

## Original Article

# Relationship between carotid artery intima-media thickness and cardiovascular risk factors in Chinese Uygur population

Fenglei Zhang<sup>1\*</sup>, Lingzhou Feng<sup>1\*</sup>, Yao Chen<sup>2</sup>, Zhiying Geng<sup>1</sup>, Xinsheng Xu<sup>1</sup>

<sup>1</sup>Department of Cardiology, Dongying People's Hospital of Shandong Provincial Hospital Group, Dongying 257091, Shandong, China; <sup>2</sup>Department of Internal Medicine, People's Hospital of Shule County, Kashi 844200, Xinjiang, China. \*Equal contributors.

Received October 7, 2014; Accepted December 8, 2014; Epub December 15, 2014; Published December 30, 2014

**Abstract:** Aims: To investigate the relationships between carotid intima-media thickness (IMT) and conventional cardiovascular risk factors in Uygur population. Methods: In totally 226 Uygur subjects, common carotid IMT values were detected, and the anthropometric and laboratory measurements were recorded. Results: Correlation analysis showed that the factors of age, BMI, SBP, DBP, PP, hypertension, TC, LDL-C, TG, Apo B, diabetes mellitus, glucose, smoking status, creatinine, IHD, and stroke were significantly and positively associated with carotid IMT in Uygur males. In Uygur females, significant positive associations with carotid IMT were observed for age, BMI, SBP, DBP, PP, hypertension, TC, LDL-C, TG, diabetes mellitus, glucose, IHD, and stroke, and a significant inverse association was found for HDL-C. Multiple regression analyses suggested that LDL-C, age, TG, creatinine, BMI, smoking, hypertension, and diabetes were independently associated with carotid IMT in Uygur males. However, for carotid IMT in Uygur females, SBP, age, TG, HDL-C, BMI, and diabetes were independent determinants. Conclusion: Carotid artery IMT could be used as a predictive tool for atherosclerotic lesions and cardiovascular diseases in Uygur population, which might contribute to the prevention and management of the local disease.

**Keywords:** Intima-media thickness, atherosclerosis, carotid arteries, Uygur population, ultrasonography

## Introduction

Cardiovascular disease (CVD) is one of the leading causes of morbidity and mortality worldwide. First clinical manifestations of CVD often occur in the advanced stage of atherosclerosis. However, the arterial wall change has actually been a long-term subclinical process. Recently, researches on atherosclerosis have been mainly focused on identifying markers of early atherosclerosis, in which carotid intima-media thickness (IMT) represents an intermediate phenotype for the disease. There is evidence that the increased carotid IMT is related to various cardiovascular risk factors, including hypertension, smoking, obesity, dyslipidemia, and diabetes mellitus. Moreover, increased carotid IMT has also been closely linked with future myocardial infarction, stroke, and cardiovascular death, which could influence a clinician to use more aggressive treatment in prevention. In addition, carotid IMT assessment with high-

resolution B-mode ultrasonography is safe, inexpensive, reliable, reproducible, and non-invasive, which makes it more and more popular in detecting and monitoring atherosclerosis.

Along with the development of society, lifestyles and dietary habits in Uygur area have drastically changed in the past few decades, which might be partially responsible for the local increase in cardiovascular diseases [1, 2]. Therefore, it would be important to identify and address the cardiovascular risk factors in Uygur population. Associations between the carotid IMT and these cardiovascular risk factors have been widely reported, however few studies have been conducted in Uygur population in Northwest China.

In the present study, we evaluated the associations between carotid IMT and conventional cardiovascular risk factors in Uygur adults. Our study provides a predictive tool for atheroscle-

## Carotid intima-media thickness in Uygurs

rotic lesions and cardiovascular diseases in these people, which might contribute to the prevention and management of the local disease.

### Materials and methods

#### *Study population*

Totally 226 Uygur participants (114 males and 112 females, aged from 40-96 years) were recruited in this study, who had been admitted into the People's Hospital of Shule County due to the presence of cardiovascular risk factors, CVD, and health check-up, from May 2011 to April 2012. Exclusion criteria were as follows: serological evidence of hepatitis B virus or HIV infection, malignancy, acute or chronic liver and kidney disease, connective tissue disease, recent infection, chronic heart failure, alcoholism, and carotid artery surgery. Patients eligible for the study were subsequently subjected to detailed medical history evaluation, physical examination, and ultrasonography of the carotid arteries. Prior written and informed consent were obtained from every patient and the study was approved by the ethics review board of the local ethics committee.

#### *Carotid ultrasonography*

High-resolution B mode ultrasonography was performed with a 7.5 MHz linear array imaging transducer (Vivid 7; GE Corporation, Milwaukee, WI, USA) in a quiet, semi-dark room. Subjects were asked not to drink coffee or tea for at least 2 h before the detection. For the common carotid artery (CCA) examination, the patients were lying in the supine position, with the head turned contralateral to the detecting side, and the neck extended slightly. Magnified pictures were frozen incidentally with the R wave on the ECG. The IMT values were defined as the distance between the characteristic echoes from the lumen-intima and the media-adventitia interfaces. Because the near wall is different for accurate measurement, IMT was measured on the longitudinal views of the far wall of the bilateral distal common carotid arteries (1 cm proximal to the beginning of the dilatation of the carotid bulb). Carotid IMT was calculated as the mean from eight measurements (four on each side). No measurement was made on the sites where a plaque existed. The intra-observer reproducibility of the carotid artery examination was assessed by a repeated examination of 10 study subjects within 4 weeks from the initial examination. The coefficient of variation for

carotid IMT measurement was 11.5% (mean difference: 0.01 mm).

