ABSTRACT

Association of Increased Pulse Wave Velocity and Augmentation index after Isometric Handgrip Exercise with Coronary Revascularization

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Background; Arterial stiffness is associated with myocardial ischemia and incident coronary artery disease (CAD), and indexes of arterial stiffness are usually increased in patients with CAD. However, these indexes are often increased in elderly without CAD because systolic pressure increases with aging, and both vascular aging and hypertension are the powerful factors determining arterial stiffness. Arterial stiffness in patients with CAD may become more evident after isometric handgrip exercise which increases systolic pressure and ventricular afterload. We investigated the association of the change of stiffness indexes after isometric handgrip exercise with the lesion severity of CAD and the necessity for coronary revascularization.

Methods; Patients who were scheduled a routine coronary angiography via a femoral artery were enrolled. Arterial waveforms were traced at aortic root and external iliac artery using coronary catheters at baseline and 3 minutes after handgrip exercise. Augmentation index (AIx) was measured on the recorded aortic pressure waveform, and pulse wave velocity (PWV) was calculated using the ECG-gated time difference of the upstroke of arterial waveforms and distance between aortic root and external iliac artery.

Results: Total 37 patients were evaluated. Both PWV and AIx increased after handgrip exercise. ΔPWV was significantly correlated with ΔAIx (r = 0.344, *P* = 0.037). Patients were divided into higher and lower ΔPWV or ΔAIx groups based on the median values of 0.4 m/sec and 3.3%, respectively. Patients with higher PWV had more 2- or 3-vessel CAD (69% vs. 27%, *P* = 0.034), and underwent percutaneous coronary intervention (PCI) more frequently (84% vs. 50%, *P* = 0.038), but higher ΔAIx was not associated with either the lesion severity or PCI. Area under curve (AUC) of ΔPWV in association with PCI by C-statistics was 0.70 (95% confidence interval [CI] 0.51-0.88; *P* = 0.056). In multiple logistic regression analysis, ΔPWV was significantly associated with PCI (odds ratio 7.78; 95% CI 1.26-48.02; *P* = 0.027).

Conclusions: Increased PWV after isometric handgrip exercise was associated with the lesion severity of CAD and the necessity for coronary revascularization, but increased AIx was not.

Keywords: Arterial stiffness, Pulse wave velocity, Pulse wave analysis, Isometric exercise, Percutaneous coronary intervention

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LIST OF ABBREVIATIONS

AIx, augmentation index

AP, augmentation pressure

BMI, body mass index

BP, blood pressure

CAD, coronary artery disease

CAG, coronary angiography

CKD, chronic kidney disease

DBP, diastolic blood pressure

DM, diabetes mellitus

FP, forward pressure

PCI, percutaneous coronary intervention

PP, pulse pressure

PWV, pulse wave velocity

RAS, renin-angiotensin system

SBP, systolic blood pressure

ΔPWV, changes of PWV

ΔAIx, changes of AIx

I. Background

Normal or accelerated vascular aging and hypertension are two main factors determining arterial stiffness because they are basically related to the change of the arterial media [1]. However, diabetes, dyslipidemia, and smoking in addition to vascular aging and hypertension, all of which are shared common risk factors for coronary artery disease (CAD), may also change the mechanical properties of the arterial wall to make a stiff artery [2]. In a stiff arterial system, the velocities of the incident flow and the backward reflection flow are rapid enough for the early return of reflected waves during arterial systole rather than diastole, and the incident and reflected pressure waves are summed to increase aortic or central systolic pressure, but decrease central diastolic pressure, resulting in widened central pulse pressure [3]. Augmented central systolic pressure increases ventricular afterload and myocardial oxygen demand, and lowered diastolic pressure decreases coronary blood perfusion: the net results are myocardial ischemia and ventricular dysfunction [3-6]. For this reason, a stiff arterial system is associated with incident CAD, heart failure or stroke [7-9], and indexes of stiffness are related to the presence and severity of CAD [5]. Therefore, a stiff large artery is another feature of patients with CAD.

One of the popular methods evaluating arterial stiffness is measuring pulse wave velocity (PWV), a speed of an arterial pulsation through the arterial tree, usually between carotid and femoral arteries [6]. A number of studies reported that PWV was increased in patients with CAD, and correlated with the severity of coronary atherosclerosis [5,10-14]. Increased aortic PWV (>10 m/sec) is considered as a marker for detecting hypertension-mediated organ damage in guidelines for the management of arterial hypertension [15,16]. Another method for measuring the arterial stiffness is central pulse wave analysis. Augmentation by the summation of incident and reflected waves in the aortic pressure waveform is expressed as augmentation pressure (AP) or augmentation index (AIx). AIx is a percentage of AP on aortic pulse pressure [3,6]. The earlier studies showed that AIx was increased in patients with CAD and was associated with the severity of CAD, especially in younger patients (<60 years of age) [10,17,18]. We already reported that AIx was negatively correlated with minimal luminal area of coronary atherosclerosis measured by intravascular ultrasound, and was associated with coronary revascularization [19]. However, other studies showed no association of AIx with CAD, especially in elderly patients [8,12,20].

