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Comparison of Carotid Plaque Burden among Healthy Middle-aged Men Living in the US, Japan, and South Korea

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Abstract

Background—Carotid plaque has emerged as a marker of coronary heart disease (CHD) risk. Comparison of carotid plaque burden between different race/ethnic groups may provide a relative estimate of their future CHD risk.

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Methods—We conducted a population-based study among apparently healthy middle-aged men aged 40–49 years (ERA JUMP study (n=924)) and recruited 310 Whites in Pittsburgh, US, 313 Japanese in Otsu, Japan, and 301 Koreans in Ansan, South Korea. Number of carotid plaque and CHD risk factors was assessed using a standardized protocol across all centers. The burden of carotid plaque was compared between race/ethnic groups after adjustment for age and BMI, and after multivariable adjustment for other CHD risk factors using marginalized zero-inflated Poisson regression models. Cross-sectional associations of risk factors with plaque were examined.

Results—Whites (22.8%) had more than four-fold higher prevalence ($p<0.01$) of carotid plaque than Japanese men (4.8%) while the prevalence among Koreans was 10.6%. These differences remained significant after adjustment for age, BMI as well as other risk factors – incidence density ratio (95% confidence interval) for plaque was 0.13 (0.07, 0.24) for Japanese and 0.32 (0.18, 0.58) for Koreans as compared to Whites. Age, hypertension and diabetes were the only risk factors significantly associated with presence of carotid plaque in the overall population.

Conclusion—Whites have significantly higher carotid plaque burden than men in Japan and Korea. Lower carotid plaque burden among Japanese and Koreans is independent of traditional CVD risk factors.

Keywords

atherosclerotic plaque; carotid stenosis; carotid intima-media thickness; risk factors; epidemiology; global health

Introduction

Presence of plaque in the carotid artery has emerged as a strong predictor of coronary heart disease (CHD).[1] Carotid plaque is recently reported to be a stronger predictor of CHD than carotid intima-media thickness (IMT) [1, 2] which is commonly used as a surrogate measure of subclinical atherosclerosis in epidemiological studies. Thus, comparison of carotid plaque burden between different race/ethnic groups may provide a relative estimate of their future risk of CHD.

CHD remains the leading cause of mortality in the United States (US), with more than three-fold higher CHD mortality rates in the US than in Japan.[3] Although being industrialized for several decades with westernization of diet and lifestyle, Japan continues to have extremely low CHD rates. Similar to Japan, South Korea has extremely low CHD rates in spite of rapid westernization.[3] While several studies have examined racial/ethnic differences in CHD as well as markers of subclinical disease such as carotid IMT,[4, 5] only a few studies have compared prevalence of carotid plaque across different race/ethnic groups.[6] Further, previous studies have used varying methodology to examine and define carotid plaque,[1] thus limiting the validity of any post-hoc comparison of plaque prevalence between different studies. With the emergence of carotid plaque as a predictor of CHD, it is now important to systematically examine the differences in carotid plaque burden between populations in the US and Japan.

Although many population-based studies have assessed the prevalence of carotid plaque,[6, 7] no study has compared the burden of carotid plaque between the US and Japan or South

Korea. We used a standardized protocol to compare the number of carotid plaques among Whites in the US, Japanese in Japan, and Koreans in South Korea in the ERA JUMP study, an international population-based study for assessing subclinical atherosclerosis in 40–49 year-old men. We have previously reported lower coronary atherosclerosis and lower IMT among Japanese men than US whites.[8] Therefore, we hypothesized that the burden of carotid plaque is highest among Whites. We further examined which CHD risk factors were associated with the presence of carotid plaque in this sample population.

Methods and Materials

Participants

During 2002–2006, a population-based sample of 925 men aged 40–49 years, with no clinical cardiovascular disease (CVD) or other severe diseases was recruited from 3 centers: 310 Whites from Pittsburgh, Pennsylvania; 313 Japanese from Kusatsu city, Shiga, Japan; and 302 Koreans from Ansan, Gyeonggi-do, South Korea as previously described.[8] The final sample for this study consisted of 924 men (310 Whites, 313 Japanese men in Japan, and 301 Koreans) with complete data. Written informed consent was obtained from all participants. The study was approved by the Institutional Review Boards of the following institutions: the University of Pittsburgh, Pittsburgh, Pennsylvania, US; Shiga University of Medical Science, Otsu, Japan; and Korea University, Seoul, South Korea.

