Predictors of Carotid Intima-Media Thickness and Plaque Progression in a Chinese Population

Ling-Chun Huang¹, Ruey-Tay Lin^{1,2}, Chien-Fu Chen^{1,2}, Chun-Hung Chen¹, Suh-Hang Hank Juo^{3,4} and Hsiu-Fen Lin^{1,2}

¹Department of Neurology, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan

²Department of Neurology, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan

³Department of Medical Research, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan

⁴Department of Medical Genetics, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan

Aim: Atherosclerotic diseases are the leading cause of death worldwide. Longitudinal changes in carotid intima-media thickness (IMT) and plaque are being increasingly used as markers of atherosclerosis progression and may predict future cardiovascular events. This study aimed to investigate the predictors of carotid IMT and plaque progression in a Chinese population and to determine whether these predictors differ by gender.

Methods: Segment-specific carotid IMT and plaque were measured in 712 stroke- and myocardial infarction-free subjects at baseline and after an average interval of 4.3 ± 0.9 years. Multivariate linear regression and logistic regression analyses were conducted to investigate the predictive effect of age, gender, and cardiovascular risk factors on carotid IMT and plaque progression. Gender-specific analyses were also performed.

Results: Overall, age and smoking were predictors of common carotid artery IMT progression (adjusted $p < 0.001$ and $p = 0.045$, respectively). Age, hypertension, and use of antihypertensive medication were predictors of bifurcation IMT progression (adjusted $p < 0.001$, $p = 0.033$, and $p < 0.001$, respectively). The use of antihypertensive medication was associated with less annual IMT progression in hypertensive subjects than in those who did not take medication, which was most prominent in the bifurcation segment. In addition, most predictors of IMT progression were identified in women in a gender-specific analysis. For plaque progression, age and gender were independent predictors.

Conclusions: The predictors of carotid atherosclerosis progression were gender and segment specific. The detection and control of hypertension may prevent atherosclerosis progression, particularly in women.

Key words: Intima-media thickness, Plaque, Cardiovascular risk factors, Progression, Atherosclerosis

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Introduction

Atherosclerotic diseases are the leading cause of death in developed countries. Events because of atherosclerosis, such as cardiovascular disease, stroke, and myocardial infarction (MI), often occur without warning¹. The key factor for the primary prevention of

atherosclerotic events is to identify asymptomatic individuals who are at a high risk² and then implement strategies that are directed at risk factors, which are known to be related to clinical events.

Carotid intima-media thickness (IMT) and plaque, which are surrogate markers of subclinical atherosclerosis, are considered to predict future MI and stroke³⁻⁶, and changes in carotid IMT and plaque, which are noninvasively assessed by ultrasound, are being increasingly used as markers of atherosclerosis progression^{7, 8}. Several studies have investigated the predictors of carotid IMT and plaque progression⁹⁻¹⁵. However, most of these longitudinal studies have

Address for correspondence: Hsiu-Fen Lin, Kaohsiung Medical University, 100 TzYou First Road, Kaohsiung City 807, Taiwan

E-mail: sflin@kmu.edu.tw

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focused on Caucasian populations, and only a few studies have investigated the predictors of atherosclerosis progression in Asian populations¹⁶⁻¹⁹.

In a recent study on a Chinese population, the 5-year change in systolic blood pressure was found to be associated with the incidence of carotid plaque and total plaque area progression¹⁹. Moreover, in a Korean study on an elderly population (>60 years of age), metabolic syndrome was found to be associated with the occurrence of new plaque and changes in common carotid artery (CCA) IMT after excluding subjects with thicker carotid IMT and carotid plaque at baseline¹⁸. Another longitudinal study that was conducted in Japan also demonstrated the impact of metabolic syndrome on the progression of CCA IMT. The authors found that an increasing number of metabolic syndrome components was related to a larger annual IMT change, particularly in women¹⁷. Carotid plaque and IMT may reflect the different biological aspects of atherogenesis with distinct relationships with cardiovascular risk factors²⁰. However, none of these studies on Asian populations explored the association of conventional cardiovascular risk factors with carotid IMT and plaque progression. In addition, no studies evaluated the association between vascular risk factors and carotid IMT progression at different segments in Asian patients.