Increased PWV or AIx in patients with CAD may become more evident with a maneuver that influences the velocities of incident and reflected pressure waves. Isometric handgrip exercise, which increases systolic blood pressure (BP) and ventricular afterload [21-23], is a suitable and easily applicable tool for this purpose. The changes of PWV and AIx after isometric handgrip exercise may unmask the lesion severity and the necessity for coronary revascularization in elderly patients with CAD. In this study, the association of the change of PWV or AIx after isometric handgrip exercise with the lesion severity of CAD and the necessity for coronary revascularization was investigated.

II. Methods

Study patients

Patients who were scheduled a routine coronary angiography (CAG) via a femoral artery for the evaluation of the coronary atherosclerosis, and agreed to participate in the study were enrolled. Patients with acute coronary syndrome, or valvular heart disease were excluded. CAD was defined as ≥70% stenosis in at least one major epicardial coronary artery or a past medical history of coronary revascularization. The severity of coronary atherosclerosis was classified as 1-, 2- or 3-vessel disease by the number of the major epicardial coronary arteries with a significant stenosis. Patients with a significant stenosis in the left main coronary artery were counted as having 2-vessel disease.

The study protocol was approved by the institutional review board of Jeju National University Hospital. Written informed consents were obtained from participating patients or legal representative.

Study protocol

The maximal voluntary forearm contraction power was measured with a JAMAR dynamometer (Sammons Preston Rolyan, Nottinghamshire, UK), and a submaximal target at 30~40% of maximal handgrip power was used for 3-minute isometric handgrip exercise.

After routine CAG, arterial pressure waveforms were traced using a right coronary catheter and a fluid-filled pressure transducer system. Central arterial waveforms were recorded at the aortic root and traced before and at 1, 2 and 3 minutes after handgrip exercise (Figure 1). Forward pressure was measured at a merging point of the forward and the reflected waves on the recorded aortic pressure waveform. Augmentation pressure was defined as maximal central systolic pressure minus forward pressure. AIx was defined as augmentation pressure divided by central pulse pressure and expressed as a percentage (Figure 2). Peripheral arterial waveforms were recorded at the external iliac artery before and after 3-minute handgrip exercise (Figure 1).

The ECG-gated time difference (ΔTime) of the upstroke of the central and peripheral arterial waveforms was measured. The distance (D) between the aortic root and the external iliac artery was determined by a tape measure of the catheter length from the tip to the entry point at an arterial sheath minus the length of an arterial sheath (12 cm). PWV was defined as D divided by ΔTime (Figure 2) [24].

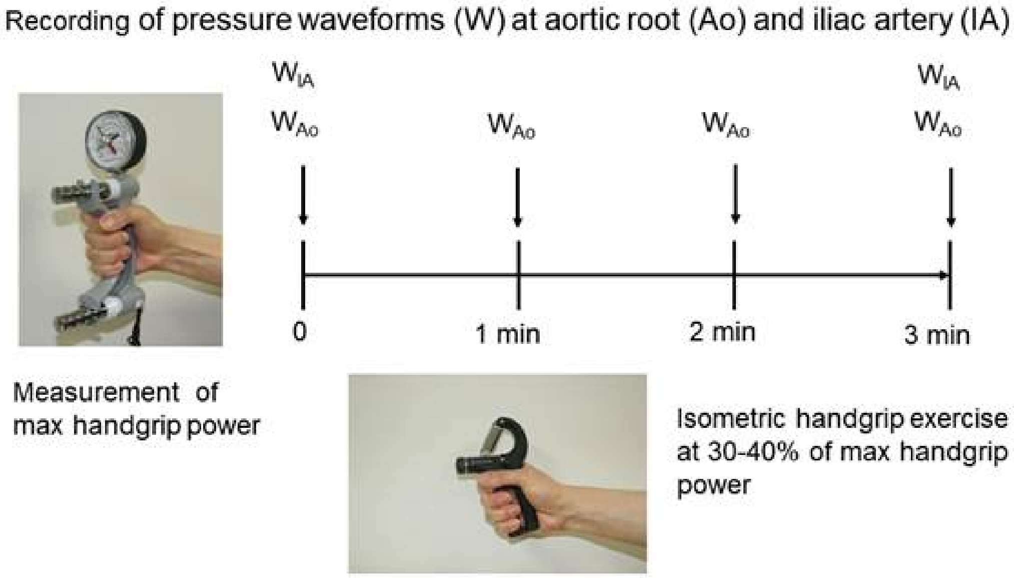


Figure 1. Study protocol. Baseline arterial pressure waveforms were traced at the aortic root (W_{Ao}) and external iliac artery(W_{IA}). A submaximal targetat 30~40% of maximal handgrip power was used for isometric handgrip exercise. Arterial waveforms were recorded at 1, 2 and 3 min in the aortic root and at 3 min in the external iliac artery after exercise.

