

Muscle strength and carotid artery flow velocity is associated with increased risk of atherosclerosis in adults

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Abstract

Background: Carotid intima–media thickness (CIMT) has been proposed as a surrogate marker of atherosclerotic disease. In addition, carotid flow velocity (FV) and muscle strength (MS) are reported to be associated with increased CIMT. As there remains insufficient evidence for a complex association of CIMT with FV and MS, the aim of this study was to examine this association in adults.

Methods: A total of 426 adults participated in this study. MS in all subjects was measured by hand grip strength. Carotid variables were measured with B-mode ultrasound. Analysis of covariance (ANCOVA) was performed to assess independent differences in the CIMT among four groups, according to the level of peak systolic flow velocity (PSV) and MS after multivariate adjustment. Logistic regression analysis was performed to calculate odds ratios (OR) and 95% confidence intervals (CI) for the independent associations between PSV and MS and the estimated risk of atherosclerosis.

Results: Increased CIMT is associated with MS and PSV. ANCOVA showed that the CIMT varied significantly among groups according to the level of PSV and MS after multivariate adjustment. When calculated for the estimated risk of carotid atherosclerosis, the adjusted OR for the low PSV and MS group was 3.87 (95% CI 1.78–8.44).

Conclusions: The results suggest that CIMT and risk of carotid atherosclerosis are significantly correlated with PSV and upper body MS, more closely for the PSV than for the MS after adjustment for potential confounders. PSV by itself, and/or PSV with grip strength may be an indicator of atherosclerotic plaque instability. (Cardiol J 2017; 24, 4: 385–392)

Key words: carotid intima–media thickness, carotid flow velocity, muscle strength, atherosclerosis, adults

Introduction

Carotid artery intima–media thickness (CIMT) has been proposed as a surrogate marker of atherosclerotic disease, including cardiovascular disease (CVD), myocardial infarction (MI), stroke, and all-cause mortality. Therefore, prevention of increased CIMT may prevent atherosclerotic disease [1–4].

Increased CIMT is affected by CVD risk factors such as aging, body composition, blood pressure, and cardiorespiratory fitness in adults [5–10]. Moreover, two follow-up studies reported that carotid artery peak systolic flow velocity (PSV) and end diastolic flow velocity (EDV) are negatively associated with CIMT in Taiwanese adults [11, 12]. Another cross-sectional study reported that

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CIMT was independently associated with muscle strength (MS) evaluated by hand grip strength in children [13].

PSV and EDV are reported risk factors for development of CVD and ischemic stroke [11, 12, 14, 15]. MS evaluated by hand grip strength is also reportedly an important predictor of risk for CVD, coronary heart disease, and stroke [16–19]. Thus, PSV and MS are common risk factors for CVD. Meanwhile, two recent cross-sectional studies reported that combinations of CVD risk factors (aging and smoking or body mass index (BMI) and waist circumference) is associated with acceleration of the increase in CIMT [20, 21]. As there is still insufficient evidence for a complex association between CIMT, carotid artery flow velocity, and MS, this study aimed to examine this association in adults aged 19 to 64 years.

Methods

Subjects

This cross-sectional study was performed between June and December 2015. A total of 450 adults (19–64 years of age) submitted an application to participate after reading an advertisement for the study in community and health centers. The participation rate according to advertisement was 76%. Healthy adults aged 19–64 years were included. The initial exclusion criteria were under 19 years of age and those over 65, current CVD, stroke history of CVD (angina, MI) or stroke. Five subjects were excluded with a history of CVD or stroke. The secondary exclusion criterion was failure to complete the entire test. Nineteen subjects who did not complete the entire test were excluded from the analysis. In total, data of 426 adults were analyzed (mean age 43.9 ± 14.7 years) (Table 1). Hypertension was defined as a systolic blood pressure (SBP) ≥ 140 mm Hg or diastolic blood pressure (DBP) at least 90 mm Hg, and/or current treatment with antihypertensive medication [22]. Diabetes and hyperlipidemia were defined as current medication use (hypoglycemic and lipid-lowering). Information on clinical outcomes was obtained through a questionnaire. The institutional review board approved the study and informed consent was obtained in writing from all subjects participating in the study.