B-Mode Carotid Ultrasound Scanning

Presence and extent of plaque were evaluated in each of 4 segments of the left and right carotid arteries i.e., distal and proximal common carotid artery (CCA), carotid bulb, and the proximal internal carotid artery (ICA). Plaque was defined as a distinct area of the vessel wall protruding into the vessel lumen that was at least 50% thicker than the adjacent IMT. Number of distinct plaques was counted in the abovementioned carotid segments on both sides and used as a measure of the carotid plaque burden.[9]

Before the start of the study, sonographers at all centers received training for carotid scanning provided by the Ultrasound Research Laboratory at the University of Pittsburgh. Continuous-quality assessment programs developed by the Ultrasound Research Laboratory to assure scanning quality were applied across all study sites throughout the study.[9] Pittsburgh and Kusatsu sites used a Toshiba 140A scanner (Tokyo, Japan) equipped with a 7.5-MHz-linear-array imaging probe while the Ansan site used a Titan high-resolution ultrasound system with a 10.5 MHz linear array. Readers were blinded to participants' characteristics and the study centers. Under continuous-quality assessment programs, there was excellent agreement between sonographers for carotid plaque assessment (kappa statistic, $\kappa=0.78$). For IMT measurement, digitized carotid artery images were sent to the University of Pittsburgh from other centers, and were read by a trained reader using a standardized protocol and a semi-automated edge detection software. The sonographer measured the average IMT across 1-cm segments of near and far walls of the common carotid arteries and the far wall of the carotid bulb and internal carotid arteries on both sides. Average IMT was calculated by taking a mean of the IMT measurements.[8]

Risk Factor Assessment

All participants underwent a physical examination, completed a lifestyle questionnaire and a laboratory assessment as described previously.[8, 10, 11] Body weight and height were measured while the participant was wearing light clothing without shoes. Body-mass index (BMI) was calculated as weight in kilograms divided by the square of the height in meters. Blood pressure was measured—after the participants emptied their bladder and sat quietly for 5 minutes—twice on the right arm with an automated sphygmomanometer (BP-8800, Colin Medical Technology, Komaki, Japan) using an appropriate sized cuff width; the average of the two measurements was used. Hypertension was defined as systolic blood pressure (SBP) ≥ 140 mmHg and/or diastolic blood pressure (DBP) ≥ 90 mmHg or use of anti-hypertensive medications. [12] Venipuncture was performed early in the clinic visit after a 12-hour fast. Blood samples were stored at -80°C and shipped on dry ice to the University of Pittsburgh. Serum lipids were determined using the protocol standardized by the Centers for Disease Control and Prevention.[13] Dyslipidemia was defined as LDL-c ≥ 160 mg/dL or use of lipid-lowering medications.[14] Serum glucose was determined by using hexokinase–glucose-6-phosphate-dehydrogenase enzymatic assay. Diabetes was defined as individuals with fasting glucose ≥ 126 mg/dl or use of medications for diabetes. [15] Alcohol drinking was defined as intake ≥ 2 times/week. Ever smoking was defined as current or past cigarette smoking. Use of blood pressure-lowering, diabetes, and lipid-lowering medication was ascertained through questionnaire. Data collection procedures were standardized across all centers.

Statistical Methods

Descriptive characteristics and segment-wise presence of carotid plaque were assessed after stratification by race/ethnicity. The overall population was also described in terms of carotid plaque presence. To compare the burden of carotid plaque between these population groups, crude, age-BMI adjusted, and multivariable-adjusted incidence density ratios were calculated using a marginalized zero-inflated Poisson regression model with NLMIXED procedure in SAS.[16, 17] This approach allowed us to account for the large fraction of sample population with no plaque (inflated zeroes), and provided incidence density ratio as the measure to compare plaque between the three racial groups.

To examine which CVD risk factors were associated with the presence of carotid plaque, we performed forward-selection logistic regression analyses in a combined sample of the three race/ethnic groups. We kept carotid plaque presence as the outcome variable and the following variables as independent variables in the regression model – age, race/ethnicity, BMI, SBP, glucose, ever smoking, alcohol drinking status, TC/HDL-c, LDL-c, and triglycerides (log-transformed). Alpha (two-sided) was set at 0.05 for determining statistical significance. As a confirmatory analysis, we performed the above analyses using a traditional logistic regression model forcing all the above variables into the regression equation. All analyses were performed using SAS/STAT software v 9.4 of the SAS System, Cary, NC, USA.

