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The Relationship between Brachial-Ankle Pulse Wave Velocity and Depressive Symptoms among Patients with Coronary Artery Disease

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Background: Noninvasive brachial-ankle pulse wave velocity (baPWV) is an index for arterial stiffness in coronary artery disease (CAD). Depression has been connected to increased adverse cardiac events and mortality among patients with CAD. The aim of this study was to investigate the relationship between arterial stiffness and depressive symptoms among patients with CAD.

Methods: Eighty-six patients with CAD were recruited. Demographic characteristics and Beck Depressive Inventory II scores were obtained from the study participants, and resting baPWV was measured by using a noninvasive device. Thereafter, the participants were divided into mild and severe arteriosclerosis groups according to baPWV values.

Results: After adjusting the age, use of β-blockers, and left ventricular ejection fraction, there were higher somatic symptoms of depression in the severe arteriosclerosis group than those in the mild arteriosclerosis group, in particular concentration difficulty, changes in appetite, and fatigue. A multiple regression analysis indicated that baPWV was related to somatic symptoms of depression after adjusting the covariates of CAD risk factors. However, this association was not found between baPWV and cognitive symptoms of depression, and the total score of depression.

Conclusions: This study supports the proposition that somatic symptom of depression was related to arterial stiffness among patients with CAD.

Key Words: Arterial stiffness • CAD • Depression

INTRODUCTION

Arterial stiffness is a pathological process of coronary artery disease (CAD), and progressive arterial stiffness can cause damage in coronary vessel walls, increasing the risk of developing atherosclerotic cardiovascular disease, peripheral vascular disease, and stroke.[1-3] Brachial-ankle pulse wave velocity (baPWV) and ankle-brachial index (ABI) are two simple and noninvasive diagnostic tools for measuring arterial stiffness in cardiovascular disease, atherosclerosis, and peripheral arterial disease.[1,2] Previous studies found that baPWV was higher in patients with CAD than in those without CAD or healthy controls.[2,4,5] baPWV was related to the severity of CAD[4] and was a useful predictor of cardiovascular events among patients with acute coronary syndrome and CAD.[1,2]

Previous studies found that depression can predict

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elevated central augmentation index, which will increase the development and progression of atherosclerosis, other cardiovascular diseases, or heart failure.[6-8] For example, Satoh et al. found that persistent depression was a significant risk factor for the development of arteriosclerosis.[9] In prognostic studies, CAD comorbid with depression was associated with an increased risk of adverse cardiac events or mortality.[10-12] Carney and colleagues found that 15-20% of patients with myocardial infarction had depressive symptoms.[13,14] Durmaz et al.[15] found that depressive mood was related to coronary slow flow. Smolderen et al.[16] indicated that 26.6% of patients with CAD had somatic symptoms of depression, and 25.1% of 2,347 patients with CAD had cognitive symptoms of depression. Moreover, somatic symptoms of depression also related to re-hospitalization and mortality in four years of follow-up.[16] In addition, prognostic studies also found that somatic symptoms of depression were better predictors of cardiac events than cognitive symptoms of depression among patients with CAD or acute myocardial infraction.[17,18] ABI was related to poor health status and caused the symptoms of depressionin the long-term follow-up.[19]

Therefore, depression screening and defining the high-risk group in order to prevent adverse cardiac outcomes in CAD prognosis are important. However, the relationship between baPWV and depression in CAD prognostic studies is still unknown. The purpose of the present study was to investigate the relationship between depression, somatic symptoms of depression, cognitive symptoms of depression, and arterial stiffness among patients with CAD.

METHODS

Participants

Patients with CAD were recruited from the outpatient services section of the division of cardiology from Kaohsiung Medical University Hospital and Kaohsiung Municipal Ta-Tung Hospital. The inclusion criterion were as follows: 1) documented CAD with blockage greater than 50% in the left main artery or greater than 70% in the left circumflex, left anterior descending, and right coronary arteries as identified by using coronary angiography; or 2) a history of coronary intervention such as percutaneous transluminal coronary angioplasty, stent or laser, or a history of coronary artery bypass surgery. Participants with class III and IV congestive heart failure, arrhythmia, unstable angina, atrial fibrillation, other severe physical illness or mental disorder, or a pacemaker were excluded. Institutional review board approval was obtained from the ethics committee of Kaohsiung Medical University Hospital, and informed consent was obtained from each participant before the start of this study.

Materials and measurements

The demographic characteristics, smoking frequency, exercise frequency and duration, and Beck Depressive Inventory II (BDI-II) responses were obtained for all patients. Disease information, medications, and laboratory data were collected from medical records, and baPWV was measured by using a noninvasive vascular screening device.