#### *Physical and biochemical examinations*

Blood pressures were measured in the right arm using standard mercury sphygmomanometers in seated participants who had rested for 5 min. The blood pressure values were the average of the second and third measurements. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were defined by Korotkoff phase I and V, respectively. Hypertension was defined as a systolic blood pressure  $\geq 140$  mmHg, diastolic blood pressure  $\geq 90$  mmHg, or use of antihypertensive medication. Pulse pressure was calculated as  $PP = SBP - DBP$ . Height and weight were determined for all participants, and then body mass index (BMI) was calculated as weight divided by the square of height. BMI between 25 and 29.9 kg/m<sup>2</sup> was considered as overweight, and BMI of 30 kg/m<sup>2</sup> or more indicated obesity. Diabetes mellitus was defined as fasting glucose level  $\geq 7.0$  mmol/L, or non-fasting glucose level  $\geq 11.1$  mmol/L, and/or use of medication for diabetes. Information of smoking was collected by interviews. Smoking status was classified as either "never smoking" or "smoking" (the latter group included both former and current smokers). History of stroke or coronary heart disease was ascertained from previous medical records of these subjects.

Fasted blood samples (10-14 h overnight) were drawn from the antecubital vein to determine the levels of lipids and glucose, between 7 and 8 AM after an overnight fast. Serum levels of lipids, including total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), triglycerides (TG), apolipoprotein A1 (Apo A1), apolipoprotein B (Apo B), urea, creatinine, and uric acid were determined using a standard laboratory technique in the central laboratory of People's Hospital of Shule County. Low-density lipoprotein cholesterol (LDL-C) was calculated by the Friedewald's formula:  $LDL (mg/dl) = TC - HDL - (TG/5)$ . Levels of blood glucose were determined by routine enzymatic method.

#### *Statistical analysis*

Data were expressed as mean  $\pm$  SD. Comparison of categorical and continuous variables between groups was performed using  $\chi^2$  test and unpaired t-test, respectively. Analysis of normality of the continuous variables was performed with the Kolmogorov-Smirnov test. For

## Carotid intima-media thickness in Uygurs

**Table 1.** Baseline characteristics and laboratory measurements of the Uygur subjects

	All	Males	Females	<i>P</i>
Number of subjects	226	114	112	
Mean age (years)	59.86 ± 11.17	60.82 ± 12.48	58.89 ± 9.60	0.196
BMI (kg/m <sup>2</sup> )	24.90 ± 3.52	25.20 ± 3.18	24.59 ± 3.82	0.200
Normal	129 (57.1%)	52 (45.6%)	77 (68.8%)	0.002
Overweight	75 (33.2%)	49 (43.0%)	26 (23.2%)	0.002
Obese	22 (9.7%)	13 (11.4%)	9 (8.0%)	0.002
Ischemic heart disease, n (%)	44 (19.5%)	21 (18.4%)	23 (20.5%)	0.688
Cerebrovascular disease (stroke), n (%)	34 (15.0%)	21 (18.4%)	13 (11.6%)	0.152
Diabetes mellitus, n (%)	53 (23.5%)	27 (23.7%)	26 (23.2%)	0.934
Hypertension, n (%)	108 (47.8%)	62 (54.4%)	46 (41.1%)	0.045
Total cholesterol (mmol/L)	4.44 ± 0.89	4.38 ± 0.93	4.51 ± 0.85	0.276
LDL-C (mmol/L)	2.52 ± 0.67	2.46 ± 0.55	2.57 ± 0.77	0.205
HDL-C (mmol/L)	0.91 ± 0.24	0.89 ± 0.23	0.93 ± 0.25	0.200
Triglycerides (mmol/L)	1.96 ± 1.09	1.87 ± 1.11	2.05 ± 1.09	0.206
Apo A1 (g/L)	1.12 ± 0.27	1.09 ± 0.27	1.15 ± 0.26	0.099
Apo B (g/L)	1.03 ± 0.31	1.0 ± 0.27	1.06 ± 0.35	0.143
Fasting plasma glucose (mmol/L)	6.29 ± 2.48	6.40 ± 2.89	6.18 ± 1.99	0.518
Urea (mmol/L)	5.31 ± 1.17	5.45 ± 1.21	5.17 ± 1.12	0.081
Creatinine (umol/L)	84.52 ± 14.59	86.08 ± 12.99	82.93 ± 15.96	0.104
Uricacid (umol/L)	258.26 ± 74.99	256.53 ± 77.24	250.87 ± 72.23	0.142
Systolic blood pressure (mmHg)	132.65 ± 19.70	134.56 ± 20.75	130.70 ± 18.47	0.141
Diastolic blood pressure (mmHg)	79.87 ± 13.75	81.32 ± 14.41	78.39 ± 12.95	0.110
Pulse pressure (mmHg)	52.56 ± 12.79	52.89 ± 13.43	52.21 ± 12.17	0.690
Never smoking, n (%)	163 (72.1%)	51 (44.7%)	112 (100%)	< 0.001
Smoking, n (%)	63 (27.9%)	63 (55.3%)	0 (0%)	< 0.001
Carotid IMT (mm)	0.75 ± 0.17	0.77 ± 0.18	0.73 ± 0.16	0.157