Results

Comparison of Risk Factors

The mean age was approximately 45 years in all three population groups. Whites had significantly higher BMI than the Japanese and Koreans, although they had much lower smoking rates than the Japanese and Koreans. LDL-c among Whites was similar to Japanese, while it was lowest among Koreans. Whites had higher HDL-c than the Koreans but less than the Japanese. Whites and Koreans had lower hypertension rates than Japanese. Whites had the lowest prevalence of diabetes of the three groups although the differences were not statistically significant. (Table 1)

When comparing population characteristics by presence or absence of carotid plaque in the combined population of the three groups, those with plaque (n=117, 12.7%) were older (46.1 ± 2.8 years vs. 44.8 ± 2.8 years, $p = 0.01$), had higher BMI (26.9 ± 4.4 kg/m² vs. 25.2 ± 3.7 kg/m², $p = 0.01$), SBP (125.5 ± 14.6 mmHg vs. 122.7 ± 13.9 mmHg, $p = 0.04$), diabetes (12.8% vs. 5.2%, $p = 0.01$), and hypertension (29.9% vs. 17.4%, $p = 0.01$), while they had similar rates of glucose (105.4 ± 17.9 mg/dl vs. 103.2 ± 16.4 mg/dl, $p = \text{ns}$), alcohol drinking (50.4% vs. 52.2%, $p = \text{ns}$) and smoking (53.8% vs. 62.3%, $p = \text{ns}$). (online supplement)

Carotid plaque

Whites (22.8%) had significantly higher prevalence of carotid plaque as compared to Japanese (4.8%, $P = 0.0001$) and Koreans (10.6%, $P = 0.0001$). A majority of participants with prevalent carotid plaque had only one plaque in the carotid arteries. In all three race/ethnic groups, more plaques were present in the carotid bulb than in the common carotid or internal carotid artery. The race/ethnic differences remained significant within individual carotid segments, i.e. Whites > Koreans > Japanese within carotid bulb and internal carotid artery. These differences were not seen in the CCA due to lower plaque prevalence in the CCA (Table 2)

The differences in number of plaques were independent of age and BMI. (Figure 1) The differences remained significant even after further adjusting for other CVD risk factors including hypertension and diabetes. As compared to Whites, the multivariable-adjusted incidence density ratio for carotid plaque was 0.13 (95% CI: 0.07, 0.24) for Japanese and 0.32 (95% CI: 0.18, 0.58) for Koreans. (Figure 1) Similar results were seen after excluding participants with hypertension, diabetes, and hyperlipidemia from the analysis. (online supplement)

Risk factors for Carotid Plaque

In a race/ethnicity-adjusted logistic regression model created using forward-selection strategy (Model I), age, hypertension, diabetes, and ever smoking were significantly associated with the cross-sectional presence of carotid plaque. (Table 3) These risk factors together explained 18% of the total variance (R^2) in carotid plaque. When we force-entered other cardiovascular risk factors in the model (Model II), the results were similar, and the R^2 increased only marginally to 19%. (Table 3) When carotid IMT was further included in the

model, the R^2 increased from 19% to 33%. In this regression model, carotid IMT had the strongest association with the presence of carotid plaque with a β_{std} of 0.56.

Discussion

In our population-based international study among middle-aged men without CVD, we observed wide variations in the prevalence of carotid plaque, with Whites having nearly five-fold higher burden of carotid plaque as compared to Japanese. The differences in plaque burden remained significant within individual segments of carotid plaque. We further showed that age, hypertension, diabetes, and smoking were independently associated with carotid plaque burden, while other cardiovascular risk factors added little to explain the presence of plaque. This is the first population-based international study to compare the burden of carotid atherosclerotic plaque among different race/ethnic populations living in different countries.