Aim

This study aimed to investigate the predictors of the progression of segment-specific carotid IMT and plaque in a stroke- and MI-free Chinese population residing in Taiwan. In addition, we investigated the gender-specific predictors of carotid IMT and plaque progression.

Methods

Subjects

This prospective study was initiated in August 2006²¹. The stroke- and MI-free participants were recruited through an advertisement that was posted in the Kaohsiung Medical University Hospital. From November 2008 to September 2014, 879 subjects who completed baseline surveys between August 2006 and December 2009 were contacted. The Kaohsiung Medical University Hospital Institutional Review Board approved the study, and all participants provided their written informed consent.

Cardiovascular Risk Factors

At baseline and follow-up visits, a self-administered structured questionnaire was provided to collect

sociodemographic information, medical history, medication exposure, and smoking habits. Total cholesterol and glucose levels were measured from venous blood after fasting for at least 8 h. A calibrated standard aneroid sphygmomanometer (Omron; Vernon Hills, Illinois) was used to measure blood pressure after resting for 5 min. Two measurements of blood pressure were taken, and the average of these two measurements was used for analysis. Hypertension was defined as systolic or diastolic blood pressure of $\geq 140/90$ mmHg or the use of antihypertensive medications. Diabetes was defined as a fasting blood glucose level of ≥ 126 mg/dl or current treatment for diabetes. Hypercholesterolemia was defined as a serum total cholesterol level of ≥ 200 mg/dl or the use of lipid-lowering medications. Participants were defined as smokers if they had ever smoked or were current smokers. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2).

Carotid IMT and Plaque Measurement

Carotid IMT was measured on enrollment and during the follow-up period for each participant by an experienced technician who was blinded to the patients' clinical data. Carotid IMT was assessed using a Philips HD 11 ultrasonography system that was equipped with a broadband linear array transducer. The transducer scanning direction was anterior oblique insonation while the subject was in the supine position. IMT was bilaterally visualized and measured at the plaque-free area of the CCA (10–20-mm proximal to the tip of the flow divider), carotid bifurcation (BIF) (tip of the flow divider extending 10-mm proximal), and internal carotid artery (ICA) (10-mm proximal above BIF). If a carotid plaque was insonated, carotid IMT was measured outside the plaque portion. The far wall of the carotid IMT was analyzed using an off-line automatic computerized analysis system (Philips QLAB quantification software). Mean IMT values of both the right and left arteries from each segment were used for analysis. The annual progression of IMT ($\mu m/year$) was calculated as the difference between the IMT value that was measured at enrollment and during follow-up divided by the follow-up period in years. The intra-reader absolute IMT differences and standard deviations between the two readings were 0.01 ± 0.01 mm in CCA, 0.03 ± 0.04 mm in BIF, and 0.02 ± 0.01 mm in ICA.

A plaque was defined as an area of focal protrusion into the lumen at least 50% greater than the surrounding wall thickness. It was assessed by the same equipment that was used for the carotid IMT measurement. The presence of carotid plaques at 10 locations in the carotid arteries (proximal and distal CCA,

BIF, ICA, and external carotid artery) was recorded. The total number of plaques was counted offline, and the changes in the number of plaques that were measured at enrollment and during follow-up were calculated. We defined plaque progression as an increase in the number of plaques by one or more during the follow-up compared with the number at enrollment. All ultrasound data were interpreted by a single neurologist (Dr. Hsiu-Fen Lin).

Statistical Analysis

Data were presented as mean $\pm$ standard deviation or proportions. The χ^2 test was used for categorical data and the t-test for continuous data. The independent relationships between baseline risk factors and IMT progression were assessed by multivariate linear regression analysis. We created dummy variables to group hypertension and hypercholesterolemia status as no disease, disease with treatment, and disease without treatment. Logistic regression analysis was conducted to investigate the predictive effect of baseline risk factors on the progression of plaque. We further analyzed these effects by gender. All analyses were performed using SPSS version 17.0 (SPSS Inc., Chicago, IL, USA). A two-tailed p value of <0.05 was considered to be statistically significant.