Note: BMI, body mass index; LDL-C, low density lipoprotein-cholesterol; HDL-C, high density lipoprotein-cholesterol; Apo A, apolipoprotein A1; Apo B, apolipoprotein B; IMT, intima-media thickness.

non-normally distributed data, Mann-Whitney tests were used to assess univariate correlations. Bivariate correlations between parameters were assessed with the Pearson or Spearman correlation coefficient for normally or non-normally distributed variables, respectively. Multiple stepwise linear regression analyses were used to determine the independent predictors for carotid IMT. All comparisons were performed using the statistical package SPSS 13.0 for Windows. *P* < 0.05 was considered statistically significant.

### Results

#### *Baseline characteristics and laboratory assessments in the Uygur subjects*

The baseline characteristics and laboratory assessments of all 226 Uygur subjects were summarized in **Table 1**. Among these eligible

Uygur individuals, there were 114 males and 112 females, with the average age of 59.86 ± 11.17 years (ranged 40-96 years). The incidence rates of the medically documented ischemic heart disease (IHD), stroke, diabetes mellitus, as well as TC, TG, LDL-C, HDL-C, Apo A1, Apo B, glucose, urea, creatinine, uricacid, SBP, DBP, and PP, did not show statistically significant differences between males and females. However, significant differences were observed for hypertension (*P* < 0.05), smoking status (*P* < 0.05), and body shapes indicated by BMI (normal weight, overweight, and obese) (*P* = 0.002). Uygur males had slightly higher BMI compared with females (25.20 ± 3.18 vs. 24.59 ± 3.82 kg/m<sup>2</sup>; *P* = 0.20) at the baseline assessment. Moreover, the mean carotid IMT value was 0.75 ± 0.17 mm for the overall population, ranged from 0.42 to 0.91 mm, and the mean carotid IMT had no significant differences between

## Carotid intima-media thickness in Uyghurs

**Table 2.** Associations between mean carotid IMT and conventional cardiovascular risk factors in Uyghur subjects

	Q1	Q2	Q3	Q4	P
	0.42-0.63 mm	0.63-0.76 mm	0.76-0.91 mm	> 0.91 mm	
Number of subjects	57	56	56	57	
Mean age (years)	52.02 ± 7.52	61.95 ± 9.53***	61.96 ± 11.80***	63.60 ± 11.54***	< 0.001
BMI (kg/m <sup>2</sup> )	23.29 ± 2.47	23.27 ± 2.48	26.38 ± 3.42***###	26.63 ± 3.95***###	< 0.001
Ischemic heart disease, n (%)	0 (0%)	4 (1.8%)	11 (4.9%)	29 (12.8%)	< 0.001
Stroke, n (%)	0 (0%)	3 (1.3%)	10 (4.4%)	21 (9.3%)	< 0.001
Diabetes mellitus, n (%)	2 (0.9%)	4 (1.8%)	18 (8.0%)	29 (12.8%)	< 0.001
Hypertension, n (%)	9 (4.0%)	21 (9.3%)	33 (14.6%)	45 (19.9%)	< 0.001
Total cholesterol (mmol/L)	4.00 ± 0.85	4.29 ± 0.82	4.68 ± 0.84***#	4.79 ± 0.86***#	< 0.001
LDL-C (mmol/L)	2.29 ± 0.67	2.40 ± 0.60	2.59 ± 0.62*	2.76 ± 0.68***#	0.001
HDL-C (mmol/L)	0.90 ± 0.29	0.87 ± 0.17	0.91 ± 0.23	0.94 ± 0.26	0.47
Triglycerides (mmol/L)	1.33 ± 0.68	1.84 ± 0.96*	2.29 ± 1.39***#	2.40 ± 0.93***#	< 0.001
Apo A1 (g/L)	1.13 ± 0.27	1.07 ± 0.24	1.14 ± 0.25	1.14 ± 0.31	0.433
Apo B (g/L)	0.96 ± 0.28	1.0 ± 0.31	1.06 ± 0.34	1.10 ± 0.31	0.08
Fasting plasma glucose (mmol/L)	5.36 ± 0.87	5.56 ± 1.33	6.75 ± 2.76*#	7.50 ± 3.43***###	< 0.001
Urea (mmol/L)	5.21 ± 1.09	5.31 ± 1.23	5.33 ± 1.37	5.40 ± 0.99	0.857
Creatinine (μmol/L)	82.16 ± 13.64	83.11 ± 13.97	85.18 ± 14.33	87.62 ± 16.07*	0.196
Uric acid (μmol/L)	261.63 ± 76.65	244.58 ± 69.65	268.20 ± 68.02	258.56 ± 84.36	0.399
Systolic blood pressure (mmHg)	119.65 ± 11.64	130.50 ± 21.91***	136.79 ± 19.92***	143.68 ± 15.66***###&	< 0.001
Diastolic blood pressure (mmHg)	72.37 ± 9.45	77.59 ± 13.62*	83.66 ± 15.24***#	85.87 ± 12.11***###	< 0.001
Pulse pressure (mmHg)	47.28 ± 9.45	52.55 ± 14.23*	52.94 ± 12.46*	57.45 ± 12.82***#	< 0.001
Never smoking, n (%)	46 (20.4%)	44 (19.5%)	40 (17.7%)	33 (14.6%)	0.029
Smoking, n (%)	11 (4.9%)	12 (5.3%)	16 (7.1%)	24 (10.6%)	0.029