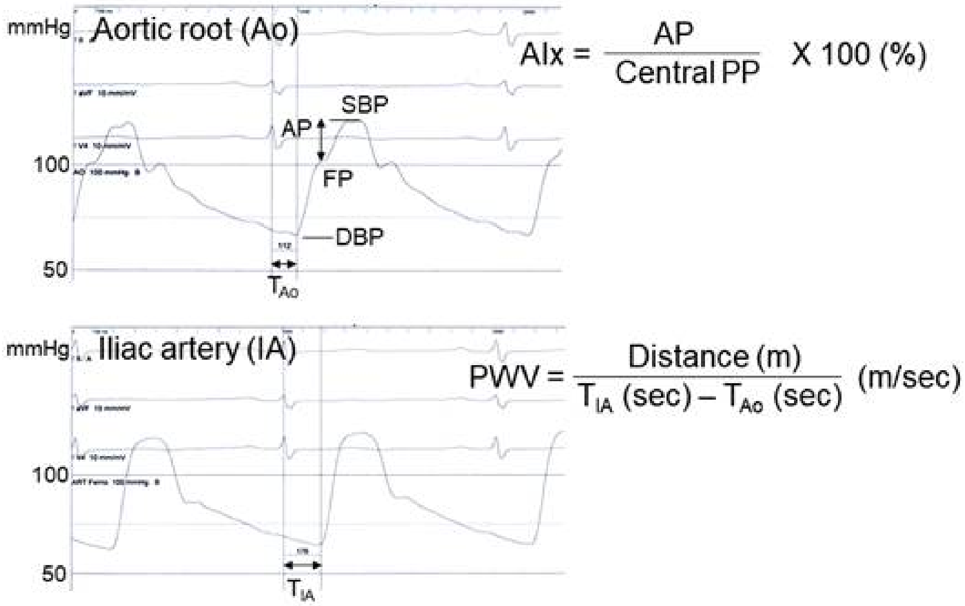


Figure 2. Measurements of augmentation index (AIx), and pulse wave velocity (PWV). Forward pressure (FP) was measured at a merging point of the forward and the reflected waves on the recorded aortic pressure waveform. AIx was defined as augmentation pressure (AP) divided by central pulse pressure (PP), and expressed as a percentage. PWV was calculated using the ECG-gated time difference of the upstroke of the arterial waveforms between the aortic root (T_{AO}) and the external iliac artery(T_{IA}), and the distance between them determined by a tape measure of the catheter length after removal of a coronary catheter. DBP; diastolic blood pressure, SBP; systolic blood pressure

Statistics

Data were expressed as mean ± standard deviation for continuous variables, and as number (percentage) for categorical variables. Changes of hemodynamic parameters after handgrip exercise were analyzed using paired t-test, or where appropriate, Wilcoxon signed rank test. The association between changes of PWV (ΔPWV) and AIx (ΔAIx) after handgrip exercise was evaluated using correlation analysis. Patients were divided into higher and lower ΔPWV or ΔAIx groups based on the each median value. Data between groups were compared using unpaired t-test for continuous variables, and chi-square test for categorical variables. The association between higher ΔPWV or ΔAIx and coronary revascularization was evaluated using C-statistics and multiple logistic regression analysis after adjusting for age, gender, height, body mass index (BMI), hypertension, diabetes mellitus (DM) and chronic kidney disease (CKD). CKD was defined as estimated glomerular filtration rate <60 mL/min/1.73m^{2}by Modification of Diet in Renal Disease equation.

All statistical analyses were performed with the statistical package SPSS version 23 (IBM Co, Armonk, NY, US). Clinical significance was defined as $P < 0.05$.

III. Results

Total 42 patients were enrolled. After excluding 4 patients without a definite inflection point of augmentation pressure on the central arterial waveform and 1 patient without a peripheral arterial waveform, final 37 patients were evaluated. The mean age of study patients was 63.3±9.4 years (range 41-82 years), 24 patients (65%) were older than 60 years, 26 patients (70%) had hypertension, and 27 patients (73%) had CAD. Percutaneous coronary intervention (PCI) was conducted in 25 patients (68%): one year ago in 20 patients and on the day of the study in 5 patients. One patient underwent both PCI and coronary artery bypass graft.

Heart rate, central systolic and diastolic BP, central pulse pressure, forward pressure, augmentation pressure, and AIx increased progressively from 1 minute after handgrip exercise, and reached the maximal level at 2 minutes. Peripheral systolic BP, diastolic BP, pulse pressure and PWV also increased after 3-minute handgrip exercise (Table 1). ΔPWV was significantly correlated with ΔAIx (r = 0.344, P = 0.037) (Figure 3). The median values of ΔPWV and ΔAIx were 0.4 m/sec and 3.3%, respectively.

Table 1. Changes of hemodynamic parameters after isometric handgrip exercise (N=37)

	Baseline	1 min	2 min	3 min
Heart rate (/min)	64.2±9.2	67.5±10.1*	68.9±10.2*†	70.6±12.9*†
Central systolic BP (mmHg)	118.4±20.6	135.1±21.4*	138.9±22.5*†	140.4±22.9*†
Central diastolic BP (mmHg)	63.4±10.3	71.0±10.6*	72.1±11.3*†	72.7±11.2*†
Central PP (mmHg)	55.0±17.6	64.2±18.2*	66.8±19.2*†	67.7±18.7*†
Forward pressure (mmHg)	108.7±19.4	121.4±20.7*	124.7±21.8*†	126.2±22.6*†
Augmentation pressure (mmHg)	9.7±6.6	13.7±8.3*	14.2±8.5*	14.2±8.7*
Augmentation index (%)	17.4±10.5	21.2±11.5*	21.5±11.5*	21.4±11.7*
Peripheral systolic BP (mmHg)	125.0±20.4			140.7±25.0*
Peripheral diastolic BP (mmHg)	62.2±10.1			65.1±10.3*
Peripheral PP (mmHg)	62.8±18.4			75.7±21.4*
Pulse wave velocity (m/sec)	9.99±1.84			10.81±2.33*

Values are mean ± standard deviation.