Body composition, blood pressure, and muscle strength

After measuring the subject height and body mass, using body composition analyzer (Inbody

370, Biospace, Seoul, Korea) body fat mass (BFM) percentage and appendicular skeletal muscle (ASM) were measured respectively by the bio-electrical impedance analysis method. Waist circumference was measured to the nearest 0.1 cm at the level of the umbilicus using a flexible plastic tape with the participant standing. BMI was calculated by this formula. Two days prior to body composition measurement, the subjects were instructed to avoid physical exertion other than routine daily activity and to eat a light diet. SBP and DBP were measured with a mercury sphygmomanometer (HICO, Tokyo, Japan) after a 10-min rest. Grip strength in the dominant hand was measured using an isometric dynamometer (TKK-5401, Japan). MS per body weight was calculated using the body weight and grip strength value. Reproducibility was assessed by test-retest in 30 participants in this study. Pearson correlation coefficients between test-retest were 0.94 for the mean hand grip strength.

Carotid artery ultrasound

Carotid artery variables were measured using B-mode ultrasound and 10-MHz probe (LOGIQ 3, GE Healthcare, Wauwatosa, WI, USA). The left carotid artery was measured by ultrasound. CIMT, and systolic and diastolic carotid artery luminal diameter (CLD) were measured from the far wall of the distal common carotid, 1 cm proximal to the carotid bifurcation. The CIMT was defined as the distance from the lumen-intima interface to the intima-adventitia interface, and systolic and diastolic CLD was defined as the distance between the near and far wall intima-media interfaces [23]. For Doppler spectral analysis, PSV and EDV were measured by continuous-wave Doppler examination in the common carotid, 1–3 cm proximal to the bifurcation [12]. Reproducibility was assessed by test-retest in 30 participants in this study. Pearson correlation coefficients between test-retest were 0.90 for the mean CIMT and 0.81 for the mean PSV.

Statistical analysis

SPSS ver. 17.0 (SPSS Inc., Chicago, IL, USA) was used for the statistical analysis, and the measurement results were presented as averages and standard deviation. Compared to the other variables between two groups in which all subjects were divided into Low and High groups depending on each PSV average (under 30 years: 110.0 cm/s, 30–49 years: 90 cm/s, and 50–64 years: 75 cm/s) and MS average (under 30 years: 0.63 kg/weight, 30–49 years: 0.56 kg/weight, and 50–64 years:

Table 1. Anthropometric characteristics, body composition, blood pressure, muscle strength, and carotid artery variables.