We found that the prevalence of carotid plaque among Whites was 22.8%, which is significantly higher than that in Japanese and Koreans. Similar prevalence (26.6%) of carotid plaque among Whites has been reported from the Atherosclerosis Risk in Communities study among 45–49 year old men.[18] However, in the Multi-Ethnic Study of Atherosclerosis, 46% of the White men and women aged 45–84 years had carotid artery plaque.[7] Previous studies among older Japanese populations have reported much higher prevalence than among Japanese in our study. In the Suita Study of 1,694 Japanese in Japan, men (n=814) in age groups of 50–59 years, 60–69 years and 70–79 years had 79%, 91% and 98% prevalence of carotid plaque respectively.[19] In a smaller Japanese study consisting of 100 patients with CVD (age: 61 ± 14 years, 76% male) and 132 participants without CVD (age: 58 ± 14 years, 67% male), prevalence of carotid plaque was 59% and 41% respectively.[20] However, carotid plaque was defined as $IMT > 1.1$ mm and $IMT > 1.0$ mm in these Japanese studies, respectively. It is likely that the higher prevalence observed in these studies was due to an older sample population and use of a different – probably more sensitive – definition for carotid plaque. In Korea, a population-based study reported approximately 31% prevalence of carotid plaque in a rural population free of CVD. This study included both men and women 40–91 years of age (mean ~ 61 years).[21] Another population-based study in a similar age group reported 37% prevalence of plaque among men.[22] The prevalence of plaque reported in these studies is higher probably due to their populations being older than in our study.

Our finding of higher plaque burden among Whites was consistent even when we compared segment-specific prevalence of carotid plaque. While carotid plaque was rare in the CCA, its prevalence was highest in the carotid bulb. Although carotid plaque is strongly associated with future CVD, the magnitude of association differs slightly by the location of carotid plaque. Nevertheless, the higher presence of plaque in the carotid bulb as well as in the ICA among Whites points to their higher overall atherosclerotic burden.

Eastern Asia vs. the US

Whites had more than four times higher burden of carotid plaque than Japanese, although Japanese had higher prevalence of hypertension, diabetes and smoking, and similar levels of

LDL-c, all potential risk factors for plaque development. The difference remained after adjustment for BMI, smoking, and other CVD risk factors. These results are also consistent with our previous report of significantly more coronary atherosclerosis and higher IMT among Whites than Japanese.[8] It is also reported that inflammation is positively associated with carotid plaque.[23, 24] Low levels of inflammation in Japan might be one of the reasons for low atherosclerosis among Japanese as compared to Whites.[25] However, in a supplementary analysis, CRP (log-transformed) was not significantly associated with prevalence of carotid plaque in our study after adjusting for race/ethnicity and other risk factors (data not shown). Although no study has examined the genetic reasons for lower atherosclerosis in Japan, it is possible that genetic markers such as variation in lipoprotein lipase gene may also be responsible for lower carotid atherosclerosis seen among Japanese in our study. [26, 27]

Koreans had about half the burden of carotid plaque than Whites, even after adjusting for traditional risk factors. Although Koreans are genetically similar to the Japanese,[28] and have similar or more favorable profile of risk factors, they have twice the burden of carotid plaque as the Japanese. We have shown that Koreans also had higher carotid IMT than Japanese.[29] Additionally, CHD mortality among Koreans is also higher than among the Japanese.[30] Given the genetic similarities between Koreans and Japanese, higher burden of atherosclerosis and CHD among Koreans is likely due to some environmental factors. Thus, further investigations are warranted to examine the reasons for these differences between Koreans and Japanese.

Risk Factors for Plaque

Of all the traditional CVD risk factors, age, hypertension, and diabetes were significantly associated with carotid plaque after adjusting for race/ethnicity in this cross-sectional study. Even in this relatively homogenous population of men aged 40–49 years, of all the risk factors, age had the strongest association with carotid plaque. In the NOMAS study, i.e. an older population-based cohort in the US comprising of 60% Hispanics, age, smoking, SBP, DBP, diabetes, and blood pressure medication use were significant predictors of carotid plaque.[31] Similarly, Klein et al. reported that in a sample of 876 clinical patients (mean age: 53.4±12.0 years; 47% female), age, sex, SBP, smoking, diabetes, and lipid medication were significant predictors of carotid plaque.[32] A lack of association for many of these risk factors seen in our study may be because our study included a relatively younger and healthier population.

In our study, 18% of the variance in the prevalence of carotid plaque was explained by the three significant risk factors in the model. Forcing other variables in the model did not result in a significant increase in the R^2 . Previous studies have reported similar results – in the NOMAS study, risk factors explained 19.5% of the carotid plaque variance.[31] Similar to our study, age as the single largest contributor to the R^2 . Klein et al reported from a clinical population a R^2 of 48.6% for total carotid plaque area, and a R^2 of 13.9% for total carotid stenosis.[32]

The differences in plaque prevalence remained significant even after adjusting for IMT. This was somewhat expected as the definition used to identify plaque includes a measure of IMT,

i.e. plaque was defined as focal protrusion at least 50% thicker than the surrounding IMT. Thus, assessment of plaque in an individual was based on his IMT. Further, while IMT is strongly associated with age and blood pressure,[33] carotid plaque is atherosclerotic in origin and has a lipid core.[34] Thus, it is possible that IMT and carotid plaque have different pathophysiological origins even though they are both markers of cardiovascular risk. In another population-based study in France, IMT was a significant predictor of carotid plaque occurrence in a 59 to 71 year old population followed over 4 years.[35] In our study as well, IMT was the strongest determinant of plaque among all factors. Thus, it seems that IMT is a significant, but not the sole, determinant of carotid plaque.

