briefly, baPWV was automatically calculated using a Colin Waveform Analyzer (Colin, Komaki, Japan) according to the following equation: baPWV (cm/s) = (D1-D2)/T, where D1 is the distance from heart to the right ankle, D2 is the distance from the heart to the right upper arm and T is the time from onset of the rise in pulse-volume record of the right upper arm to the onset of the rise in pulse-volume record of the right ankle. Distance were calculated automatically on the basis of participant height. The intra and interobserver variabilities of baPWV are reportedly 3.8-10.0% and 3.6-8.4%, respectively, representing a reproducibility that is not problematic in clinical use.[30,31] High baPWV was defined as ≥1,600 cm/s because this value is an independent variable for risk stratification from previous reports of patients with cardiovascular events.[32,33]

Statistical Analysis

Continuous variables are presented as mean ± standard deviation. To achieve a normal distribution, the hs-CRP value was log-transformed before analysis. Categorical variables are presented as number of participants and proportion (percentage). Participants were stratified into two groups according to high IMT (IMT>0.9mm), presence of atherosclerosis (PS≥1.1 mm), presence of advanced atherosclerosis (PS≥5.1 mm) and high baWPV (baPWV≥1,600 cm/s) based on the classifications used in previous reports.[25,27-29,33] Variables were compared between the two groups using the t-test for continuous variables and the χ^2 test for categorical variables. The annual proportion of IMT>0.9mm, PS>1.1mm, PS>5.1 mm and baPWV>1,600cm/s were calculated for each year from 2004 to 2015. We used the Cochran-Armitage trend test to assess the statistical significance of changes by year. The test was two-sided, and a p-value of < 0.01 was considered significant given the large sample size of our data. The Z test-statistics values corresponding to the Cochran-Armitage trend test was also provided.

Logistic regression analysis was applied to assess the odds ratios of obesity, smoking history, high BP, IFG, DL and log hs-CRP for high IMT, presence of atherosclerosis, advanced atherosclerosis and high baPWV. Multivariate logistic regression analysis adjusted for age and the enrolled-year was performed and obesity, smoking history, high BP, IFG, DL and log hs-CRP were used as covariates. Statistical analysis was performed using JMP pro 14 (SAS Institute Inc, Cary, NC, USA) for Windows. Statistical significance was accepted at $p<0.05$.

Results

Characteristics of the study participants

After the application of exclusion criteria, a total 3,128 male participants were included in analysis (Figure 1). Characteristics of the final study population are shown in

Table 1. Mean age was 56±11 years, and mean value of hs-CRP was 0.11±0.24 mg/dL. Mean IMT, mean total PS, and mean baPWV were 0.76±0.13 mm, 3.3±3.1 mm, and 1552±326 cm/s, respectively. The rate of risk factors was as follows: obesity 34%, high BP 55%, IFG 31%, DL 56%, and smoking 66%.

Table 2 shows the clinical characteristics of participants with regards to high and low IMT, PS and baPWV. The rates of obesity, high BP and IFG were significantly higher among participants with high IMT compared with low IMT. Hs-CRP, and the rates of smoking and DL were not significantly different between participants with high and low IMT. Log hs-CRP and the rate of DL were not significantly different when comparing participants with or without atherosclerosis, whereas those with advanced atherosclerosis had significantly higher log hs-CRP and rate of DL compared with those without advanced atherosclerosis. Log hs-CRP, pack-years, high BP, and IFG were significantly higher among participants with high baPWV than those with low baPWV; however the rate of obesity and DL were not significantly different between two groups.

Trend Analysis

Table 3 showed the result in the Cochran-Armitage trend test. The Cochran-Armitage trend test demonstrated the significance of the change by year for the percentage of IMT>0.9 mm (Z=-2.65, p=0.0079) and baPWV>1,600 cm/s (Z=2.60, p=0.0092). In contrast, the change of percentage by year of PS≥1.1 mm and PS≥5.1 mm did not show the significant changes in the Cochran-Armitage trend test.