Results

Demographic Data

Among the 879 eligible subjects, 98 were lost to follow-up, 60 refused to complete the second survey, and nine died. In total, 712 subjects were successfully followed up. Comparisons of the baseline characteristics between the patients who completed follow-up and those who dropped out are shown in **Supplementary Table 1**. The demographic and basic clinical characteristics of 712 subjects (274 men and 438 women) who completed the study are shown in **Table 1**. The age at enrollment was 54.7 ± 9.4 years, and the mean duration of follow-up was 4.3 ± 0.9 years. At baseline, more men had diabetes, a higher BMI, and smoked than women. Men also had a thicker IMT and higher rate of plaques compared with women at baseline and follow-up. Although there was no statistically significant difference in IMT progression between men and women, men had a higher rate of plaque progression.

Predictors of Carotid IMT Progression

Multivariate regression analysis was used to identify independent predictors of IMT progression (**Table 2**). We found a significantly inverse correlation between baseline IMT and its annual rate of progres-

sion (**Supplementary Table 2**), which is consistent with previous reports^{11, 12}. Therefore, in addition to conventional risk factors at baseline (i.e., age, gender, diabetes, hypertension, hypercholesterolemia, smoking, BMI, antihypertensive and lipid-lowering medications), baseline IMT was selected as a covariate. We found that the statistical significance of conventional risk factors varied in different carotid segments. Age and smoking were independent predictors of CCA IMT progression (adjusted $p < 0.001$ and $p = 0.045$, respectively). Age and hypertension were independent predictors of BIF IMT progression (adjusted $p < 0.001$ and $p = 0.033$, respectively), while the use of antihypertensive medication could slow down the progression (adjusted $p < 0.001$). There were no significant predictors of ICA IMT progression.

Relationship between Hypertension Treatment and IMT Progression

Because hypertension and the use of antihypertensive medication at baseline were related to IMT progression, we further investigated the relationship between antihypertensive treatment and IMT progression in hypertensive subjects. As shown in **Fig. 1**, the rate of annual IMT progression was slower in patients who took medication than in those who did not in all segments of IMT (9.60 vs. 10.86 $\mu\text{m}/\text{year}$ in CCA; 12.00 vs. 25.76 $\mu\text{m}/\text{year}$ in BIF; 11.30 vs. 14.63 $\mu\text{m}/\text{year}$ in ICA). The difference was most prominent in the BIF segment ($p = 0.015$).

Differences between Genders in Predicting IMT Progression

To investigate gender-specific predictors of IMT progression, further multivariate regression analysis was performed (**Table 3**). In women, age and smoking were statistically significant predictors of CCA IMT progression (adjusted $p < 0.001$ and $p = 0.011$, respectively). Age, hypertension, and antihypertensive medication were associated with BIF IMT progression (adjusted $p < 0.001$, $p = 0.005$, and $p = 0.002$, respectively). The use of antihypertensive medication was associated with slower progression in the ICA IMT segment (adjusted $p = 0.001$). However, in men, there were no associations between any cardiovascular risk factors and IMT progression except for age in predicting CCA and BIF IMT progression ($p = 0.041$ and $p < 0.001$, respectively).

Predictors of Plaque Progression

Age was a predictor of carotid plaque progression (**Table 4**), and the risk of plaque progression was 1.05-fold each year (adjusted $p < 0.001$). In addition, gender was also associated with plaque progression.