Variable	Total (n = 426)	Peak systolic flow velocity PSV [cm/s]		Muscle strength — MS [kg/weight]	
		Low (n = 212)	High (n = 214)	Low (n = 219)	High (n = 207)
Female	315	174	140	162	153
Age [years]	43.9 ± 14.7	47.2 ± 13.4	40.8 ± 15.2***	45.2 ± 14.4	42.6 ± 15.0
Height [cm]	160.7 ± 7.7	158.7 ± 6.0	162.7 ± 8.6***	160.8 ± 7.7	160.6 ± 7.7
Body mass [kg]	60.4 ± 9.7	58.6 ± 8.2	62.2 ± 10.6***	63.7 ± 10.1	56.9 ± 7.8***
Body mass index [kg/m ²]	23.4 ± 3.0	23.3 ± 3.0	23.4 ± 3.0	24.6 ± 3.0	22.0 ± 2.3***
Body fat mass percent [%]	28.8 ± 8.2	30.4 ± 7.8	27.4 ± 8.0***	31.3 ± 7.6	26.2 ± 8.1***
Waist circumference [cm]	85.8 ± 4.6	86.5 ± 4.6	85.1 ± 4.55**	87.1 ± 4.3	84.4 ± 4.5***
Appendicular skeletal muscle mass [kg]	17.6 ± 4.0	16.6 ± 2.9	18.6 ± 4.6***	18.0 ± 4.0	17.3 ± 3.9*
Systolic blood pressure [mm Hg]	123.1 ± 12.3	123.8 ± 12.2	122.4 ± 12.4	123.8 ± 12.3	122.4 ± 12.4
Diastolic blood pressure [mm Hg]	78.0 ± 8.6	79.2 ± 8.4	76.8 ± 8.7**	79.1 ± 8.5	76.8 ± 8.6**
Dominant grip strength [kg]	28.5 ± 8.6	27.1 ± 7.4	29.9 ± 9.4**	26.0 ± 7.5	31.2 ± 8.8***
Carotid intima-media thickness [mm]	0.57 ± 0.15	0.62 ± 0.15	0.53 ± 0.13***	0.60 ± 0.15	0.54 ± 0.14***
Diastolic carotid luminal-diameter [cm]	0.60 ± 0.06	0.61 ± 0.07	0.60 ± 0.06	0.61 ± 0.07	0.60 ± 0.06
Systolic carotid luminal-diameter [cm]	0.56 ± 0.06	0.57 ± 0.06	0.55 ± 0.06**	0.56 ± 0.06	0.55 ± 0.06
Peak-systolic flow velocity [cm/s]	81.8 ± 22.5	66.4 ± 12.5	97.0 ± 19.8***	81.4 ± 22.8	82.1 ± 22.4
End-diastolic flow velocity [cm/s]	25.12 ± 5.4	22.9 ± 4.4	27.3 ± 5.5***	25.1 ± 5.8	25.1 ± 5.1
Smoking	18 (4.2%)				
Diabetes	10 (2.3%)				
Hypertension	16 (3.8%)				
Hyperlipidemia	10 (2.3%)				

Values are means ± standard deviation. All subjects were divided into Low and High groups depending on each PSV average (under 30 years: 110.0 cm/s, 30–49 years: 90 cm/s, and 50–64 years: 75 cm/s) and MS average (under 30 years: 0.63 kg/weight, 30–49 years: 0.56 kg/weight, and 50–64 years: 0.53 kg/weight for men; under 30 years: 0.46 kg/weight, 30–49 years: 0.45 kg/weight, and 50–64 years: 0.41 kg/weight for women) per age. *p < 0.05; ** p < 0.01; *** p < 0.001

0.53 kg/weight for men; under 30 years: 0.46 kg/weight, 30–49 years: 0.45 kg/weight, and 50–64 years: 0.41 kg/weight for women). An independent sample t-test was used to identify differences in variables between the groups according to the two groups for the PSV and MS.

Also, subjects were divided into four groups (group I: both low PSV and low MS, group II: low PSV and high MS, group III: high PSV and low MS, and group IV: both high PSV and high MS) according to the level of the PSV and MS. Analysis of covariance (ANCOVA) was used to evaluate independent differences in CIMT among four groups according to the level of PSV and MS, after adjustment for smoking, diabetes, hypertension, hyperlipidemia, gender, age, BMI, BFM percent, waist circumference, ASM, and DBP. And the post-hoc was performed according to Tukey's method.

CIMT is considered to be a marker of generalized atherosclerosis [24, 25]. Sun et al. [24]

reported the value of CIMT over the cut-off point of 0.68 mm correlated with increased risk of carotid atherosclerosis. The mean CIMT value of 0.68 mm was used as the cut-off point between thick and thin CIMT, and risk factors of thick CIMT were studied. Logistic regression analysis was used to calculate the odds ratio (OR) and 95% confidence interval (CI) for the assessment of atherosclerosis risk according to the decrease in PSV and MS after adjustment for multiple covariates. The statistical level of significance was set at less than p < 0.05.