*$p<0.05$ vs. baseline, †$p<0.05$ vs. 1 min

BP; blood pressure, PP; pulse pressure

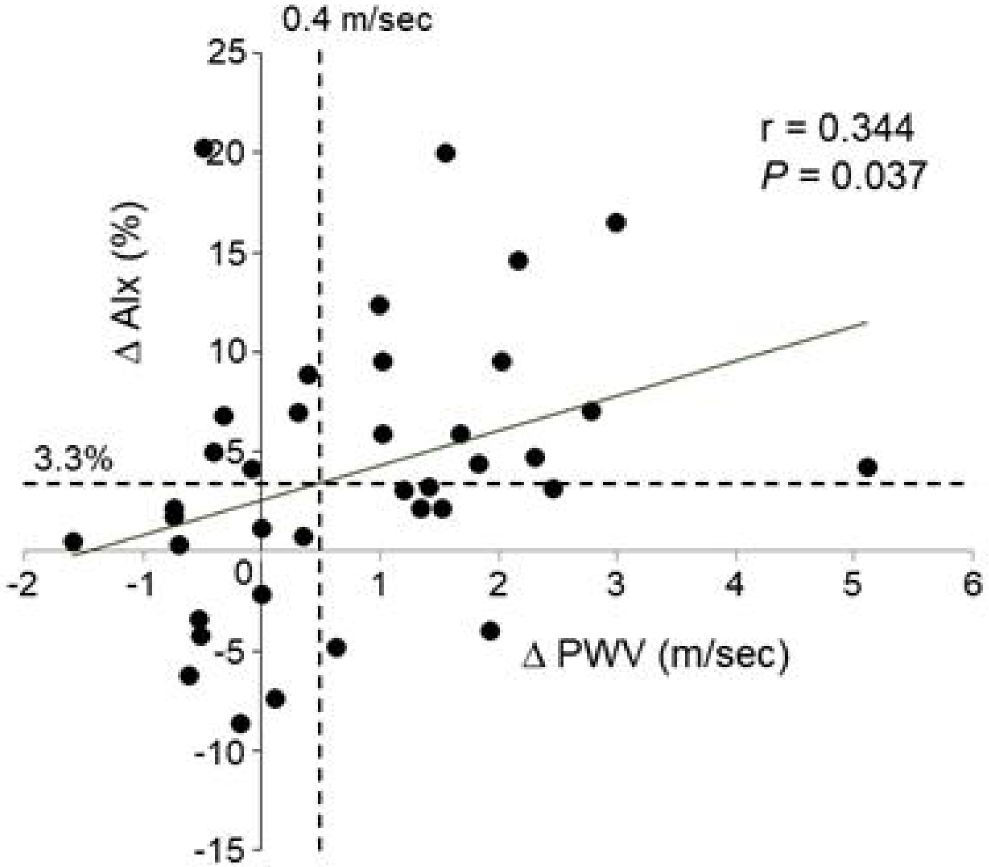


Figure 3. Correlation between changes of pulse wave velocity (ΔPWV) and augmentation index (ΔAIx) after isometric handgrip exercise. The median values of ΔPWV and ΔAIx were 0.4 m/sec and 3.3%, respectively.

Patients were divided into higher and lower ΔPWV (≥0.4 vs. <0.4 m/sec) groups. Age, gender, BMI, smoker, co-morbid condition such as hypertension, DM, CKD or prior myocardial infarction, and medications were not significantly different between higher and lower ΔPWV groups except hyperlipidemia. Patients with higher PWV had more 2- or 3-vessel CAD (69% vs. 27%, P = 0.034). PCI was more frequently performed in patients with higher PWV (84% vs. 50%, P = 0.038) (Table 2). Baseline hemodynamic parameters including PWV and AIx were not significantly different between two groups. After 3-minute handgrip exercise, PWV, Δcentral systolic BP, ΔAIx, and Δperipheral systolic BP were greater in patients with higher ΔPWV (Table 3)

Table 2. Comparison of baseline characteristics according to the changes of pulse wave velocity after isometric handgrip exercise