Table 1. Demographic features of the study participants

	All (N=712)	Women (N=438)	Men (N=274)	P value
Baseline				
Age (years)	54.7 ± 9.4	53.9 ± 9.1	55.9 ± 9.7	0.007**
Diabetes	64 (9.0)	21 (4.8)	43 (15.7)	<0.001**
Hypertension	216 (30.3)	123 (28.1)	93 (33.9)	0.099
Using antihypertensive medication	165 (76.4)	90 (73.2)	75 (80.6)	0.107
Hypercholesterolemia	157 (22.1)	91 (20.8)	66 (24.1)	0.308
Using lipid-lowering medication	84 (53.5)	42 (46.2)	42 (63.6)	0.054
Ever and current smoking	114 (16.0)	10 (2.3)	104 (38.0)	<0.001**
BMI (kg/m ²)	24.3 ± 3.2	23.7 ± 3.1	25.3 ± 3.1	<0.001**
Baseline IMT(mm)				
CCA	0.62 ± 0.15	0.59 ± 0.12	0.67 ± 0.17	<0.001**
BIF	0.65 ± 0.13	0.63 ± 0.12	0.68 ± 0.14	<0.001**
ICA	0.50 ± 0.09	0.48 ± 0.08	0.53 ± 0.09	<0.001**
Follow up IMT(mm)				
CCA	0.67 ± 0.15	0.64 ± 0.13	0.72 ± 0.17	<0.001**
BIF	0.72 ± 0.14	0.70 ± 0.13	0.76 ± 0.15	<0.001**
ICA	0.54 ± 0.10	0.53 ± 0.10	0.57 ± 0.10	<0.001**
Baseline plaque presence	242 (34.0)	128 (29.2)	114 (41.6)	0.001**
Follow-up plaque presence	301 (42.3)	159 (36.3)	142 (51.8)	<0.001**
Annual IMT progression rate (μm/year)				
CCA	11.82 ± 19.95	11.72 ± 16.99	11.99 ± 24.01	0.873
BIF	17.39 ± 28.94	17.31 ± 27.72	17.50 ± 30.87	0.931
ICA	10.37 ± 20.13	10.42 ± 19.38	10.27 ± 21.32	0.923
Progression of plaque	167 (23.5)	84 (19.2)	83 (30.3)	0.001**

p values comparing men and women using the Student's *t* test or chi-squared test.

Data are shown as mean ± SD for quantitative variables and *n* (%) for qualitative variables.

Abbreviations: IMT, intima-media thickness; CCA, common carotid artery; BIF, bifurcation; ICA, internal carotid artery; BMI, body mass index

p* < 0.05, *p* < 0.01

Men had a 1.62-fold higher risk of plaque progression than women (adjusted *p* = 0.039).

Discussion

In this prospective follow-up study, the predictors of carotid IMT progression were gender and segment specific. Age was a risk factor for the progression of CCA and BIF IMT in both genders, while smoking and hypertension were the predictors of CCA and BIF IMT progression only in women. Antihypertensive medication could slow down the rate of IMT progression, particularly in women. Therefore, our findings may imply the importance of blood pressure control in hypertensive subjects to prevent the progression of atherosclerosis, particularly in women.

Ethnic differences have been reported in the risk factors for cardiovascular disease and atherosclerosis progression²²⁻²⁴. The Northern Manhattan Stroke study demonstrated that the effect of hypertension

and diabetes on the risk of stroke was greater among blacks and Caribbean Hispanics than among whites; whereas the number of strokes that were attributable to atrial fibrillation was higher in whites than in blacks²³. Results from the Multi-Ethnic Study of Atherosclerosis also demonstrated that the effect of diabetes was strongest in blacks and weakest in Hispanics in coronary artery calcium progression²². Therefore, the risk factors and their effect on the progression of carotid atherosclerosis may vary between different ethnic groups.

Few studies have evaluated the predictors of carotid atherosclerosis progression in Asian patients¹⁶⁻¹⁹, and most of these studies have focused on special groups (diabetes mellitus, elderly) or on specific carotid atherosclerotic parameters (IMT or plaque). It is known that plaque and IMT may represent different phenotypes of atherosclerosis with different relationships to cardiovascular risk factors and clinical vascular events^{10, 25}. IMT changes reflect an

Table 2. Association between risk factors and carotid IMT progression in a multivariate regression model