Results

Table 1 shows the differences in variables between the two groups according to the level of PSV and MS. In the PSV analysis, age, height, body mass, BFM percent, CIMT, PSV, and EDV were significantly different (p < 0.001) between the two groups. The waist circumference, DBP,

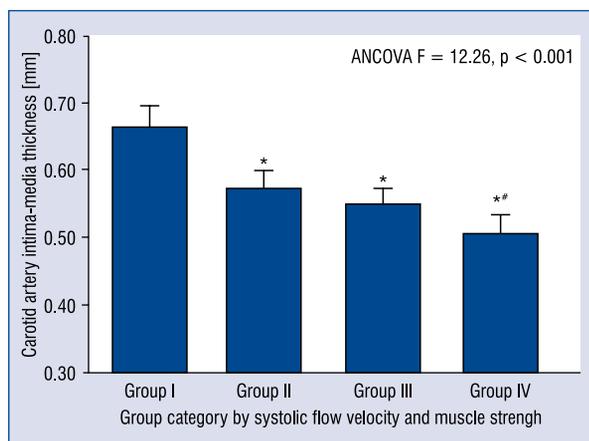


Figure 1. Differences in carotid artery intima–media thickness among four groups according to the level of peak systolic flow velocity (PSV) and muscle strength (MS); Group I: low PSV and low MS, Group II: low PSV and high MS, Group III: high PSV and low MS, and Group IV: high PSV and high MS. Covariates: smoking, diabetes, hypertension, hyperlipidemia, gender, age, body mass index, waist circumference, body fat mass percent, waist circumference, appendicular skeletal muscle mass, and diastolic blood pressure; *Differences of Group I vs. Group IV, #Difference of Group II vs. Group IV; $p < 0.05$.

dominant hand MS, and systolic CLD were also significantly different ($p < 0.01$) between the two groups. There were no differences in BMI, SBP, and diastolic CLD.

In MS analysis, body mass, BMI, BFM percent, waist circumference, MS, and CIMT were significantly different ($p < 0.001$) between the two groups. The DBP and ASM were also significantly different ($p < 0.01$, $p < 0.05$) between the two groups. There were no differences in age, height, SBP, systolic and diastolic CLD, PSV, and EDV.

CIMT was significantly negatively correlated with PSV and MS/weight ($r = -0.595$, $r = -0.416$; $p < 0.01$). CIMT was also significantly negatively correlated with EDV ($r = -0.232$, $p < 0.01$).

Figure 1 shows the results of ANCOVA analysis. CIMT was significantly different ($F = 12.26$, $p < 0.001$) among four groups according to the level of PSV and MS; CIMT in group I was the thickest, and CIMT in the group IV was the thinnest, after adjustment for smoking, diabetes, hypertension, hyperlipidemia, gender, age, BMI, BFM percent, waist circumference, ASM, and DBP. The result in group I was significantly different ($p < 0.05$) compared to that in other groups, and the result in group II was

significantly different ($p < 0.05$) compared to the result in group IV. Group III did not differ from group IV.

In Table 2, results of logistic regression analysis were adjusted for smoking, diabetes, hypertension, hyperlipidemia, gender, age, BMI, BFM percent, waist circumference, ASM, and DBP showed that risk of atherosclerosis was related to the level of PSV and MS. The OR was 5.80 (CI 2.98–11.28) for group I (reference group), when not adjusted, and when group IV was set as the reference; OR was 4.38 (CI 1.84–10.41) for group I (reference group), when smoking, diabetes, hypertension, hyperlipidemia, gender, and age were adjusted. The OR was 3.87 (CI 1.78–8.44) for group I (reference group), when smoking, diabetes, hypertension, hyperlipidemia, gender, age, BMI, BFM percent, waist circumference, ASM, and DBP were adjusted.

Discussion

This study examined the association of CIMT with levels of carotid PSV and MS in adults. The primary findings are that CIMT was different among four groups according to the level of PSV and MS. Individuals with low PSV and low MS have thicker CIMT compared to those with high PSV and high MS; therefore, individuals with low PSV and low MS are more likely to have increased CIMT compared to those with high PSV and high MS.

