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ORIGINAL RESEARCH

Prevalence and Risk Factors of Abnormal Carotid Artery in Young Adults without Overt Cardiovascular Disease

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Objective: The current study was to evaluate the prevalence of increased carotid artery intimal-medial thickness (IMT) and carotid plaque in young individuals and factors associated with increased IMT and carotid plaque were also assessed.
Methods: Individuals between 18 and 44 years old who underwent an annual health examination and without cardiovascular disease were included. The value of IMT ≥0.1 cm was defined as increased IMT and IMT ≥0.15 cm was defined as carotid plaque. Based on the IMT, participants were divided into normal and abnormal groups.
Results: A total of 551 individuals were included and the mean age was 38.9 years old, with women accounting for 32.5% (n=179) and 238 (43.2%) individuals with abnormal IMT. Those with abnormal IMT was older, more likely to be male and smoking, had higher blood pressure (BP) and body mass index (BMI). Individuals with abnormal MIT also had worse lipid profiles, higher serum levels of fasting plasma glucose (FPG), HbA1c, homocysteine, and uric acid. Age, male sex, elevated systolic and diastolic BP, BMI, HbA1c, FPG, triglyceride, total cholesterol, LDL-C, homocysteine, and uric acid were positively correlated with IMT, while HDL-C was negatively correlated with IMT. Factors associated with increased IMT and carotid plaque included age, male sex, BMI, triglyceride, LDL-C, homocysteine, uric acid, and smoking.
Conclusion: Among apparent healthy young individuals, the prevalence of increased IMT was high and there were several factors associated with increased IMT. Further studies are needed to evaluate how to be better in preventing the development of subclinical atherosclerosis among young individuals.
Keywords: intimal-medial thickness, carotid plaque, risk factors

Introduction

Despite advances in primary prevention being achieved in the last two decades, atherosclerotic cardiovascular disease (ASCVD) remains the leading cause of morbidity and mortality in China and worldwide.[1–4] Prior studies have demonstrated that the factors contributing to the initiation and progress of atherosclerosis are diverse, including advancing age, smoking, obesity, diabetes mellitus, dyslipidemia, and hypertension, among others.[5,6] Notably, most of these findings were derived from middle-to-older age populations with established ASCVD, and the data on the apparent healthy young populations are limited. Furthermore, these data are remarkably lacking in the Chinese populations.

Carotid artery intimal-medial thickness (IMT) is a marker of early atherosclerosis.[7–9] With the progress of atherosclerosis, carotid plaque may develop subsequently.[10] Prior studies have shown that increased IMT or the presence of carotid plaque portends an increased risk of developing ischemic stroke and myocardial infarction.[8,11] Therefore, it is critically important to assess the carotid artery with ultrasound so as to identify high-risk populations.

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Prior epidemiologic studies show that in the last two decades, the prevalence of ASCVD has increased significantly in China, especially among young individuals, which is due to smoking, physical inactivity, environmental pollution, and unhealthy lifestyle, among others.[1,6,12] Therefore, it is clinically relevant to determine the prevalence of subclinical ASCVD, such as increased IMT or prevalent carotid plaque, in the young populations, which in turn can help inform effective targeted preventive therapy. To the best of our knowledge, there are few studies which have evaluated the prevalence of subclinical ASCVD in individuals between the ages of 18–44 years old. In addition, factors associated with the prevalence of subclinical ASCVD in young populations are also unknown. Herein, through collecting data from apparently healthy young individuals during annual health examination in the outpatient department of our hospital, the aims of the current study are to evaluate: 1) the prevalence of subclinical ASCVD (namely increased IMT and carotid plaque) in the young individuals; and 2) factors associated with increased IMT and carotid plaque.

Methods

Study Design and Participants Enrollment

This is a cross-sectional study and the current study was approved by the Clinical Research Ethics Committee of the First Affiliated Hospital of Xinjiang Medical University. Written informed consent was obtained before participants' enrollment. Individuals between the ages of 18–44 years who underwent an annual health examination were screened for eligibility of the current study. All the examinations were conducted in accordance with the Declaration of Helsinki. Individuals who had a documented history of hypertension, diabetes mellitus, abnormality in liver or kidney function, coronary artery disease, infectious disease, malignant disease, systemic inflammatory disease, or therapy with lipid lower medications were excluded.