Risk factors at baseline	IMT progression		
	CCA	BIF	ICA
Age	$\beta = 0.183$ $p < 0.001^{**}$	$\beta = 0.216$ $p < 0.001^{**}$	$\beta = 0.002$ $p = 0.964$
Gender	$\beta = 0.014$ $p = 0.759$	$\beta = 0.036$ $p = 0.393$	$\beta = 0.081$ $p = 0.070$
Diabetes	$\beta = 0.065$ $p = 0.107$	$\beta = -0.014$ $p = 0.706$	$\beta = 0.041$ $p = 0.291$
Hypertension	$\beta = -0.083$ $p = 0.074$	$\beta = -0.092$ $p = 0.033^*$	$\beta = 0.043$ $p = 0.340$
Hypercholesterolemia	$\beta = -0.061$ $p = 0.250$	$\beta = -0.073$ $p = 0.142$	$\beta = -0.071$ $p = 0.165$
Ever and current smoking	$\beta = 0.089$ $p = 0.045^*$	$\beta = 0.067$ $p = 0.106$	$\beta = 0.035$ $p = 0.414$
BMI	$\beta = 0.030$ $p = 0.456$	$\beta = 0.012$ $p = 0.756$	$\beta = 0.022$ $p = 0.564$
Baseline IMT	$\beta = -0.289$ $p < 0.001^{**}$	$\beta = -0.460$ $p < 0.001^{**}$	$\beta = -0.380$ $p < 0.001^{**}$
Antihypertensive medication	$\beta = -0.061$ $p = 0.164$	$\beta = -0.149$ $p < 0.001^{**}$	$\beta = -0.065$ $p = 0.120$
Lipid-lowering medication	$\beta = -0.002$ $p = 0.975$	$\beta = -0.012$ $p = 0.794$	$\beta = -0.042$ $p = 0.389$

Abbreviations: IMT, intima-media thickness; CCA, common carotid artery; BIF, bifurcation; ICA, internal carotid artery; BMI, body mass index

* $p < 0.05$, ** $p < 0.01$

Fig. 1. Carotid IMT progression rate of hypertension treatment status

p value comparing the IMT progression rate between those with hypertension using and not using antihypertensive medication using the Student's t -test.

Abbreviations: IMT, intima-media thickness; CCA, common carotid artery; BIF, bifurcation; ICA, internal carotid artery

Table 3. Association between risk factors and carotid IMT progression by gender

Risk factors at baseline	IMT progression					
	CCA		BIF		ICA	
	Women	Men	Women	Men	Women	Men
Age	$\beta = 0.207$ $p < 0.001^{**}$	$\beta = 0.160$ $p = 0.041^*$	$\beta = 0.196$ $p < 0.001^{**}$	$\beta = 0.251$ $p < 0.001^{**}$	$\beta = -0.035$ $p = 0.485$	$\beta = 0.031$ $p = 0.648$
Diabetes	$\beta = 0.071$ $p = 0.163$	$\beta = 0.050$ $p = 0.460$	$\beta = 0.051$ $p = 0.274$	$\beta = -0.089$ $p = 0.157$	$\beta = -0.023$ $p = 0.622$	$\beta = 0.078$ $p = 0.238$
Hypertension	$\beta = -0.070$ $p = 0.244$	$\beta = -0.098$ $p = 0.190$	$\beta = -0.157$ $p = 0.005^{**}$	$\beta = -0.010$ $p = 0.886$	$\beta = 0.001$ $p = 0.991$	$\beta = 0.111$ $p = 0.127$
Hypercholesterolemia	$\beta = -0.072$ $p = 0.304$	$\beta = -0.028$ $p = 0.734$	$\beta = -0.067$ $p = 0.307$	$\beta = -0.067$ $p = 0.381$	$\beta = -0.073$ $p = 0.273$	$\beta = -0.073$ $p = 0.365$
Ever and current smoking	$\beta = 0.126$ $p = 0.011^*$	$\beta = 0.060$ $p = 0.353$	$\beta = 0.022$ $p = 0.633$	$\beta = 0.080$ $p = 0.178$	$\beta = 0.016$ $p = 0.736$	$\beta = 0.047$ $p = 0.457$
BMI	$\beta = 0.076$ $p = 0.126$	$\beta = -0.032$ $p = 0.642$	$\beta = 0.027$ $p = 0.557$	$\beta = 0.001$ $p = 0.993$	$\beta = 0.079$ $p = 0.090$	$\beta = -0.073$ $p = 0.269$
Baseline IMT	$\beta = -0.259$ $p < 0.001^{**}$	$\beta = -0.301$ $p < 0.001^{**}$	$\beta = -0.423$ $p < 0.001^{**}$	$\beta = -0.482$ $p < 0.001^{**}$	$\beta = -0.376$ $p < 0.001^{**}$	$\beta = -0.362$ $p < 0.001^{**}$
Antihypertensive medication	$\beta = -0.109$ $p = 0.052$	$\beta = 0.016$ $p = 0.822$	$\beta = -0.166$ $p = 0.002^{**}$	$\beta = -0.120$ $p = 0.064$	$\beta = -0.176$ $p = 0.001^{**}$	$\beta = 0.098$ $p = 0.149$
Lipid-lowering medication	$\beta = 0.035$ $p = 0.611$	$\beta = -0.020$ $p = 0.803$	$\beta = -0.016$ $p = 0.807$	$\beta = -0.002$ $p = 0.974$	$\beta = -0.038$ $p = 0.553$	$\beta = -0.048$ $p = 0.528$