Logistic Regression Analysis

Table 4 and 5 detail the results of univariate and multivariate logistic regression analysis of IMT, PS and baPWV and risk factors for atherosclerosis. In univariate logistic regression analysis, high IMT was significantly correlated with obesity, high BP, and IFG. The presence of atherosclerosis was significantly associated with smoking, high BP and IFG. Furthermore, in the case of advanced atherosclerosis, log hs-CRP and DL were also significant risk factors. High baPWV was significantly correlated with smoking, high BP, IFG and log hs-CRP.

Multivariate logistic regression analysis adjusted age and the enrolled-year for carotid atherosclerosis revealed high IMT to be independently correlated with obesity and high BP. The presence of atherosclerosis was independently associated with high BP, IFG and DL. Log hs-CRP and smoking were independently associated with advanced atherosclerosis. High baPWV was significantly correlated with high BP, IFG and log hs-CRP.

Discussion

This investigation of the relationship between three atherosclerotic indexes and risk factors including hs-CRP demonstrated several novel findings. The impact of each risk factor was different for each of the atherosclerotic indexes. High BP was a common risk factor for three parameters. Although IFG and DL were significantly associated with the presence or advanced atherosclerosis, both smoking and hs-CRP were significantly associated with advanced atherosclerosis only. High baPWV was significantly associated with IFG and hs-CRP.

Although IMT, PS and baPWV are parameters relating to the degree of atherosclerosis, they represent different aspects of the pathology. Specifically, IMT indicates arterial wall thickness, PS represents the degree of plaque formation and baPWV is an index of arterial stiffness. Therefore, the atherosclerotic risk factors that are associated with these three parameters can be expected to be different. To the best of our knowledge, this is the first study to demonstrate differences in the associations between IMT, PS and baPWV and risk factors in the same participants.

With regards to the development of atherosclerosis in the context of elevated BP, the main cause is considered to be vascular endothelial dysfunction due to excessive shear stress on blood vessels. The production of endothelium-derived vascular relaxation factor occurs during the early stages. [34] This could explain the association of high BP with IMT, which is increased in the early stage of atherosclerosis.

We did not find a significant association between IFG and IMT.[32] However, there are several reports which show no relationship between IFG and IMT in adjusted analysis.[35,36] Furthermore, Kowall et al have reported that there is no relationship between blood glucose and IMT after adjustment for age, gender and anthropometric variables.[37] Therefore, it is unclear whether blood glucose level is associated with IMT. Further study is needed to clarify this point.

On the other hand, we found DL to be significantly associated with PS only. A previous study has demonstrated a lack of significant association between DL and IMT or arterial stiffness.[32] Although the reason was not fully elucidated, it has been reported that lipids play a central role in plaque formation.[38] Thus, because PS is a parameter of plaque formation, it is perhaps unsurprising that DL had a relationship with PS but not with IMT or baPWV which are indicators of early atherosclerosis.

Inflammation plays an important role in the progress of atherosclerosis and hs-CRP, a marker of inflammation, is closely related to development of atherosclerosis.[39] In participants with advanced atherosclerosis, progression may have been accompanied by inflammation, indicated by factors such as hs-CRP, caused by various risk factors or activated by atherosclerosis itself. This may explain why we observed a relationship of hs-CRP with advanced, but not early-stage, atherosclerosis. Optimal medical treatment for atherosclerotic risk factors may therefore be important in preventing progression of atherosclerosis. There are several reports on the relationship between hs-CRP and arterial stiffness. Previous reports have shown baPWV to be significantly associated with hs-CRP in multivariate regression analysis of the general population.[40,41] In addition, this association has been shown to differ according to age.[40] Therefore, when we evaluate the relationship between baPWV and hs-CRP, it may be necessary to consider the background characteristics of participants.

In our study, high BP may have affected the process of atherosclerosis formation and arterial stiffness. Taken together, our results indicate that high BP, IFG and DL may be involved in the initiation of atherosclerosis, while hs-CRP appears to play an important role in the progression, but not initiation of the condition.