	All patients (N = 37)	ΔPWV ≥0.4 m/sec (N = 19)	ΔPWV <0.4 m/sec (N = 18)	P value
Age (years)	63.3±9.4	63.7±8.4	62.9±10.5	0.800
Male	23 (62)	14 (74)	9 (50)	0.184
Height (cm)	160.8±8.9	162.0±8.3	160.0±9.6	0.422
Weight (kg)	65.7±12.4	66.5±12.1	64.9±13.0	0.703
Body mass index (kg/m^2)	25.27±3.30	25.2±3.0	25.3±3.7	0.902
Smoker	9 (24)	5 (26)	4 (22)	0.459
Hypertension	26 (70)	14 (74)	12 (67)	0.728
Diabetes mellitus	8 (22)	5 (26)	3 (17)	0.693
Hyperlipidemia	33 (89)	19 (100)	14 (78)	0.046
Chronic kidney disease	19 (51)	9 (47)	10 (56)	0.746
Prior myocardial infarction	11 (30)	7 (37)	4 (22)	0.476
Coronary artery disease	27 (73)	16 (84)	11 (61)	0.151
CAG findings				0.051
1 vessel disease	13 (48)	5 (31)	8 (73)	0.034*
2 vessel disease	9 (33)	6 (38)	3 (27)	
3 vessel disease	5 (19)	5 (31)	0 (0)	
PCI	25 (68)	16 (84)	9 (50)	0.038
Medications				
Calcium channel blockers	16 (43)	10 (53)	6 (33)	0.325
RAS inhibitors	18 (49)	9 (47)	9 (50)	1.000
Beta-blockers	22 (60)	12 (63)	10 (56)	0.743
Nitrate	8 (22)	4 (21)	4 (22)	1.000
Statins	31 (84)	18 (95)	13 (72)	0.090

Values are mean ± standard deviation or number (%).

*1 vessel vs. 2- or 3-vessel disease

CAG; coronary angiography, PCI; percutaneous coronary intervention, PWV; pulse wave velocity, RAS; renin-angiotensin system

Table 3. Comparison of hemodynamic parameters according to the changes of pulse wave velocity after isometric handgrip exercise

	ΔPWV ≥ 0.4 m/sec (N = 19)	ΔPWV <0.4 m/sec (N = 18)	P value
Isometric handgrip exercise			
Handgrip power, maximal (kg)	36.2±13.2	31.0±11.1	0.207
Handgrip power at exercise (kg)	13.3±2.3	11.9±3.3	0.134
Handgrip power %	38.9±6.6	39.6±5.8	0.736
Hemodynamic parameters, baseline			
Heart rate (/min)	62.5±9.0	66.1±9.3	0.240
Central systolic BP (mmHg)	114.3±18.3	122.7±22.4	0.216
Central diastolic BP (mmHg)	60.6±7.1	66.4±12.2	0.082
Central pulse pressure (mmHg)	53.7±15.6	56.3±19.8	0.660
Forward pressure (mmHg)	104.6±17.3	113.1±21.1	0.186
Augmentation pressure (mmHg)	9.7±7.3	9.6±5.9	0.974
Augmentation index (%)	17.9±11.9	16.8±9.2	0.742
Peripheral systolic BP (mmHg)	122.3±19.4	127.8±21.5	0.414
Peripheral diastolic BP (mmHg)	60.3±7.7	64.2±12.0	0.244
Peripheral pulse pressure (mmHg)	62.0±17.3	63.6±19.9	0.787
PWV (m/sec)	10.15±2.07	9.83±1.61	0.610
Exercise 3 min			
Heart rate (/min)	68.7±13.9	72.7±11.9	0.355
Central systolic BP (mmHg)	140.7±20.9	140.1±25.4	0.935
Central diastolic BP (mmHg)	70.7±7.1	74.7±14.2	0.289
Central pulse pressure (mmHg)	70.0±18.0	65.3±19.5	0.455
Forward pressure (mmHg)	124.1±20.2	128.4±25.3	0.567
Augmentation pressure (mmHg)	16.6±9.3	11.7±7.3	0.081
Augmentation index (%)	24.3±12.4	18.3±10.3	0.121
Peripheral systolic BP (mmHg)	144.3±23.6	136.9±26.5	0.377
Peripheral diastolic BP (mmHg)	65.7±7.7	64.4±12.7	0.708
Peripheral pulse pressure (mmHg)	78.6±21.3	72.6±21.6	0.395
PWV (m/sec)	12.03±2.37	9.51±1.44	<0.001
Δ Central systolic BP (mmHg)	26.4±10.3	17.3±15.6	0.043
Δ Forward pressure (mmHg)	19.5±7.5	15.3±13.4	0.245
Δ Augmentation index (%)	6.3±6.3	1.5±6.8	0.033
Δ Peripheral systolic BP (mmHg)	22.1±11.8	9.1±8.7	0.001
Δ PWV (m/sec)	1.89±1.00	-0.32±0.49	<0.001

Values are mean ± standard deviation.

BP; blood pressure, PWV; pulse wave velocity

Patients were also divided into higher and lower ΔAIx (≥3.3 vs. <3.3%) groups. Age, BMI, smoker, co-morbid condition such as hypertension, DM, hyperlipidemia, CKD, prior myocardial infarction, or CAD, and medications except gender were not significantly different between higher and low ΔAIx groups (Table 4).