A systematic review and meta-analysis reported that CIMT evaluated by ultrasound is a strong predictor of future CVD in middle-aged and older adults [26]. Some studies demonstrated that an increase in CIMT is associated with common risk factors such as aging, body composition, blood pressure, serum lipids, and cardiorespiratory fitness [5–10].

Meanwhile, recent cross-sectional studies have reported that CIMT had a significant negative association with carotid artery flow velocity [11, 12], and that CIMT was more highly associated with EDV than PSV in a large population [12]. However, another cross-sectional study reported that PSV is more associated with a cardiovascular event than EDV in hypertensive patients [15]. This study revealed that CIMT was more highly associated with PSV ($r = -0.595$) than with EDV ($r = -0.232$), and that CIMT was different between groups according to the level of PSV. Additionally, it was shown that the high PSV group was significantly different from the low PSV group with regard to other CVD risk factors. Therefore, high PSV is

Table 2. Odds-ratio with 95% confidence interval for cut-off point of carotid artery intima-media thickness in four groups according to the level of peak systolic flow velocity (PSV) and muscle strength (MS).

Category	N (%)	Age [years]	Odds ratio	95% confidence interval	
Carotid artery intima-media thickness cutoff point of 0.68 mm					
Crude model					
	426				
Group I	100 (23.5)	48.1 ± 13.5	5.80	2.98	– 11.28
Group II	112 (26.3)	46.3 ± 13.4	2.24	1.15	– 4.38
Group III	119 (27.9)	41.8 ± 15.4	1.52	0.77	– 3.01
Group IV (reference)	95 (22.3)	43.9 ± 14.7	1.00		
Model I					
Group I	4.38		1.84	–	10.41
Group II	1.59		0.72	–	3.34
Group III	1.48		0.65	–	3.37
Group IV (reference)	1.00				
Model II					
Group I	3.87		1.78	–	8.44
Group II	1.55		0.71	–	3.37
Group III	1.31		0.59	–	2.90
Group IV (reference)	1.00		1.00		

All subjects were divided into Low and High groups depending on each PSV average (under 30 years: 110.0 cm/s, 30–49 years: 90 cm/s, and 50–64 years: 75 cm/s) and MS average (under 30 years: 0.63 kg/weight, 30–49 years: 0.56 kg/weight, and 50–64 years: 0.53 kg/weight for men; under 30 years: 0.46 kg/weight, 30–49 years: 0.45 kg/weight, and 50–64 years: 0.41 kg/weight for women) per age.

Group I: low PSV and low MS, Group II: low PSV and high MS, Group III: high PSV and low MS, and Group IV: high PSV and high MS
Crude model, not adjusted

Model I, adjusted for smoking, diabetes, hypertension, hyperlipidemia, gender, and age

Model II, adjusted as for Model I plus gender, age, body mass index, body fat mass percent, waist circumference, appendicular skeletal muscle mass, and diastolic blood pressure

considered to be associated with a delay in CIMT increase. The present study also demonstrated that high PSV has a positive effect on CVD risk factors.

Previous studies demonstrated that high cardiorespiratory fitness [10, 27] and walking speed [28, 29] were independently associated with a delay in CIMT increase. Meanwhile, MS is closely associated with metabolic risk factors and CVD risk in adults [17, 30]. Furthermore, a recent cross-sectional study reported that CIMT was negatively associated with level of the MS index [13]. This research indicated that CIMT was significantly associated ($r = -0.481$) with MS, and that the high MS group also showed a significantly thinner CIMT compared with that in the low MS group. Results suggested that high MS might be effective in preventing an increase in CIMT in adults. Additionally, it was shown that the high MS group was significantly different from the low MS group with regard to body composition and blood pressure. Therefore, high MS is considered to be associated with reduced risk for CVD.