Study Limitations

Our study has several limitations, which should be acknowledge. First, this is a cross-sectional study. A prospective longitudinal study is needed to confirm the relationship between hs-CRP and the change in IMT, PS and baPWV. Second, the population of this study was made up of participants who underwent health checkups at a single facility in Japan. We will need to collect the health checkups data in many facilities. Third, the proportion of females recruited for this study was 23%, and we therefore excluded female participants from analysis. Further investigation, including females, are required. Fourth, we were not able to analyze the relationship between IMT, PS or baPWV and exercise habits, because we had not the information about the exercise habits. There are several reports on the exercise effects of arterial stiffness improving and IMT reduction. Therefore, further studies are needed to clarify the relationship with exercise habits. Fifth, although IMT and PS were measured by several skilled sonographers and cardiologists, there may be a measurement error. This study is a retrospective study, thereby we cannot investigate the measurement error at individual level.

Conclusions

Risk factors for atherosclerosis depending on IMT, PS and baPWV differ in Japanese male participants. Only high BP was a significant common risk factor of atherosclerosis associated with all three parameters. Hs-CRP related with the advanced atherosclerosis, not but with the presence of atherosclerosis.

Conflict of interest

The authors declare that there are no known competing financial interests or personal relationships that could have influenced the work reported in this paper.

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Figure legend

Figure1. Flowchart of participants enrollment. In total, 3,128 participants were included in analysis.

Abbreviations: baPWV, brachial-ankle pulse wave velocity; ABI, ankle-brachial pressure index; PS, plaque score; hs-CRP, high-sensitivity C-reactive protein; LDL-C, low-density lipoprotein cholesterol.

Table 1. Participant characteristics

Variables	*Number of participants* (N=3128)
Age (years)	56±11
Body mass index (kg/m^2)	24.1±3.1
Systolic blood pressure (mm Hg)	125±17
Diastolic blood pressure (mm Hg)	79±11
Triglyceride (mg/dL)	135±143
HDL-C (mg/dL)	55±14
LDL-C (mg/dL)	126±30
Fasting blood sugar (mg/dL)	108±22

hs-CRP (mg/dL)	0.11±0.24
Pack-years of cigarette smoking	19±23
Atherosclerotic risk factors	
Obesity	1,069 (34)
High blood pressure	1,711 (55)
Impaired fasting glucose	976 (31)
Dyslipidemia	1,755 (56)
Smoking	2,065 (66)
Alcohol	2,855 (91)
Intima-media thickness (mm)	0.76±0.13
Plaque score (mm)	3.3±3.1

baPWV (cm/s)	1552±326

Categorical data are presented as number (%), continuous data are presented as mean ± standard deviation. Pack-years is defined as the number of packets smoked per day multiplied by the number of years of smoking.

Abbreviations: HDL-C, high density lipoprotein-cholesterol; LDL-C, low density lipoprotein-cholesterol; hs-CRP, high sensitivity C-reactive protein; baPWV, brachial-ankle pulse wave velocity.

Table 2. Comparison of participant characteristics among high and low intima-media thickness, plaque score, and brachial-ankle pulse wave velocity