Data Collection

Data was collected during the health examination. Demographics (eg, age and sex) and anthropometrics (eg, body weight and height) were collected and entered into the standardized health record form. Body weight in kilograms and height in meters were used to calculate body mass index (BMI) based on the formula as follows: BMI=weight (kg)/height (m^2). Fasting venous blood was used to measure lipid profiles, fasting plasma glucose (PFG), glycated hemoglobin A1c (HbA1c), renal function, uric acid, and homocysteine. Blood pressure (BP) was measured according to the China hypertension guideline recommendation. Specifically, participants were required to stay at rest in a sitting position for 5 minutes, and two BP measurements were performed with a 1-minute interval with the arm positioned at the heart level using an Omron HEM-7051 device (Omron HealthCare, Kyoto, Japan). The average value of two BP readings was used. If the first two BP readings differed by >5 mm Hg, an additional measurement was performed and the mean value of three readings was used.

Assessment of Carotid Artery Using Ultrasound

Assessment of the carotid artery was performed using a 7.5–10 MHz linear array transducer (Siemens ACUSON Cypress) by experienced ultrasonographers who were blinded to the characteristics of all participants. Common carotid artery (1 mm below the carotid artery bifurcation) was chosen to evaluate IMT, and measurements were performed 3-times on both sides. The values of IMT were averaged by the left- and right-sided IMT values, and the largest average value was used in the current study. In brief, IMT ≥0.1 cm was defined as increased IMT and IMT ≥0.15 cm was defined as carotid plaque accordingly.[13] Based on the IMT, participants were divided into normal (IMT <0.1 cm) and abnormal (IMT ≥0.1 cm) groups.

Statistical Analysis

Continuous variables with normal distribution were expressed as mean±standard deviation, or presented as median (interquartile range). Categorical variables were presented as frequencies and percentages. Student's *t*-test was used to compare continuous variables with normal distribution and Mann–Whitney *U*-test was used to evaluate variables with skewed distribution. Comparisons of categorical variables were performed using Chi-squared test or Fisher's exact test.

Pearson or Spearman correlation analysis was performed to evaluate the relationship between IMT and factors of interest. Univariate binary logistic regression analyses were performed to evaluate the association between factors with increased IMT or carotid plaque. In addition, factors in the univariate analysis with a *P*-value <0.1 were entered into the multivariate logistic regression analyses to further evaluate the association between factors with increased IMT or carotid plaque. Odds ratio (OR) and 95% confidence interval (CI) were reported. All analyses were performed with SPSS version 17.0 for Windows, and a two-sided *P*-value of less than 0.05 was considered to indicate statistical significance.

Results

Baseline Characteristics

A total of 551 individuals aged 18–44 years old were included for the current analysis. The mean age was 38.9±5.7 years old, women accounted for 32.5% (n=179), and 238 individuals had abnormal IMT (43.2%). As presented in Table 1, compared to individuals with normal IMT, those with abnormal IMT were older, more likely to be male and smoking, and had higher blood pressure and BMI. In addition, individuals with abnormal MIT also had worse lipid profiles, higher serum levels of FPG, HbA1c, homocysteine, and uric acid. Among individuals with abnormal IMT, 117 (49.2%) had increased IMT, 114 (47.9%) had isolated carotid plaque, and seven (2.9%) had multiple carotid plaque, respectively.

Factors Correlated with IMT

As presented in Table 2, age, male sex, systolic and diastolic BP, BMI, HbA1c, FPG, triglyceride, total cholesterol, low density lipoprotein-cholesterol, homocysteine, and uric acid were positively correlated with IMT, while high density lipoprotein-cholesterol was negatively correlated with IMT. The correlation coefficient was the largest with BMI and followed by age.

Table 1 Baseline Characteristics

Variables	Abnormal Group	Normal Group	*P*-value
n	238	313	
Female, n (%)	60 (25.2)	119 (38.0)	<0.001
Age (years)	41.1±4.3	37.2±6.0	0.005
Smoking, n (%)	150 (63.0)	97 (31.0)	<0.001
Systolic blood pressure (mm Hg)	124.0±15.9	120.8±15.0	0.009
Diastolic blood pressure (mm Hg)	78.1±11.3	75.1±11.3	0.012
Body mass index (kg/m^2)	25.5±3.8	22.4±3.8	<0.001
Triglyceride (mmol/L)	2.11±1.50	1.55±0.97	<0.001
Total cholesterol (mmol/L)	4.88±0.85	4.53±0.78	<0.001
HDL-C (mmol/L)	1.29±0.35	1.35±0.33	<0.001
LDL-C (mmol/L)	3.03±0.73	2.82±0.64	<0.001
HbA1c (%)	5.49±0.79	5.34±0.59	0.006
Fasting plasma glucose (mmol/L)	4.86±1.26	4.69±0.85	0.010
Homocysteine (μmol/L)	15.40±2.91	10.22±2.34	<0.001
Creatinine (μmol/L)	75.8±14.9	73.7±14.9	0.209
Uric acid (μmol/L)	336.3±91.7	314.9±96.5	<0.001
BUN (mmol/L)	5.06±1.35	4.96±1.24	0.108
IMT (mm)	1.33±0.13	0.59±0.16	<0.001
Increased IMT, n (%)	117 (49.2)	–	
Isolated carotid plaque, n (%)	114 (47.9)	–	
Multiple carotid plaque, n (%)	7 (2.9)	–	

Abbreviations: HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; HbA1c, glycated hemoglobin A1c; BUN, blood urea nitrogen; IMT, intima media thickness.