Abbreviations: IMT, intima-media thickness; CCA, common carotid artery; BIF, bifurcation; ICA, internal carotid artery; BMI, body mass index
 $^*p < 0.05$, $^{**}p < 0.01$

Table 4. Predictors of carotid plaque progression

Risk factors at baseline	Odds Ratio (95% CI)	<i>p</i> value
Age	1.05 (1.02-1.07)	$< 0.001^{**}$
Gender(Men/Women)	1.62 (1.03-2.55)	0.039 *
Diabetes mellitus	1.43 (0.76-2.69)	0.270
Hypertension status		
No hypertension	1.00	
Hypertension with antihypertensive medication	1.51 (0.94-2.43)	0.088
Hypertension without antihypertensive medication	1.64 (0.78-3.39)	0.179
Hypercholesterolemia status		
No hypercholesterolemia	1.00	
Hypercholesterolemia with lipid-lowering medication	1.34 (0.76-2.38)	0.313
Hypercholesterolemia without lipid-lowering medication	1.18 (0.65-2.16)	0.588
Ever and current smoking	1.46 (0.85-2.50)	0.173
BMI	0.95 (0.90-1.02)	0.146
Follow up duration (years)	0.98 (0.79-1.22)	0.870
Baseline plaque presence	0.70 (0.46-1.07)	0.098

Abbreviations: BMI, body mass index
 $^*p < 0.05$, $^{**}p < 0.01$

adaptive process and represent an early carotid atherosclerosis, while plaque formation may reflect a more significant alteration in vessel walls and represent an estimate of more advanced status²⁶⁾. Thus, these two aspects of atherosclerosis reflect different biological aspects of atherogenesis. By evaluating both the early and late stages of carotid atherosclerosis progression and conventional cardiovascular risk factors, our study may provide important clinical information.

In agreement with previous studies^{10, 13-15, 19)}, the most consistent predictors of carotid IMT and plaque progression in this study were age and hypertension. Antihypertensive medication use may be the strongest modifiable predictor of slowing IMT progression over time^{27, 28)}, and may be able to further prevent the development of stroke and coronary heart disease. In this study, we demonstrated that antihypertensive medication was associated with slowing carotid IMT progression. Furthermore, its effect on carotid IMT progression differed by a segment, which has not been reported before.

Few studies have reported on the association between vascular risk factors and carotid IMT progression at different segments^{11, 13, 14)}, and most previous studies have only focused on the progression in the CCA IMT segment^{9, 10, 12, 15)}. Theoretically, these segments histologically differ and their walls are differentially exposed to turbulent flow²⁹⁾. Therefore, it is reasonable that IMT progression is segment specific and governed by different cardiovascular risk factors. The Carotid Atherosclerosis Progression Study reported that the predictors of ICA IMT progression were age, male gender, hypertension, diabetes, and currently smoking and that age and currently smoking were predictors of IMT progression at BIF¹³⁾. In the Bogalusa Heart Study, Nguyen *et al.* also found different predictors of CCA, BIF, and ICA IMT progression in young adults¹⁴⁾. However, our study is the first to demonstrate different risk predictors for all segments of carotid IMT progression in an Asian population. The identification of these specific risk markers may be important with regard to the pathophysiology and early prevention of IMT progression.