	IMT			*PS*						*baPWV*		
	>0.9 mm (n=*363*)	*≤0.9 mm* (n=*2,765*)	p *value*	*≥1.1 mm* (n=*2,517*)	*<1.1 mm* (n=*611*)	p *value*	*≥5.1 mm* (n=*739*)	*<5.1 mm* (n=*2,389*)	p *value*	*≥1,600 cm/s* (n=*1,135*)	*<1,600 cm/s* (n=*1,993*)	p *value*
Age (years)	63±9	56±10	<0.0001	58±10	48±10	<0.0001	63±9	54±10	<0.0001	63±9	53±9	<0.0001
BMI (kg/m^2)	24.6±2.8	24.0±3.1	0.0009	24.0±3.0	24.2±3.3	0.2160	24.0±2.8	24.1±3.1	0.6246	24.0±2.8	24.1±3.2	0.2555
SBP (mm Hg)	134±16	123±16	<0.0001	126±17	118±15	<0.0001	131±17	123±16	<0.0001	136±16	118±14	<0.0001
FBS (mg/dL)	114±26	108±22	<0.0001	110±24	103±16	<0.0001	114±27	107±20	<0.0001	113±26	106±19	<0.0001
LDL-C (mg/dL)	128±29	125±30	0.0654	127±30	121±29	<0.0001	127±31	125±29	0.0739	124±31	127±29	0.0098
Hs-CRP (mg/dL)	0.11±0.22	0.11±0.24	0.8909	0.11±0.24	0.11±0.21	0.9457	0.12±0.28	0.10±0.22	0.0249	0.12±0.28	0.10±0.21	0.0021
Log hs-CRP	-2.92±1.06	-3.01±1.09	0.1482	-3.00±1.09	-3.00±1.11	0.9573	-2.87±1.09	-3.04±1.09	0.0003	-2.87±1.10	-3.07±1.08	<0.0001
Pack-years	24±27	19±22	<0.0001	20±24	16±19	0.0003	26±27	17±21	<0.0001	21±26	18±21	0.0077
Obesity	39%	33%	0.0293	34%	36%	0.3418	34%	34%	0.9293	34%	34%	0.9375
Smoking	66%	66%	0.8597	65%	72%	0.0014	70%	65%	0.0209	62%	68%	0.0001
Alcohol	92%	91%	0.8431	91%	91%	0.5759	91%	91%	0.6020	91%	91%	0.8954
High BP	78%	52%	<0.0001	59%	38%	<0.0001	71%	50%	<0.0001	81%	40%	<0.0001
IFG	40%	30%	0.0003	34%	21%	<0.0001	41%	28%	<0.0001	42%	25%	<0.0001
DL	59%	56%	0.2607	57%	53%	0.0927	62%	54%	0.0007	57%	56%	0.7080

Continuous data are presented as mean ± standard deviations, categorical data are presented as percentage.

Abbreviations: IMT, intima-media thickness; PS, plaque score; baPWV, brachial-ankle pulse wave velocity; BMI, body mass index; SBP, systolic blood pressure; FBS, fasting blood
sugar; LDL-C, low density lipoprotein-cholesterol; hs-CRP, high-sensitivity C-reactive protein; BP, blood pressure; IFG, impaired fasting glucose; DL, dyslipidemia.

Table 3. The proportion by year of IMT>0.9 mm, PS≥1.1 mm, 5.1 mm or baPWV≥1,600 cm/s

	years												Z	*p value*
	2004	*2005*	*2006*	*2007*	*2008*	*2009*	*2010*	*2011*	*2012*	*2013*	*2014*	*2015*		
IMT>0.9 mm	7.3%	13.4%	12.3%	12.0%	18.2%	16.7%	13.1%	8.6%	9.2%	2.5%	5.9%	0.0%	-2.65	0.0079
PS≥1.1 mm	86.3%	79.3%	80.6%	73.4%	80.5%	84.0%	86.9%	76.8%	82.4%	77.0%	80.9%	69.2%	-0.90	0.3691
PS≥5.1 mm	24.6%	19.4%	23.9%	20.9%	24.2%	29.5%	29.7%	21.2%	23.5%	23.6%	25.0%	10.3%	0.83	0.4056
baPWV≥1,600 cm/s	35.6%	30.2%	34.1%	32.3%	42.1%	44.1%	41.1%	31.8%	34.6%	38.5%	43.4%	33.3%	2.60	0.0092

data are presented as percentage

Abbreviations: IMT, intima-media thickness; PS, plaque score; baPWV, brachial-ankle pulse wave velocity.

Table 4 . Results of univariate logistic regression analysis for intima-media thickness (>0.9 mm), plaque score (≥1.1 mm or ≥5.1 mm), and brachial-ankle pulse wave velocity (≥1,600 cm/s)