Table 2 Factors Correlated with IMT

Factors	r	*P*-value
Age (years)	0.511	<0.001
Male	0.281	<0.01
Systolic blood pressure (mm Hg)	0.306	<0.001
Diastolic blood pressure (mm Hg)	0.212	<0.001
Body mass index (kg/m^2)	0.701	<0.001
HbA1c (%)	0.194	<0.001
Fasting plasma glucose (mmol/L)	0.141	<0.05
Triglyceride (mmol/L)	0.469	<0.05
Total cholesterol (mmol/L)	0.334	<0.001
HDL-C (mmol/L)	−0.245	<0.001
LDL-C (mmol/L)	0.209	<0.001
Homocysteine (μmol/L)	0.306	<0.001
Uric acid (μmol/L)	0.207	<0.001

Abbreviations: HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; HbA1c, glycated hemoglobin A1c; IMT, intima media thickness.

Table 3 Association Between Factors with Increased IMT and Carotid Plaque (Univariate Analysis)

Factors	Increased IMT		Carotid Plaque	
	Odds Ratio (95% CI)	***P*-value**	**Odds Ratio (95% CI)**	***P*-value**
Age (years)	2.114 (2.061–2.870)	<0.001	2.227 (2.149–3.011)	<0.001
Male vs female	1.181 (1.047–1.396)	0.012	2.307 (1.993–3.361)	0.030
Body mass index (kg/m^2)	2.988 (2.009–3.573)	<0.001	3.986 (3.403–4.077)	<0.001
Triglyceride (mmol/L)	1.379 (1.062–1.791)	<0.001	1.564 (1.309–1.869)	<0.001
LDL-C (mmol/L)	1.696 (1.572–2.102)	0.003	1.721 (1.546–2.301)	0.021
Homocysteine (μmol/L)	2.011 (1.872–2.702)	0.018	2.311 (1.916–3.402)	0.004
Uric acid (μmol/L)	1.201 (1.004–1.309)	0.011	1.304 (1.101–1.507)	0.024
Smoking (yes vs no)	1.390 (1.277–1.718)	<0.001	1.498 (1.076–2.320)	<0.001

Abbreviations: LDL-C, low-density lipoprotein cholesterol; IMT, intima media thickness; CI, confidence interval.

Association Between Factors with Increased IMT and Carotid Plaque

In the univariate binary logistic regression analysis (Table 3), factors associated with increased IMT included age, male sex, BMI, triglyceride, low density lipoprotein-cholesterol, homocysteine, uric acid, and smoking. These factors were also associated with carotid plaque. After multivariate regression analysis, factors which remained associated with increased IMT included age, BMI, low density lipoprotein-cholesterol, homocysteine, and smoking; and factors which remained associated with carotid plaque included age, male sex, BMI, triglyceride, low density lipoprotein-cholesterol, homocysteine, and smoking (Table 4).

Discussion

There are two potentially clinical important findings of the current study: 1) among apparent healthy young individuals, the prevalence of subclinical atherosclerosis, including increased IMT or the presence of carotid plaque, was high, with a prevalence of 43.2%; and 2) there were several factors associated with increased IMT and carotid plaque. These findings together suggest that it is warranted to routinely assess IMT in apparent healthy young individuals and interventions are needed to target several common risk factors such as BP and metabolic disorder.

Table 4 Association Between Factors with Increased IMT and Carotid Plaque (Multivariate Analysis)

Factors	Increased IMT		Carotid Plaque	
	Odds Ratio (95% CI)	*P*-value	Odds Ratio (95% CI)	*P*-value
Age (years)	1.563 (1.243–2.157)	<0.001	2.086 (1.805–2.670)	<0.001
Male vs female	1.072 (0.956–1.212)	0.056	2.004 (1.674–3.018)	0.044
Body mass index (kg/m^2)	2.324 (1.568–3.098)	<0.001	3.475 (3.112–3.684)	<0.001
Triglyceride (mmol/L)	1.112 (0.943–1.430)	0.163	1.341 (1.068–1.773)	0.023
LDL-C (mmol/L)	1.408 (1.226–1.864)	0.015	1.553 (1.263–2.007)	0.036
Homocysteine (μmol/L)	1.698 (1.245–2.227)	0.043	2.006 (1.503–3.012)	0.009
Uric acid (μmol/L)	1.080 (0.925–1.117)	0.078	1.118 (0.904–1.308)	0.065
Smoking (yes vs no)	1.237 (1.114–1.405)	0.008	1.402 (1.033–2.158)	0.006

Abbreviations: LDL-C, low-density lipoprotein cholesterol; IMT, intima media thickness; CI, confidence interval.