Coronary artery disease in women lags behind men by 10–15 years. This delay is believed to be caused by the protective effect of estrogen on coronary atherosclerosis³⁰⁾. The average age of women in our study population was 54 years at baseline, with up to 67% having had menopause, which has been reported to have unfavorable effects on lipid metabolism, and increased incidence, mortality and morbidity due to cardiovascular disease as compared with premenopausal control³¹⁻³³⁾. A previous study reported a ceiling effect in arterial stiffness³⁴⁾ and that men have a

thicker IMT, which could possibly explain why most of the underlying risk factors for IMT progression were identified in women rather than in men in this study.

There are strengths and limitations to this study. Carotid IMT and plaque were separately measured, and thus, atherosclerosis progression was more thoroughly evaluated than in previous Asian studies. Measuring the progression of IMT is more difficult than making a single measurement because random measurement errors at baseline and follow-up can accumulate. However, in this study, all measurements were performed by a single experienced sonographer, and the IMT measurement was performed by a single neurologist, which would counteract the inherent measurement errors. In this study, we did not measure IMT in a specific cardiac phase. However, the Chinese population has the smallest changes in IMT during the cardiac cycle as compared with the non-Hispanic whites³⁵⁾, which may minimize the impact of the cardiac phase to IMT data in this study. The subjects enrolled in this study were followed up for >2 years. The timing of the second survey was in accordance with the participants' will. Therefore, the follow-up period was heterogeneous. However, annual IMT progression could overcome this limitation. The other potential limitation is that some clinical profiles differed between those who dropped out and those who completed follow-up. Those who dropped out had a higher prevalence of diabetes, hypertension, and hypercholesterolemia, which could limit the conclusiveness of the findings.

Conclusion

In conclusion, there were differences in the gender and segmental predictors of carotid atherosclerosis progression in our Taiwan Chinese population. In women, hypertension was more strongly associated with carotid IMT progression and the use of antihypertensive medication protected against carotid IMT progression. Therefore, the detection and control of hypertension may prevent atherosclerosis progression and may reduce cardiovascular disease, particularly in women.

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Conflicts of Interest

None.

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Supplementary Table 1. Comparison of baseline characteristic between those who did and did not complete the study

	Participants (<i>N</i> =712)	Dropped out (<i>N</i> =167)	<i>P</i> value
Age (years)	54.7 ± 9.4	53.6 ± 15.4	0.251
Gender-Men	38.5%	39.5%	0.804
Diabetes	9.1%	15.6%	0.014*
Hypertension	30.5%	41.3%	0.007**
Hypercholesterolemia	22.3%	30.5%	0.025*
Ever and current smoking	16.7%	19.2%	0.448
BMI (kg/m ²)	24.7 ± 3.4	25.1 ± 3.8	0.177

p values comparing the participants and those who dropped out using the Student's *t* test or chi-squared test.

Data are shown as mean ± SD for quantitative variables and *n* (%) for qualitative variables.

Abbreviations: BMI, body mass index

p* < 0.05, *p* < 0.01

Supplementary Table 2. Pearson's correlation between baseline carotid IMT and IMT progression

Baseline IMT	IMT progression		
	CCA	BIF	ICA
CCA	<i>r</i> = −0.23, <i>p</i> = <0.001**	<i>r</i> = −0.09, <i>p</i> = 0.016*	<i>r</i> = −0.02, <i>p</i> = 0.669
BIF	<i>r</i> = −0.03, <i>p</i> = 0.447	<i>r</i> = −0.41, <i>p</i> = <0.001**	<i>r</i> = −0.07, <i>p</i> = 0.068
ICA	<i>r</i> = 0.07, <i>p</i> = 0.072	<i>r</i> = −0.04, <i>p</i> = 0.365	<i>r</i> = −0.37, <i>p</i> = <0.001**

Abbreviations: IMT, intima-media thickness; CCA, common carotid artery; BIF, bifurcation; ICA, internal carotid artery

p* < 0.05, *p* < 0.01