Table 4. Comparison of baseline characteristics according to the changes of augmentation index after isometric handgrip exercise

	All patients (N = 37)	ΔAIx ≥ 3.3% (N = 19)	ΔAIx < 3.3% (N = 18)	P value
Age (years)	63.3±9.4	61.7±10.4	65.0±8.1	0.288
Male	23 (62)	15 (79)	8 (44)	0.045
Height (cm)	160.8±8.9	162.6±8.4	158.9±9.3	0.213
Weight (kg)	65.7±12.4	69.2±13.1	62.1±10.8	0.081
Body mass index (kg/m^2)	25.27±3.30	25.98±3.17	24.51±3.36	0.180
Smoker	9 (24)	5 (26)	4 (22)	0.124
Hypertension	26 (70)	13 (68)	13 (72)	1.000
Diabetes mellitus	8 (22)	3 (16)	5 (28)	0.447
Hyperlipidemia	33 (89)	18 (95)	15 (83)	0.340
Chronic kidney disease	19 (51)	8 (42)	11 (61)	0.330
Prior myocardial infarction	11 (30)	5 (26)	6 (33)	0.728
Coronary artery disease	27 (73)	15 (79)	12 (67)	0.476
CAG findings				0.620
1 vessel disease	13 (48)	6 (40)	7 (58)	0.313*
2 vessel disease	9 (33)	6 (40)	3 (25)	
3 vessel disease	5 (19)	3 (20)	2 (17)	
PCI	25 (68)	13 (68)	12 (67)	1.000
Medications				
Calcium channel blockers	16 (43)	10 (53)	6 (33)	0.325
RAS inhibitors	18 (49)	9 (47)	9 (50)	1.000
Beta-blockers	22 (60)	13 (68)	9 (50)	0.325
Nitrate	8 (22)	4 (21)	4 (22)	1.000
Statins	31 (84)	18 (95)	13 (72)	0.090

Values are mean ± standard deviation or number (%).

*1 vessel vs. 2- or 3-vessel disease

AIx; augmentation index, CAG; coronary angiography, PCI; percutaneous coronary intervention, RAS; renin-angiotensin system

Patients with 2- or 3-vessel CAD were not significantly different (60% vs. 42%, P = 0.313), and PCI was similarly performed in both groups (68% vs. 67%, P = 1.000). Baseline central systolic BP and pulse pressure, augmentation pressure, AIx, peripheral systolic BP, and PWV were lower in higher ΔAIx group. However, after 3-minute handgrip exercise, these hemodynamic parameters became not significantly different between both groups (Table 5).

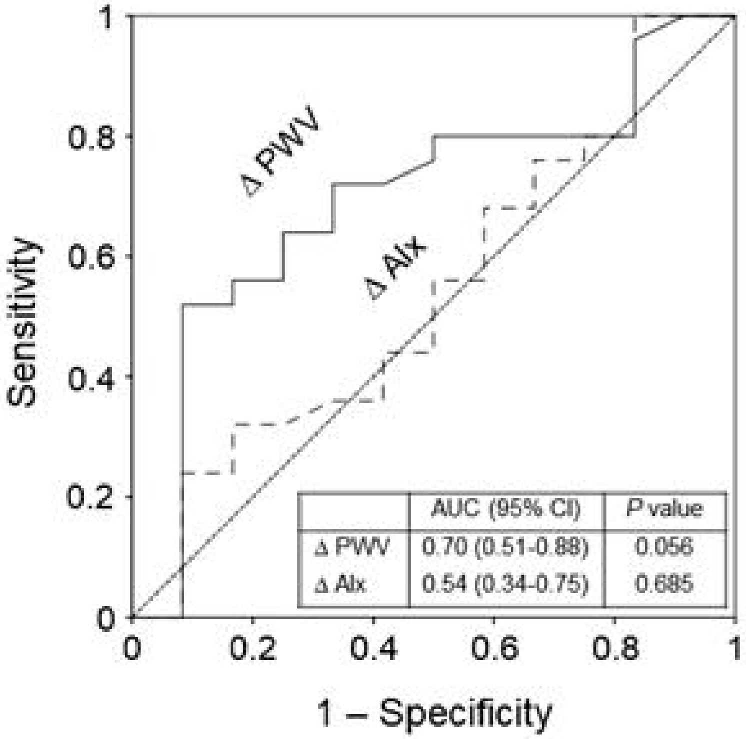
Table 5. Comparison of hemodynamic parameters according to the changes of augmentation index after isometric handgrip exercise

	ΔAIx ≥ 3.3% (N = 19)	ΔAIx < 3.3% (N = 18)	P value
Isometric handgrip exercise			
Handgrip power, maximal (kg)	37.0±14.4	30.1±8.7	0.089
Handgrip power at exercise (kg)	13.5±2.8	11.7±2.7	0.060
Handgrip power %	38.7±6.7	39.8±5.6	0.566
Hemodynamic parameters, baseline			
Heart rate (/min)	65.7±9.9	62.7±8.4	0.334
Central systolic BP (mmHg)	109.9±16.2	127.3±21.3	0.008
Central diastolic BP (mmHg)	62.0±8.4	65.0±12.0	0.373
Central pulse pressure (mmHg)	48.0±14.7	62.3±17.7	0.011
Forward pressure (mmHg)	103.7±15.8	114.1±21.9	0.105
Augmentation pressure (mmHg)	6.2±4.9	13.3±6.2	<0.001
Augmentation index (%)	13.3±9.6	21.7±10.0	0.013
Peripheral systolic BP (mmHg)	118.5±19.3	131.8±19.8	0.045
Peripheral diastolic BP (mmHg)	61.3±8.3	63.2±11.9	0.562
Peripheral pulse pressure (mmHg)	57.2±17.8	68.6±17.6	0.058
Pulse wave velocity (m/sec)	9.30±1.72	10.72±1.72	0.017
Exercise 3 min			
Heart rate (/min)	70.5±13.4	70.8±12.9	0.948
Central systolic BP (mmHg)	135.0±19.7	146.1±25.1	0.140
Central diastolic BP (mmHg)	71.5±7.2	73.9±14.4	0.527
Central pulse pressure (mmHg)	63.5±18.7	72.2±18.0	0.157
Forward pressure (mmHg)	120.9±17.0	131.7±26.7	0.154
Augmentation pressure (mmHg)	14.1±9.1	14.4±8.5	0.908
Augmentation index (%)	22.2±11.6	20.4±12.0	0.648
Peripheral systolic BP (mmHg)	136.2±22.6	145.6±27.1	0.259
Peripheral diastolic BP (mmHg)	64.5±7.6	65.6±12.8	0.754
Peripheral pulse pressure (mmHg)	71.6±21.1	79.9±21.4	0.242
Pulse wave velocity (m/sec)	10.68±2.59	10.94±2.10	0.747
Δ Central systolic BP (mmHg)	25.1±11.7	18.8±15.3	0.169
Δ Forward pressure (mmHg)	17.2±7.8	17.7±13.6	0.900
Δ Augmentation index (%)	9.0±5.3	-1.3±3.8	<0.001
Δ Peripheral systolic BP (mmHg)	17.7±11.2	13.7±13.1	0.330
Δ Pulse wave velocity (m/sec)	1.38±1.39	0.21±1.08	0.008