Note: Apo A, apolipoprotein A1; Apo B, apolipoprotein B. Compared with the Q1 group, \*P < 0.05, \*\*P < 0.01, \*\*\*P < 0.001; compared with the Q2 group, #P < 0.05, ##P < 0.01, ###P < 0.001; compared with the Q3 group, &P < 0.05, &&P < 0.01, &&&P < 0.001.

Uyghur males and females ( $0.77 \pm 0.18$  vs.  $0.73 \pm 0.16$  mm;  $P = 0.16$ ). These results indicate that there are slight differences in baseline characteristics and laboratory assessments between Uyghur males and females.

### Correlations between carotid IMT and traditional cardiovascular risk factors in the Uyghur subjects

To investigate the relationships between the carotid IMT and the cardiovascular risk factors, all Uyghur subjects were divided into 4 groups according to the quartiles of the mean carotid IMT values (Q1, 0.42-0.63 mm; Q2, 0.63-0.76 mm; Q3, 0.76-0.91 mm; Q4, > 0.91 mm). As shown in **Table 2**, significant increases in the factors of age, BMI, TC, TG, LDL-C, glucose, SBP, DBP, and PP were observed across the quartiles of the mean carotid IMT values ( $P < 0.001$ ). Compared with the lowest quartile Q1, the incidences of IHD, stroke, diabetes mellitus, hypertension, and smoking tended to increase in the higher IMT quartiles ( $P < 0.001$ ). These results suggest that there are significant correlations between the carotid IMT and the cardiovascular risk factors in Uyghur subjects,

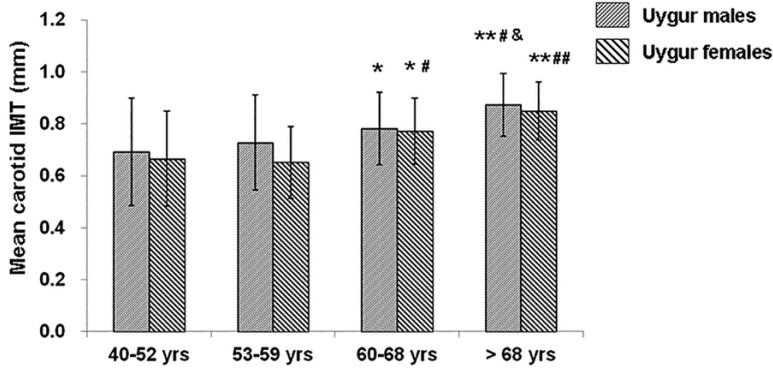
including age, BMI, TC, TG, LDL-C, glucose, SBP, DBP, and PP.

### Correlation analyses in the Uyghur male and female subgroups

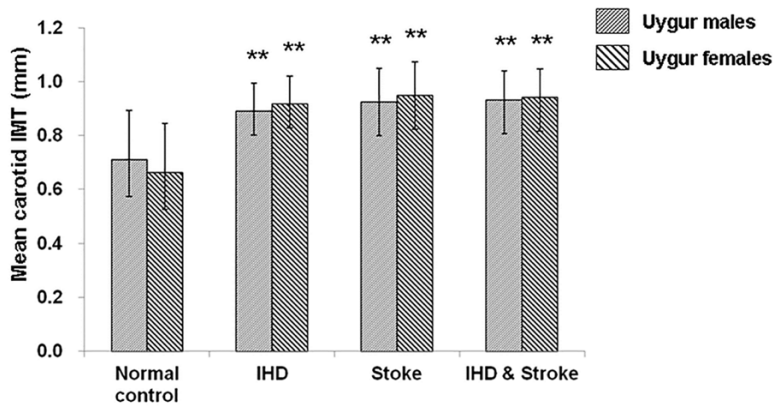
There are differences in the lifestyles and dietary habits between Uyghur males and females. So the correlation between these cardiovascular risk factors and carotid IMT values were separately analyzed in the Uyghur male and female subgroups. Our results indicated that in both Uyghur males and females, the carotid IMT values were significantly increased as age increased (carotid IMT values of  $0.69 \pm 0.21$ ,  $0.67 \pm 0.19$ ,  $0.87 \pm 0.13$ , and  $0.86 \pm 0.12$  mm for the ages of 40-52, 53-59, 60-68, and > 68 years, respectively ( $P < 0.001$ ) (**Figure 1**). Similarly, the mean carotid IMT was significantly increased in patients diagnosed with stroke and/or IHD, compared with normal individuals, in both Uyghur males and females ( $P < 0.001$ ) (**Figure 2**). In details, in the Uyghur male subjects, the carotid IMT was correlated with age ( $r = 0.39$ ,  $P < 0.001$ ), BMI ( $r = 0.35$ ,  $P < 0.001$ ), SBP ( $r = 0.43$ ,  $P < 0.001$ ), DBP ( $r = 0.34$ ,  $P < 0.001$ ), PP ( $r = 0.29$ ,  $P = 0.001$ ), hypertension ( $r = 0.56$ ,  $P <$