PSV and MS are independently associated with future CVD predicted by CIMT [12, 13, 15]. Moreover, PSV and MS are closely associated with

traditional risk factors for CVD such as aging, body composition, blood pressure, and cardiorespiratory fitness [12, 13]. Two recent cross-sectional studies reported that combinations of CVD risk factors (aging and smoking or high BMI and waist circumference) are associated with an accelerated increase in CIMT [20, 21]. This study utilized the results of ANCOVA to examine the differences in CIMT among four groups according to the level of PSV and MS. CIMT was significantly different among the four groups according to the level of PSV and MS, after adjustment for multiple variables. Our study suggested that low PSV and low MS are associated with increased CIMT in adults. In this study, CIMT in group IV was significantly different from that in group II; however, CIMT in group IV showed no difference when compared to that of group III. This study suggested that increased CIMT might be associated more with PSV than with MS in adults. This was confirmed in correlation analysis.

CIMT has been proposed as a surrogate marker of atherosclerotic disease, such as CVD and stroke [1–3]. A cross-sectional study on Taiwanese adults by Sun et al. [24] reported that CIMT of 0.68 mm is a cut-off value for an obvious

increase in risk of carotid atherosclerosis. In this study, the estimated increased risk of carotid atherosclerosis was defined as a CIMT cut-off greater than 0.68 mm. When the PSV and MS data were categorized into four groups, the adjusted OR and 95% CI calculated by logistic regression analysis showed significant relationships between the estimated vulnerability to carotid atherosclerosis and the level of PSV and MS. Logistic regression analysis confirmed significant relationships between PSV and MS and risk of carotid atherosclerosis, when estimated using CIMT cut-off of 0.68 mm. In a crude model, the estimated risk of carotid atherosclerosis in group I was 5.80 times higher than that for individuals in group IV (reference). CIMT in patients with hypertension, diabetes, dyslipidemia, and metabolic syndrome is thicker than that in healthy adults [31]. Age, gender, body composition, and blood pressure are also reported risk factors for increased CIMT [5, 32–36]. Therefore, the increased risk of carotid atherosclerosis was evaluated after adjustment for covariates. The estimated risk of arteriosclerosis in the high MS and low PSV group and low PSV and low MS group were subjects under 30 years, 30–49 years, and 50–64 years, respectively were 1.55–3.87 times higher than that in the high PSV (110.0 cm/s, 90 cm/s, and 75 cm/s; under 30 years, 30–49 years, and 50–64 years, respectively) and high MS group (0.63 kg/weight, 0.56 kg/weight, and 0.53 kg/weight for men; 0.46 kg/weight, 0.45 kg/weight, and 0.41 kg/weight for women; under 30 years, 30–49 years, and 50–64 years, respectively) although the risk for the latter group did not differ significantly from that of the high PSV and low MS after controlling for smoking, diabetes, hypertension, hyperlipidemia, age, gender, BMI, BFM percent, waist circumference, ASM, and DBP.

Limitation of the study

This study has several limitations: 1) It was a cross-sectional study that examined the association of CIMT with PSV and MS. Compared to follow-up or interventional studies, a cross-sectional study could not provide more extensive information. 2) CIMT was used for prediction in a wide range of ages (childhood to the elderly) [37, 38]. This study was limited to adults. Therefore, the results for the association of CIMT with PSV and MS have limited application. 3) CVD-related biochemical markers such as serum lipids, glucose, and C-reactive protein were not examined in this study. Demonstration of the association between CVD-associated

biochemical markers and CIMT requires a cross-sectional study of a larger population [11, 39].

Conclusions

It was found that CIMT and the presence of carotid plaque probably were correlated with PSV and upper body MS. In both sexes, CIMT was associated more closely for PSV than for MS after adjustment for potential confounders. PSV by itself, and/or PSV with grip strength may be an indicator of PSV by itself, and/or PSV with grip strength may be an indicator of atherosclerotic plaque instability.

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Conflict of interest: None declared

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