Values are mean ± standard.

AIx; augmentation index, BP; blood pressure

C-statistics showed the area under curve (AUC) of ΔPWV in association with PCI was 0.70 (95% confidence interval [CI] 0.51-0.88; P = 0.056). In contrast, it was 0.54 (95% CI 0.34-0.75; P = 0.685) in case of ΔAIx (Figure 4). In multiple logistic regression analysis after adjustment, ΔPWV was significantly associated with PCI (odds ratio [OR] 7.78; 95% CI 1.26-48.02; P = 0.027), but ΔAIx was not (OR 2.81; 95% CI 0.37-21.30; P = 0.318).



	AUC (95% CI)	*P* value
Δ PWV	0.70 (0.51-0.88)	0.056
Δ AIx	0.54 (0.34-0.75)	0.685

Figure 4. Area under curve (AUC) with 95% confidence interval (CI) of Δ pulse wave velocity (PWV) or Δaugmentation index (AIx) in association with percutaneous coronary intervention by C-statistics

IV. Discussion

The main result of this study is that, although a significant correlation was observed between ΔPWV and ΔAIx after isometric handgrip exercise, only increased PWV was associated with the lesion severity of CAD and the necessity for coronary revascularization.

Atherosclerosis is a generalized process of the arterial system including not only coronary arteries but also larger arteries. The atherosclerotic change of the aorta makes the arterial system stiffer, and the stiff aorta is associated with myocardial ischemia and incident CAD [7-9]. Therefore, indexes of arterial stiffness are usually increased in patients with CAD. However, these indexes are often increased in elderly without CAD because systolic BP increases with aging, there is a close association between systolic BP and PWV, and both vascular aging and hypertension are the powerful factors determining arterial stiffness [1]. As a result, the difference of indexes of arterial stiffness between patients with and without CAD may be not evident in elderly. The previous meta-analysis showed that aortic PWV was a predictor of future cardiovascular events such as CAD or stroke even in elderly, but its relation to cardiovascular events was weaker in older than younger patients, and the hazard ratio was decreased with age (1.89, 1.77, 1.36, and 1.23 for age ≤50, 51-60, 61-70, and >70 years, respectively) [9]. The usefulness of AIx as a marker for CAD in older patients is even more unclear. Because AIx strongly correlates with age and it is also influenced by heart rate, body length or the pattern of ventricular ejection [3], AIx may not be an accurate index for arterial stiffness. The comparison of aortic PWV with AIx as a surrogate for the extent and severity of CAD was possible in one study that measured both indexes in the same patients at the time of coronary angiography. It showed the significant association of the extent and severity of CAD with PWV, but not with AIx [12].

Isometric handgrip exercise is a non-invasive and easily applicable maneuver to increase heart rate, BP and left ventricular afterload [21-23]. In this study, central systolic BP, forward and augmentation pressures, AIx, peripheral BP and PWV were increased after handgrip exercise. Although ΔPWV and ΔAIx correlated each other, the pattern of ΔPWV and ΔAIx after handgrip exercise was different. Baseline PWV was not different between higher and lower ΔPWV groups, but after 3-minute handgrip exercise, Δcentral systolic BP, Δperipheral systolic BP and PWV were greater in higher ΔPWV group. However, baseline AIx was smaller in higher ΔAIx group, and AIx after 3-minute handgrip exercise became similar between higher and lower ΔAIx groups because of more increase of augmentation pressure in lower ΔAIx group. All of these findings suggest that ΔAIx may be larger in patients with lower baseline AIx regardless of arterial stiffness and reach plateau after handgrip exercise. Therefore, ΔAIx after handgrip exercise may not be as a good index for arterial stiffness as ΔPWV.