## Carotid intima-media thickness in Uygurs



**Figure 1.** Mean common carotid IMT increases with age in Uygur males and females. Uygur males and females were divided into the following quartiles according to age: 40-52, 53-59, 60-68, and > 68 years. Common carotid IMT values were measured, and its relationship with the factor of age was analyzed. Compared with the group of 40-52 years, \* $P < 0.05$ , \*\* $P < 0.001$ ; compared with the group of 53-59 years, # $P < 0.05$ , ## $P < 0.001$ ; compared with the group of 60-68 years, & $P < 0.05$ , && $P < 0.001$ .



**Figure 2.** Mean common carotid IMT values in normal controls and Uygur participants with stroke and/or IHD. The mean carotid IMT was significantly increased in patients diagnosed with stroke and/or IHD, compared with normal individuals, in both Uygur males and females. Compared with the normal control group, \* $P < 0.05$ , \*\* $P < 0.001$ .

0.001), TC ( $r = 0.41$ ,  $P < 0.001$ ), LDL-C ( $r = 0.42$ ,  $P < 0.001$ ), TG ( $r = 0.39$ ,  $P < 0.001$ ), Apo B ( $r = 0.25$ ,  $P = 0.004$ ), diabetes mellitus ( $r = 0.37$ ,  $P < 0.001$ ), glucose ( $r = 0.25$ ,  $P = 0.003$ ), smoking status ( $r = 0.22$ ,  $P = 0.01$ ), creatinine ( $r = 0.20$ ,  $P = 0.017$ ), IHD ( $r = 0.35$ ,  $P < 0.001$ ), and stroke ( $r = 0.43$ ,  $P < 0.001$ ). However, in Uygur females, significant positive associations with the carotid IMT were found for age ( $r = 0.46$ ,  $P < 0.001$ ), BMI ( $r = 0.47$ ,  $P < 0.001$ ), SBP ( $r = 0.43$ ,  $P < 0.001$ ), DBP ( $r = 0.41$ ,  $P < 0.001$ ), PP ( $r = 0.22$ ,  $P = 0.01$ ), hypertension ( $r = 0.39$ ,  $P < 0.001$ ), TC ( $r = 0.29$ ,  $P = 0.001$ ), LDL-C ( $r = 0.22$ ,  $P = 0.01$ ), TG ( $r = 0.35$ ,  $P < 0.001$ ), diabetes mellitus ( $r = 0.58$ ,  $P < 0.001$ ), glucose ( $r = 0.52$ ,

$P < 0.001$ ), IHD ( $r = 0.52$ ,  $P < 0.001$ ), and stroke ( $r = 0.44$ ,  $P < 0.001$ ), while a significant inverse association was observed for HDL-C ( $r = -0.17$ ,  $P = 0.033$ ).

A multivariate stepwise regression model was also constructed to identify the independent factors for common carotid IMT values in these Uygur subjects. Our results indicated that, in Uygur male subjects, LDL-C, age, TG, creatinine, BMI, smoking, and medically documented history of hypertension and diabetes, were found to be statistically significant independent factors associated with common carotid IMT (as continuous variable), with an adjusted R-square of 0.676 ( $P < 0.001$ ) (Table 3). On the other hand, in Uygur females, only SBP, age, TG, HDL-C, BMI, and history of diabetes remained significant in the model (adjusted R-square: 0.622;  $P < 0.001$ ) (Table 4). These results indicate that the risk factor profiles for carotid IMT were slightly different between Uygur males and females, which might imply the need for developing differential treatment strategies for the patient subgroups.

## Discussion

Atherosclerosis and related vascular effects, including cardiovascular disease, stroke, peripheral arterial disease, and end-stage renal disease, are among the leading causes of morbidity, mortality, and disability worldwide, especially in developing countries such as China and Indian. The pathogenesis and progression of atherosclerosis have been associated with the complicated interactions between the arterial wall and pathophysiologic factors (inflammatory, dietary, hemodynamic, genetic and/or environmental influences, and lifestyle), leading to thickening, stiffening, and dysfunction of the arterial wall [3-5]. In these interactions, vascular intimal thickening, especially in the extracra-

## Carotid intima-media thickness in Uygurs

**Table 3.** Multiple stepwise regression analysis for carotid IMT in Uygur males

	$\beta$	B	SE	t	P
Hypertension	0.278	0.100	0.022	4.527	< 0.001
LDL-C	0.207	0.068	0.019	3.501	0.001
Diabetes mellitus	0.368	0.155	0.026	5.870	< 0.001
Age	0.385	0.006	0.001	6.323	< 0.001
Triglycerides	0.184	0.030	0.010	2.880	0.005
Creatinine	0.174	0.002	0.001	3.123	0.002
BMI	0.160	0.009	0.004	2.554	0.012
Smoking	0.113	0.041	0.020	2.002	0.048

Note:  $\beta$  is the standardized regression coefficients; B is the unstandardized regression coefficients; SE is the standard error for  $\beta$  and B. R Square: 0.702; adjusted R Square: 0.676.