	IMT (>0.9 mm)			*Presence of atherosclerosis (PS ≥1.1 mm)*			*Advanced atherosclerosis (PS ≥5.1 mm)*			*baPWV (≥1,600 cm/s)*		
	Odds ratio	*95% CI*	p *value*	*Odds ratio*	*95%CI*	p *value*	*Odds ratio*	*95%CI*	p *value*	*Odds ratio*	*95%CI*	p *value*
Obesity	1.29	1.03 - 1.69	0.0260	0.91	0.76 - 1.10	0.3340	0.99	0.83 - 1.18	0.8903	1.01	0.86 - 1.17	0.9306
Smoking	0.98	0.78 - 1.23	0.8468	0.73	0.60 - 0.89	0.0012	1.23	1.03 - 1.47	0.0194	0.74	0.64 - 0.86	0.0001
Alcohol	1.07	0.72 - 1.59	0.9395	1.10	0.81 - 1.49	0.5572	0.93	0.69 - 1.23	0.6015	0.98	0.76 - 1.27	0.9013
High BP	3.25	2.51 - 4.21	<0.0001	2.27	1.89 - 2.72	<0.0001	2.51	2.10 - 3.00	<0.0001	6.40	5.38 - 7.61	<0.0001
IFG	1.53	1.22 - 1.91	0.0003	1.85	1.50 - 2.28	<0.0001	1.75	1.47 - 2.07	<0.0001	2.18	1.87 - 2.55	<0.0001
DL	1.14	0.91 - 1.42	0.2439	1.17	0.98 - 1.39	0.0879	1.34	1.13 - 1.59	0.0006	1.03	0.89 - 1.19	0.6970

Log hs-CRP	1.08	0.97 - 1.19	0.1508	1.00	0.92 - 1.09	0.9573	1.15	1.06 - 1.24	0.0003	1.18	1.11 - 1.26	<0.0001

Abbreviations: IMT, intima-media thickness; PS, plaque score; baPWV, brachial-ankle pulse wave velocity; CI, confidence interval; BP, blood pressure; IFG, impaired fasting glucose; DL, dyslipidemia; hs-CRP, high-sensitivity C-reactive protein.

Table 5. Results of multivariate logistic regression analysis for intima-media thickness (>0.9 mm), plaque score (≥1.1 mm, or ≥5.1 mm), and brachial-ankle pulse wave velocity (≥1,600 cm/s)