Carotid plaque assessments were performed at the University of Pittsburgh's Ultrasound Research Laboratory (URL) and continuous quality control was maintained by the staff. URL has significant experience in serving as core lab for assessing subclinical atherosclerosis in several large epidemiological studies and clinical trials, and has made significant contributions in determining reproducibility and reliability of carotid ultrasound assessments in the past. [36] Our results should be interpreted in light of certain limitations. As our results are based on the analysis of cross-sectional data, we cannot comment on the temporality of any association. The use of non-invasive assessment prevents us from examining differences in carotid plaque characteristics such as presence of intra-plaque calcification and hemorrhage. However, we performed ultrasonographic carotid artery examination given the population-based design of this study. All the participants in this study were men 40–49 years of age, thus limiting the generalizability of the findings, especially to women. However, assessing atherosclerosis in this middle-aged sample gives the opportunity for potential intervention to prevent the development of future clinical disease. We cannot perform analyses to examine risk factors for carotid plaque in individual race/ethnicities as there were few men with carotid plaque among the Japanese and Koreans.

Conclusion

This is the first population-based epidemiological study to use a standardized protocol for risk factor and carotid plaque assessments across race/ethnicities in different geographic regions. Whites have significantly higher carotid atherosclerotic plaque burden than Japanese and Koreans, despite having a more desirable profile on several CVD risk factors. These differences are not explained by traditional cardiovascular risk factors. These results suggest higher atherosclerotic burden and consequent risk for CHD among White men in the US as compared to men in Japan and Korea.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Highlights

- White men in the US have four-fold higher carotid plaque than Japanese and twice as much as Koreans
- These differences persist after accounting for lower BMI among east Asians in the study
- Overall, age, hypertension and diabetes status are associated with higher carotid plaque burden

White was treated as the referent category in the analyses

All prevalence ratios in the analyses were significant at p-value <0.01

Crude Model: Unadjusted model

Model I: Age-, BMI- adjusted

Model II: Model I + SBP, total cholesterol: HDL-cholesterol ratio, diabetes, hypertension, smoking, and alcohol drinking

Model III: Model II + carotid intima-media thickness

Figure 1.
Incidence Density Ratio of Carotid plaque.

Table 1

Descriptive characteristics of the study population.

	Whites (W, n=310)	Japanese (J, n=313)	Koreans (K, n=301)	Differences (p<0.05)//
Age (years)	45.0 ± 2.8	45.1 ± 2.8	44.8 ± 2.8	J = W = K
BMI (kg/m ²)	28.0 ± 4.4	23.7 ± 3.1	24.7 ± 2.7	W > K = J
Systolic BP (mmHg)	122.6 ± 11.2	125.0 ± 16.1	121.6 ± 14.1	J > W = K
Hypertension (%) [*]	15.2	26.5	15.6	J > K = W
Glucose (mmol/l)	5.65 ± 0.86	5.93 ± 1.04	5.71 ± 1.0	J > K = W
Diabetes (%) [‡]	3.6	6.1	9.6	K = J = W
Ever Smoking (%)	27.1	82.8	74.1	J > K > W
Alcohol Drinker (%) [‡]	44.3	67.3	44.0	J > W = K
LDL-cholesterol (mmol/l)	3.48 ± 0.86	3.42 ± 0.93	3.00 ± 0.82	W = J > K
HDL-cholesterol (mmol/l)	1.23 ± 0.33	1.40 ± 0.35	1.18 ± 0.30	J > W > K
Triglycerides, mmol/l [§]	1.46 (1.04, 2.08)	1.55 (1.16, 2.05)	1.51 (1.08, 2.27)	J = K = W
TC:HDL ratio	4.69 ± 1.29	4.27 ± 1.29	4.43 ± 1.16	W > J > K
Medications (%)				
Hypertension	8.7	5.4	4.6	W = J = K
Diabetes	1.0	1.9	0.3	J = W = K
Lipids	12.3	3.5	1.3	W > J = K

Values are mean ± SD unless otherwise mentioned.