The mean age of patients of this study was 63.3 years, 65% were >60 years and 70% of them had hypertension. These findings may be usually seen in patients with CAD. In this clinical setting, simple PWV value may not differentiate patients with CAD and the lesion severity of CAD. In the previous study, we showed that PWV value at rest was not different between patients with and without CAD, but after 3-minute handgrip exercise, PWV was significantly increased only in patients with CAD [24]. In this study, higher ΔPWV group had more 2- or 3-vessel CAD and underwent more PCI than lower ΔPWV group. On the other hand, the lesion severity of CAD and the necessity for PCI were not different between higher and lower ΔAIx groups. In addition, C-statistics and multiple logistic regression analysis showed that ΔPWV was associated with PCI but not ΔAIx. These findings suggest that ΔPWV may be used as an index for differentiating the lesion severity of CAD and the necessity for coronary revascularization even in elderly patients with hypertension, but ΔAIx may not.

This study has several limitations. First, a fluid-filled catheter system, instead of a high-fidelity micromanometer, was used to record the pressure waveforms. A definite merging point of the forward and the reflected waves on the recorded pressure waveform was not identified in aortic pressure waveforms of 4 patients (9.5%). Second, over half of patients were taking medications with a vasodilation property, which may influence the change of BP, PWV, and AIx after handgrip exercise. However such medications were equally taken in both higher and lower ΔPWV or ΔAIx groups, and baseline central and peripheral BP were not different between groups. Third, PCI performed not only on the day of the study but also one year ago was counted as having coronary revascularization. Including only prospectively conducted coronary revascularization would have increased the feasibility of the study. Fourth, the number of patients might not be enough to accurately evaluate the changes of PWV and AIx after handgrip exercise. Nevertheless, the association between higher ΔPWV and the lesion severity of CAD or the necessity for PCI was demonstrated.

This was an invasive study that measured hemodynamic parameters during CAG. To be widely use, the applicability of a non-invasive method measuring ΔPWV or ΔAIx after handgrip exercise using an applanation tonometry needs to be validated in a future study.

V. Conclusions

Both PWV and AIx increased after isometric handgrip exercise, and ΔPWV was significantly correlated with ΔAIx. However, increased PWV was associated with the lesion severity of coronary artery stenosis and the necessity for coronary revascularization, but increased AIx was not.

VI. References

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VII. ABSTRACT IN KOREAN

등척성 악력 운동 후 맥파 속도 및 증폭 지수의 증가 정도와 관동맥중재술 시행 여부의 관련성

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배경과 목적; 동맥경직도는 심근허혈과 관동맥질환의 발생과 관련이 있으며 관동맥질환이 있는 환자의 동맥경직도 지표는 일반적으로 증가되어 있다. 그러나 노화가 진행됨에 따라서 수축기 혈압이 증가하며 혈관노화와 수축기 혈압은 동맥경직도를 결정하는 강력한 인자이기 때문에 관동맥질환이 없는 노령층에서도 동맥경직도 지표는 증가할 수 있다. 관동맥질환이 있는 환자의 동맥경직도는 수축기 혈압과 심실 후부하를 증가시키는 등척성 악력 운동 후에 더 분명해질 수 있다. 이 연구에서 등척성 악력 운동 후 동맥경직도 지표의 변화와 관동맥병변의 중증도 및 관동맥중재술 시행 필요성의 연관성에 대하여 조사하였다.

방법; 대퇴동맥을 이용한 관동맥조영술 시행 예정 환자들을 대상으로 연구하였다. 관동맥 카테터를 이용하여 대동맥근과 외장골동맥에서 동맥파형을 기록하였다. 이후 악력 운동을 3분간 시행한 후 같은 위치에서 동맥파형을 기록하였다. 악력 운동 전, 후 동맥파형에서 증폭 지수(augmentation index: AIx)와 동맥 맥파 속도(pulse wave velocity: PWV)를 측정하였다. PWV는

대동맥근과 외장골동맥 사이의 거리와 심전도 기준 각각의 동맥파형 상승의 시간차를 이용하여 계산하였다.

결과; 37명의 환자를 평가하였다. 악력 운동 후 PWV 및 AIx는 모두 증가하였다. ΔPWV와 ΔAIx 사이에 유의한 상관관계가 있었다(r=0.344, *P*=0.037). ΔPWV와 ΔAIx의 중앙값인 0.4 m/sec와 3.3%를 기준으로 높은 집단과 낮은 집단으로 분류하였을 때 높은 ΔPWV 환자군에서 두 혈관 또는 세 혈관 관동맥질환의 빈도가 높았으며(69% vs. 27%, *P*=0.034) 경피적 관동맥 중재술(percutaneous coronary intervention: PCI)의 시행 빈도도 높았다(84% vs. 50%, *P*=0.038). 그러나 높은 ΔAIx는 관동맥질환의 중증도나 PCI의 시행 여부와 관련이 없었다. C-statistics로 평가한 ΔPWV와 PCI의 연관성에 대한 area under curve (AUC) 값은 0.70(95% 신뢰구간 0.51-0.88; *P*=0.056)이었다. 다중 로지스틱 회귀 분석에서 ΔPWV은 PCI와 유의한 관련이 있었다(odds ratio 7.78; 95% 신뢰구간 1.26-48.02; *P*=0.027).

결론; 등척성 악력 운동 후 PWV의 증가는 관동맥질환의 중증도와 관동맥중재술의 필요성과 관련이 있었다.

Keywords: 동맥경직도, 맥파속도, 파형분석, 등척성 운동, 경피적관동맥중재술