Prior studies from western populations have shown that an increase in BP, low density lipoprotein cholesterol, fasting plasma glucose, smoking, physical inactivity, and obesity were associated with endothelial dysfunction, systemic inflammation, and oxidative stress.[14–16] These pathophysiological alterations together contribute to the initiation of subclinical atherosclerosis. Notably, the carotid artery is one of the vessels which develops subclinical atherosclerosis at an early stage. Epidemiologic studies have demonstrated the relationship between increased IMT and cardiovascular outcomes.[17–19] However, most of these data were from middle-to-old age Caucasian populations. The data about the prevalence of subclinical atherosclerosis in the apparent young Chinese individuals is limited. In addition, factors associated with subclinical atherosclerosis are also undetermined.

In the current study, we included 551 individuals aged 18–44 years without prevalent hypertension, dyslipidemia, diabetes mellitus, and overt cardiovascular disease. The results suggested the prevalence of increased IMT was above 40%, suggesting that subclinical atherosclerosis developed during the young age. Notably, beyond traditional risk factors, genetic background, unhealthy diet, environment pollution, and mental stress during young age, among others have also been identified as potential risk factors for ASCVD. Indeed, an epidemiologic study from Chinese adolescents shows that the prevalence of obesity was increased in the last three decades which were partly due to the unhealthy diet.[20–22] In addition, the Chinese adolescent did not have sufficient physical activity after school. Furthermore, environment pollution in the last two decades might also contribute to the early onset of atherosclerosis in the young individuals. These findings have significant clinical implications. First, we should routinely assess IMT during annual health examination for the apparent healthy young individuals. Second, targeted intervention, such as losing weight, should be implemented. Third, strategies focused on multifaceted levels are needed. In addition to body weight reduction, we consider that mitigating other risk factors, such as dyslipidemia, diabetes mellitus, and hypertension, should also be important approaches. Indeed, several studies have demonstrated that lipid lowering medications, antidiabetic drugs, and antihypertensive therapy can reduce IMT and retard carotid plaque. Further studies are needed to explore whether these strategies are effective for the apparent healthy young individuals with increased IMT and carotid plaque.

We also investigated factors associated with increased IMT and carotid plaques. Notably, age, BMI, laboratory parameters of metabolic disorders, and smoking were associated with the subclinical atherosclerosis. Notably, among these factors, most are modifiable except for age. Through regular exercise and healthy diet, it is feasible to decrease BMI and improve lipid metabolism and reduce uric acid. Discontinuation of smoking is also feasible with positive reinforcement and family support. Homocysteine is a marker which is associated with endothelial dysfunction, increased platelet activity and pro-coagulation status.[23,24] Improvements in diet and physical activity are also able to reduce the homocysteine level. These findings suggest that among young individuals without comorbidities and overt cardiovascular disease, adherence to a healthy lifestyle is essential to prevent the development of subclinical atherosclerosis.

The current study included apparent healthy young individuals and the results suggested a high prevalence of increased IMT and carotid plaque in these populations. Since increased IMT and carotid plaque are associated with cardiovascular event, we consider that preventive and therapeutic strategies are needed for these populations group. Since obesity, hypertension, dyslipidemia and diabetes mellitus are the four common risk factors for atherosclerosis, strictly controlling these risk factors through maintaining a healthy lifestyle and regular moderate-to-vigorous exercise could provide a cost-effective approach to prevent carotid plaque and reduce IMT in a population-level.

There are some limitations of the current study. First, this was an observational study and the findings could only be used for hypothesis generation. Second, we included apparent healthy young individuals and the findings might not be able to extrapolate to those with prevalent comorbidities or cardiovascular disease. Third, data were from annual health examination and whether these findings can be extrapolated to outpatient clinic patients is also unknown. Fourth, since only one person assessed the participants, there was a possible bias introduced since ultrasound is operator-dependent. Fifth, since this was a single institutional study, the findings might not be extrapolated to other population groups. Last but not the least, although we postulated that the early onset of subclinical atherosclerosis might be due to unhealthy diet and environment pollution, among others, we did not capture these data and future studies are needed to collect these data so as to better understand the mechanisms underlying early onset subclinical atherosclerosis.

Conclusion

In conclusion, results of the current study show that, among apparent healthy young individuals, the prevalence of increased IMT was high and there were several traditional factors associated with increased IMT. Further studies are needed to evaluate how be better prevent the development of subclinical atherosclerosis among young individuals.

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Disclosure

The authors report no conflicts of interest in this work.

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