^{*} Hypertension was defined as presence of one or more of following – i) Systolic blood pressure (BP) 140 mmHg, ii) Diastolic BP 90 mmHg, or iii) use of antihypertensive medication[‡] Diabetes was defined as either fasting glucose 7 mmol/L or use of diabetic medication, or both[§] Alcohol drinking was defined as 2 or more drinks per week[§] median (interquartile range)

// Inter-group differences for continuous variables were calculated using t-tests except for triglycerides (non-parametric tests), and categorical variables (chi-square tests). “=” represents no statistical significance for the difference while “>” represents p<0.05.

TC:HDL = total cholesterol: high-density lipoprotein cholesterol ratio; BP= blood pressure; LDL= low-density lipoprotein; HDL= high-density lipoprotein

Table 2

Site-specific prevalence of carotid plaque in the three populations.

	White (n=310)	Japanese (n=313)	Koreans (n=301)	Difference *
Plaque prevalence (%)	22.8	4.8	10.6	W > K > J
CCA plaque (%)	0.6	0.3	0.3	W = K = J
Bulb plaque (%)	16.9	3.5	9.3	W > K > J
ICA plaque (%)	10.1	1.6	2.3	W > K = J
Mean number of plaques (SD) [†]	1.67 (1.20)	1.27 (0.46)	1.34 (0.60)	W = K = J

* Inter-group differences were calculated using chi-square tests and t-tests as appropriate. "=" represents no statistical significance for the difference while ">" represents p<0.05

[†] Among participants with any carotid plaque present

CCA: common carotid artery; ICA: internal carotid artery

Table 3

Risk factors associated with the presence carotid plaque

Model	Variable	Standardized β (β_{std}) [*]	β	SEM	p-value	R ²
Model A ^{*,†}	Age	0.29	0.19	0.04	<0.001	18%
	Koreans vs. White	-	-1.04	0.25	<0.001	
	Japanese vs. White	-	-2.02	0.3112	<0.001	
	Hypertension	-	0.34	0.13	0.01	
	Diabetes	-	0.50	0.19	0.01	
Model B ^{*,‡}	Age	0.28	0.18	0.04	<0.001	19%
	Koreans vs. White	-	-1.12	0.30	<0.001	
	Japanese vs. White	-	-2.16	0.37	<0.001	
	Hypertension	-	0.33	0.13	0.01	
	Diabetes	-	0.49	0.19	0.01	
	TC: HDL ratio ^{//}	0.09	0.14	0.10	0.19	
	BMI	0.02	0.01	0.03	0.79	
	Ever Smoking	-	0.15	0.12	0.23	
	Drinker	-	0.06	0.11	0.60	
	Triglyceride (log)	0.01	0.04	0.24	0.87	
Model C ^{*,‡,§}	Age	0.23	0.15	0.04	<0.01	33%
	Koreans vs. White	-	-1.18	0.33	0.0003	
	Japanese vs. White	-	-1.69	0.39	<0.001	
	Hypertension	-	0.21	0.14	0.15	
	Diabetes	-	0.23	0.21	0.27	
	TC:HDL ratio ^{//}	-0.01	-0.02	0.12	0.89	
	BMI	-0.08	-0.04	0.03	0.27	
	Ever Smoking	-	0.27	0.27	0.31	
	Drinker	-	0.01	0.12	0.91	
	Triglyceride (log)	0.01	0.04	0.29	0.88	
	Carotid IMT	0.56	10.95	1.35	<0.001	

* Standardized parameter estimates were not calculated for categorical variables

† Model A was developed using forward-selection strategy in logistic regression with p-value for significance at 0.05

‡ Models B & C were traditional model with risk factors forced into the logistic regression

§ Model C: Model B + carotid intima-media thickness

|| TC:HDL ratio: total cholesterol: high-density lipoprotein cholesterol ratio

Hypertension was defined as presence of one or more of following – i) Systolic blood pressure (BP) 140 mmHg, ii) Diastolic BP 90 mmHg, or iii) use of antihypertensive medication

Diabetes was defined as either glucose 126 mg/dl or use of diabetic medication, or both Drinker was defined as alcohol drinking 2 times/week

BP= blood pressure; BMI= body-mass index; IMT = intima-media thickness