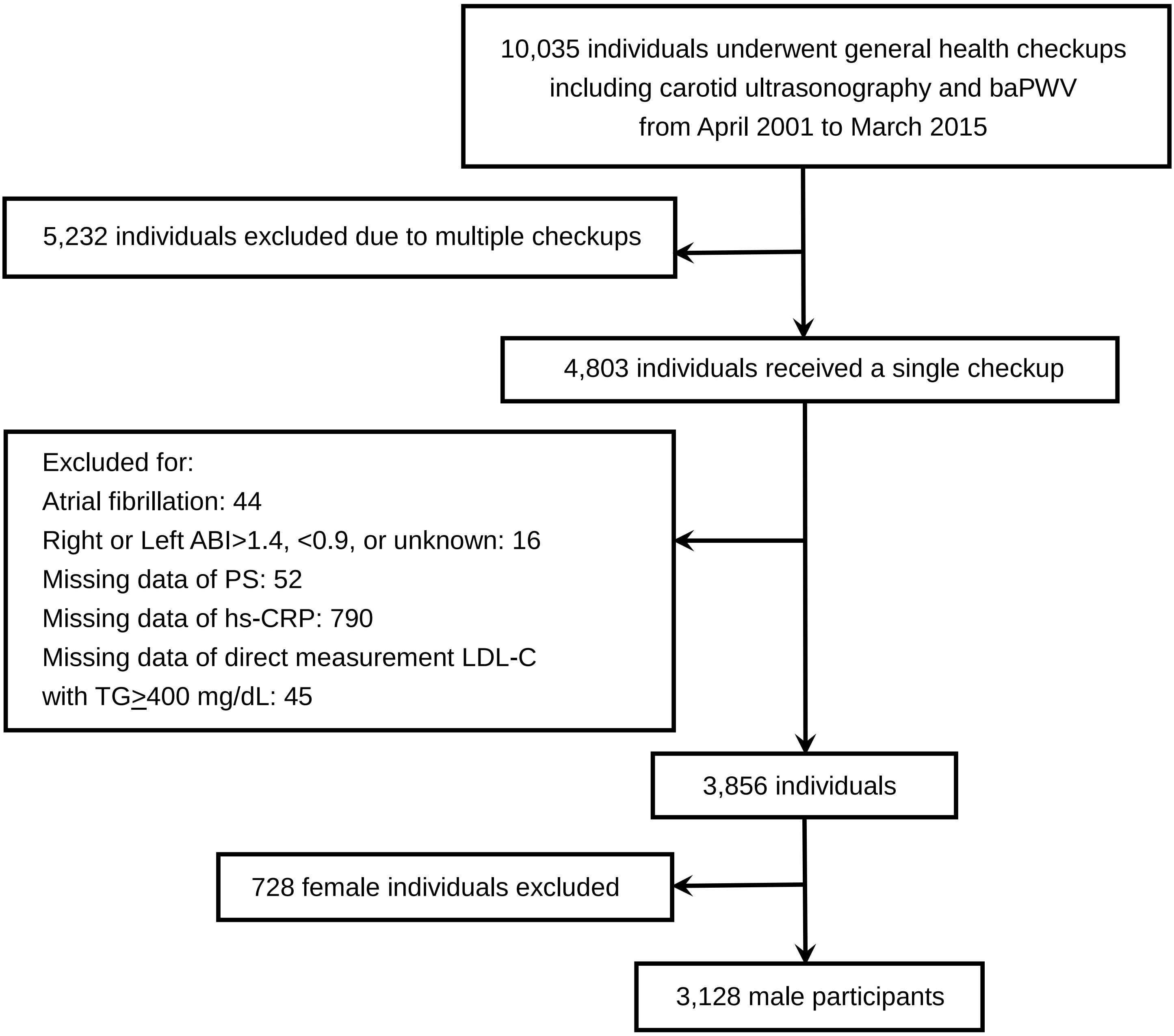
	IMT (>0.9 mm)			*Presence of atherosclerosis (PS ≥1.1 mm)*			*Advanced atherosclerosis (PS ≥5.1 mm)*			*baPWV (≥1,600 cm/s)*		
	Odds ratio	*95%CI*	p *value*	*Odds ratio*	*95%CI*	p *value*	*Odds ratio*	*95%CI*	p *value*	*Odds ratio*	*95%CI*	p *value*
Obesity	1.29	1.01 - 1.66	0.0443	1.00	0.80 - 1.24	0.9743	0.93	0.76 - 1.14	0.4842	0.82	0.67 - 1.00	0.0531
Smoking	1.28	1.00 - 1.63	0.0531	0.92	0.74 - 1.14	0.4462	1.75	1.43 - 2.14	<0.0001	0.98	0.80 - 1.19	0.8264
Alcohol	1.20	0.78 - 1.82	0.4045	1.21	0.86 - 1.72	0.2755	1.04	0.75 - 1.44	0.8029	0.98	0.71 - 1.37	0.9254
High BP	2.35	1.79 - 3.08	<0.0001	1.50	1.22 - 1.84	<0.0001	1.84	1.51 - 2.24	<0.0001	6.10	4.98 - 7.48	<0.0001
IFG	1.23	0.97 - 1.57	0.0841	1.31	1.04 - 1.65	0.0238	1.45	1.20 - 1.75	0.0001	1.88	1.55 - 2.28	<0.0001
DL	1.21	0.95 - 1.53	0.1238	1.32	1.08 - 1.62	0.0070	1.57	1.30 - 1.91	<0.0001	1.20	0.99 - 1.45	0.0641

Log hs-CRP	1.01	0.91 - 1.13	0.8046	0.99	0.90 - 1.08	0.7831	1.11	1.02 - 1.20	0.0191	1.21	1.11 - 1.32	<0.0001

Adjusted for age and the enrolled-year

Abbreviations: IMT, intima-media thickness; PS, plaque score; baPWV, brachial-ankle pulse wave velocity; CI, confidence interval; BP, blood pressure; IFG, impaired fasting glucose; DL, dyslipidemia; hs-CRP, high-sensitivity C-reactive protein.

Figure 1.


10,035 individuals underwent general health checkups including carotid ultrasonography and baPWV from April 2001 to March 2015
5,232 individuals excluded due to multiple checkups
4,803 individuals received a single checkup
Excluded for:
Atrial fibrillation: 44
Right or Left ABI>1.4, <0.9, or unknown: 16
Missing data of PS: 52
Missing data of hs-CRP: 790
Missing data of direct measurement LDL-C
with TG≥400 mg/dL: 45
3,856 individuals
728 female individuals excluded
3,128 male participants