**Table 4.** Multiple stepwise regression analysis for carotid IMT in Uygur females

	$\beta$	B	SE	t	P
Diabetes mellitus	0.409	0.159	0.021	7.654	< 0.001
Systolic blood pressure	0.244	0.002	0.001	4.302	< 0.001
Age	0.416	0.007	0.001	7.957	< 0.001
Triglycerides	0.207	0.031	0.008	3.886	< 0.001
BMI	0.219	0.009	0.003	3.675	< 0.001
HDL-C	-0.185	-0.123	0.034	-3.663	< 0.001

Note: R Square: 0.637; adjusted R Square: 0.622.

nial carotid artery system, is predictive of sub-clinical atherosclerosis and the disease progression [6]. In addition, vascular intimal thickening has also been associated with the significant angiographic coronary stenosis, increasing the incidence of myocardial infarction and stroke. Therefore, carotid IMT is widely used as a potential screening tool to identify high vascular risk factors.

Some studies have shown that there are important differences in B-mode carotid IMT detection, including the segmentation and the type of measurement. In fact, the common carotid artery (CCA) is the preferable site for IMT measurement, compared with the internal carotid artery (ICA) and the bulbous. CCA is relatively close and parallel to the skin surface, so good quality scans can be readily achieved. In contrast, ICA is rather difficult to visualize, and the IMT measurements in ICA are often incomplete, with intra-observer and/or inter-observer variabilities. In addition, common carotid IMT has been shown to be associated with cardiovascular risk factors and prevalent cardiovascular diseases [7, 8]. In this study, we chose CCA as the site for carotid IMT measurement.

Our results have shown that Uygur males have slightly higher mean carotid IMT than females, which is in line with the ARYA Study (Atherosclerosis Risk in Young Adults) [9]. We speculate that this difference could be partly attributed to the different carotid lumen diameters between Uygur males and females. Therefore, the results may reflect the differences in physiology, rather than vascular damages [10]. In Uygur males and females, factors of age, BMI, SBP, DBP, PP, hypertension, TC, LDL-C, TG, diabetes mellitus, glucose, IHD, and stroke were significantly associated with the mean carotid IMT values. Carotid IMT was markedly increased across the age quartiles. When analyzed separately, the mean carotid IMT was strongly correlated with Apo B, smoking status, and creatinine level in males. However, in Uygur females, a significant negative correlation between the mean carotid IMT and HDL-C level was found. In our study, all enrolled subjects were divided into four groups according to the mean carotid IMT quartiles. We found that age, BMI, TC, TG, LDL-C, glucose,

SBP, DBP, PP, IHD, stroke, diabetes mellitus, hypertension, and smoking were significantly different among these four groups, which was in line with the previous ultrasound studies. Acevedo *et al.* evaluated the risk factor profile of young subjects with high carotid IMT, and found that BMI, waist circumference, blood pressure, and serum lipids were significantly higher as carotid IMT increased [11]. Kaźmierski and colleagues also found a significant correlation between the carotid IMT values and the atherosclerosis risk factors [12]. Antonini-Canterin and co-workers indicated that subjects with metabolic syndrome (MetS) had a significantly higher prevalence of carotid IMT > 0.80 mm and carotid plaques. Otherwise, in participants without MetS, carotid IMT was correlated with fasting plasma glucose, serum creatinine, and uric acid levels [13].

Previous studies have demonstrated an association between CCA IMT and prevalent cardiovascular diseases. In addition, several studies have shown a strong association between IMT and the incidence of myocardial infarction and stroke [14]. In the Cardiovascular Health Study (CHS), the relationship between the CCA IMT

and the incidence of new myocardial infarction and stroke were studied in 5858 subjects, older than 65 years, without clinical cardiovascular disease. The relative risk of myocardial infarction and stroke was increased linearly with the IMT values, and the relationship remained significant after the adjustment of the traditional risk factors [15]. Hollander and colleagues have demonstrated that the increased carotid IMT is independently associated with ischemic stroke in middle-aged subjects [16]. Chuang has also observed that CCA IMT can independently predict future ischemic stroke in the Taiwanese population in 9.85-year (median) follow-up [17]. Nikic and co-workers find that mean CCA IMT was higher in patients with ischemic brain infarctions [18]. Furthermore, several studies have also demonstrated the relationship between carotid IMT and coronary artery disease [19]. Carotid IMT has been endorsed as a tool in risk assessment for IHD by the American Heart Association (AHA) and the Third Adult Treatment Panel of the National Cholesterol Education Program (NCEP ATP III) [20]. In agreement with these findings, our results indicated that the mean carotid IMT was significantly increased in patients diagnosed with stroke and/or IHD. However, no differences were found between subjects with IHD and stroke, indicating these diseases might share common risk factors and pathological mechanisms. With the stepwise multiple linear regression analysis, we also demonstrated that age, LDL-C, TG, creatinine, BMI, smoking, hypertension, and diabetes were significantly and independently associated with the mean carotid IMT in male subjects, accounting for 67.6% of the variance. However, in female subjects, only age, SBP, TG, HDL-C, BMI, and diabetes were independent predictors of carotid IMT values, accounting for 62.2% of the variance. It is well known that smoking has been considered to be a common risk factor of CVD and IMT [21]. In fact, our observation confirmed that smoking was an independent risk factor of carotid IMT in Uygur males, which is in contrast with the findings from the ARYA Study [9]. This contradiction might be partly attributed to the demographics of the study population. Unexpectedly, serum creatinine level has been shown to be an independent risk factor for carotid IMT in males, reflecting systemic atherosclerosis. In addition, the prevalence of cigarette smoking and MetS, and the meat consumption were higher in Uygur

males than females, which may promote atherosclerosis, renal injury, and consequently increase the serum creatinine levels [22].

The prevalence of overweight, obesity, and MetS has dramatically increased in Uygur population in past decades because of the changes in lifestyles and dietary habits, contributing to multiple metabolic abnormalities and the pathogenesis of cardiovascular diseases. Interestingly, majority of risk factors associated with the mean carotid IMT values in this study are also the components of MetS, implying that MetS and its components may be involved in subclinical atherosclerosis pathogenesis. In line with this, Torrejón and colleagues have found that BMI and waist circumference is associated with carotid IMT in obese adolescents [23]. Similarly, Ahn and co-workers have reported that MetS is associated with increased carotid IMT and aortic pulse wave velocity (PWV), independently of age, BP, and smoking [24]. Zou *et al.* have also indicated that common carotid artery IMT is significantly higher in the MetS groups than the groups without MetS [25]. However, further in-depth studies with enlarged samples and other ethnic people are still needed to address all these issues.

In conclusion, for the first time, our study showed that factors of age, LDL-C, TG, creatinine, urine protein, BMI, smoking, hypertension, and diabetes were significantly and independently associated with the mean carotid IMT values in Uygur males. On the other hand, in Uygur females, only age, SBP, TG, HDL-C, BMI, and diabetes were the significantly independent predictors of carotid IMT. Based on these results, modifications of these cardiovascular risk factors might be promising therapeutic strategies for primary and secondary prevention of atherosclerosis in Uygur population.

### Acknowledgements

This work was supported by the grant (grant No. 20121201) from Dongying People's Hospital of Shandong Provincial Hospital Group. We are also grateful to Ms. Fenglan Guo for the excellent technical assistance.

### Disclosure of conflict of interest

None.

**Address correspondence to:** Xinsheng Xu, Department of Cardiology, Dongying People's Hospital of

## Carotid intima-media thickness in Uygurs

Shandong Provincial Hospital Group, No. 317, Nanyi Road, Dongying 257091, Shandong, China. Tel: 86-546 8901 061; E-mail: xinshengxu163@163.com

### References

- [1] Kalibinuer Y, Buaijiaer H, Bingxian H and Binbin Y. The trend of cardiovascular disease of Uygur population in Hotan Xinjiang China. A survey from 1996 to 2005. *Heart* 2010; 96: A84-A85.
- [2] Kalibinuer Y, Buaijiaer H, Bingxian H and Binbin Y. The trend of cardiovascular disease of Uygur hospitalised patients in Xinjiang Hetian. A survey from 1996 to 2005. *Heart* 2010; 96: A85-A85.
- [3] Fenyo IM and Gafencu AV. The involvement of the monocytes/macrophages in chronic inflammation associated with atherosclerosis. *Immunobiology* 2013; 218: 1376-84.
- [4] Gardener H, Wright CB, Cabral D, Scarmeas N, Gu Y, Cheung K, Sacco RL and Rundek T. Mediterranean diet and carotid atherosclerosis in the Northern Manhattan Study. *Atherosclerosis* 2014; 234: 303-10.
- [5] Messner B and Bernhard D. Smoking and cardiovascular disease: mechanisms of endothelial dysfunction and early atherogenesis. *Arterioscler Thromb Vasc Biol* 2014; 34: 509-15.
- [6] Tran LTT, Park H and Kim H. Is the carotid intima-media thickness really a good surrogate marker of atherosclerosis? *J Atheroscler Thromb* 2012; 19: 680-90.
- [7] Stein JH, Korcarz CE, Hurst RT, Lonn E, Kendall CB, Mohler ER, Najjar SS, Rembold CM and Post WS. Use of carotid ultrasound to identify subclinical vascular disease and evaluate cardiovascular disease risk: a consensus statement from the American Society of Echocardiography Carotid Intima-Media Thickness Task Force. Endorsed by the Society for Vascular Medicine. *J Am Soc Echocardiogr* 2008; 21: 93-111; quiz 189-90.
- [8] Polak JF, Pencina MJ, Pencina KM, O'Donnell CJ, Wolf PA and D'Agostino RB. Carotid-wall intima-media thickness and cardiovascular events. *N Engl J Med* 2011; 365: 213-21.
- [9] Oren A, Vos LE, Uiterwaal CSPM, Grobbee DE and Bots ML. Cardiovascular risk factors and increased carotid intima-media thickness in healthy young adults: the Atherosclerosis Risk in Young Adults (ARYA) Study. *Arch Intern Med* 2003; 163: 1787-92.
- [10] Bots ML, Hofman A and Grobbee DE. Increased common carotid intima-media thickness. Adaptive response or a reflection of atherosclerosis? Findings from the Rotterdam Study. *Stroke* 1997; 28: 2442-7.
- [11] Acevedo M, Krämer V, Tagle R, Arnaiz P, Corbalán R, Berríos X and Navarrete C. Cardiovascular risk factors among young subjects with high carotid intima media thickness. *Rev Med Chil* 2011; 139: 1322-9.
- [12] Kaźmierski R, Michalak S and Kozubski W. Ultrasound-based markers of carotid atherosclerosis correlate well with the number of classical atherosclerotic risk factors. *Neurol Neurochir Pol* 2011; 45: 317-27.
- [13] Antonini-Canterin F, La Carrubba S, Gullace G, Zito C, Di Bello V, Di Salvo G, Benedetto F, Novo S, Pezzano A, Perticone F, Balbarini A and Carerj S. Association between carotid atherosclerosis and metabolic syndrome: results from the ISMIR study. *Angiology* 2010; 61: 443-8.
- [14] Kota SK, Mahapatra GB, Kota SK, Naveed S, Tripathy PR, Jammula S and Modi KD. Carotid intima media thickness in type 2 diabetes mellitus with ischemic stroke. *Indian J Endocrinol Metab* 2013; 17: 716-22.
- [15] O'Leary DH, Polak JF, Kronmal RA, Manolio TA, Burke GL and Wolfson SK. Carotid-artery intima and media thickness as a risk factor for myocardial infarction and stroke in older adults. Cardiovascular Health Study Collaborative Research Group. *N Engl J Med* 1999; 340: 14-22.
- [16] Hollander M, Hak AE, Koudstaal PJ, Bots ML, Grobbee DE, Hofman A, Witteman JCM and Breteler MMB. Comparison between measures of atherosclerosis and risk of stroke: the Rotterdam Study. *Stroke* 2003; 34: 2367-72.
- [17] Chuang SY, Bai CH, Chen JR, Yeh WT, Chen HJ, Chiu HC, Shiu RS and Pan WH. Common carotid end-diastolic velocity and intima-media thickness jointly predict ischemic stroke in Taiwan. *Stroke* 2011; 42: 1338-44.
- [18] Nikic P, Savic M, Jakovljevic V and Djuric D. Carotid atherosclerosis, coronary atherosclerosis and carotid intima-media thickness in patients with ischemic cerebral disease: Is there any link? *Exp Clin Cardiol* 2006; 11: 102-6.
- [19] Rohani M, Jogestrand T, Ekberg M, van der Linden J, Källner G, Jussila R and Agewall S. Interrelation between the extent of atherosclerosis in the thoracic aorta, carotid intima-media thickness and the extent of coronary artery disease. *Atherosclerosis* 2005; 179: 311-6.
- [20] National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation* 2002; 106: 3143-421.
- [21] Baldassarre D, Castelnovo S, Frigerio B, Amato M, Werba JP, De Jong A, Ravani AL, Tremoli E and Sirtori CR. Effects of timing and extent of



## Carotid intima-media thickness in Uygurs

- smoking, type of cigarettes, and concomitant risk factors on the association between smoking and subclinical atherosclerosis. *Stroke* 2009; 40: 1991-8.
- [22] Oh SM, Kim HC, Ahn SV, Chi HJ and Suh I. Association between meat consumption and carotid intima-media thickness in Korean adults with metabolic syndrome. *J Prev Med Public Health* 2010; 43: 486-95.
- [23] Torrejón C, Hevia M, Ureta E, Valenzuela X and Balboa P. Intima-media thickness in obese adolescents and their relation with metabolic syndrome. *Nutr Hosp* 2012; 27: 192-7.
- [24] Ahn MS, Kim JY, Youn YJ, Kim SY, Koh SB, Lee K, Yoo BS, Lee SH, Yoon J, Park JK and Choe KH. Cardiovascular parameters correlated with metabolic syndrome in a rural community cohort of Korea: the ARIRANG study. *J Korean Med Sci* 2010; 25: 1045-52.
- [25] Zou X, Li Y, Zhang H, Chen Z, Wang H, Guo M, Wang Q, Zhao L, Yang Y, Zheng R, Cai Y and Gu D. A community-based study on relations between metabolic syndrome and carotid atherosclerosis in a middle-aged population. *Zhonghua Liu Xing Bing Xue Za Zhi* 2010; 31: 361-5.