Background information

Background information included age, gender (0 = female and 1 male), number of vessel stenosis (range from 0 to 3, refers to coronary artery stenosis in the left circumflex, left anterior descending, and right coronary arteries), number of comorbidities (range from 0 to 18, refers to other physical illnesses except CAD), and left ventricular ejection fraction.

Beck Depressive Inventory II

The BDI-II is a multiple-choice self-report inventory used to assess patient depressive symptoms in the two-week period before the study.[20] BDI-II included 21 depressive symptoms with a 4-point scale for each item. The depression total score ranged from 0 to 63, with two subscales, namely cognitive symptoms of depression (e.g., “I feel utterly worthless” or “I criticize myself for all of my faults”) and somatic symptoms of depression (e.g., “I sleep most of the day” or “I am too tired or fatigued to do most of the things I used to do”).[20]

The noninvasive device for measuring baPWV

The VP-1000 (Colin Co, Ltd., Komaki, Japan) is a noninvasive vascular screening device used to obtained baPWV values, consistent with the measuring procedure followed by Tomiyama et al.[3] Participants were exam-

ined in the supine position, and electrocardiography electrodes were placed on the left edge of the sternum, with cuffs wrapped on both the brachia and ankles. The baPWV was calculated using the following equation: baPWV (cm/s) = Lb – La/ΔT.[3] This study used an interquartile range to define the mild (lower 75%) and severe arteriosclerosis groups (upper 25%) among the CAD participants in this study. The cutoff points lower than 75% and higher than 25% of baPWV were 1308.75 and 1585.75 cm/s, respectively.

Laboratory data

Data on plasma total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglyceride, fasting sugar, and glycated hemoglobin (HbA1c) levels were collected from medical records. All blood samples were obtained in a fasted state in the morning.

Statistics analysis

Group differences in demographic characteristics and research variables were examined by using the two-sample *t* test and chi-square test (χ^2). Fisher's exact test (P) was used to calculate 2 × 2 contingency tables to examine the gender difference between mild and severe arteriosclerosis groups. Analysis of covariance (ANCOVA) was used to examine the group differences after adjusting the covariates. The multiple regression analysis was used to examine the associations between baPWV and depression symptoms. All analyses were performed by using the SPSS predictive analytics software version 21.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

Participants' characteristics

A total of 155 patients with CAD were referred by cardiologists, and baPWV measurement was performed in 86 of those patients. Their mean age was 61.4 ± 7 years, and 93.02% of the study participatns were men. We divided the participants into a mild arteriosclerosis group (lower 75% of baPWV; n = 21) and a severe arteriosclerosis group (upper 25% of baPWV; n = 21) according to baPWV values. In the mild arteriosclerosis group, the mean ± SD age of the participants was 58.48 ± 7.40 years, and 19 were male and 2 were female. In the severe arteriosclerosis group, the mean ± SD age of the participants was 63.19 ± 5.74 years, wherein 20 were male and 1 female (Table 1). A significant difference in age was observed between the two groups (t = -2.31, p < 0.05). However, no group differences in gender, height, body mass index, number of vessel stenosis, number of comorbidities, smoking frequency, exercise frequency, and duration (p = 0.36, p > 0.05; t = 0.44, p > 0.05; t = 0.76, p > 0.05; t = 0.57, p > 0.05; t = -1.67, p > 0.05; χ^2 = 1.81, p > 0.05; χ^2 = 3.71, p > 0.05; χ^2 = 2.83, p > 0.05, respectively). There was a greater number of participants who took β-blockers and higher left ventricular ejection fraction in the mild arteriosclerosis group than in the severe arteriosclerosis group (χ^2= 4.94, p < 0.05; and t = 2.22, p < 0.05, respectively) (Table 1).

Group differences in somatic symptoms of depression

There were more somatic symptoms of depression in the severe arteriosclerosis group than in the mild arteriosclerosis group after adjusting for age, use of beta blocker, and left ventricular ejection fraction, mainly concentration difficulty, changes in appetite, and fatigue (Table 2).

baPWV was related to somatic symptoms of depression

Multiple regression analysis found a significant association between baPWV and somatic symptoms of depression after adjusting for age, gender, numbers of vessel stenosis, number of comorbidities, and left ventricular ejection fraction (β = 0.004, p < 0.05). However, no significant association was found between baPWV and cognitive symptoms of depression (β = 0.003, p > 0.05) or depression total score (β = 0.008, p > 0.05) (Table 3).

DISCUSSION

This study found higher depression total scores and somatic symptoms of depression in the severe arteriosclerosis group than in the mild arteriosclerosis group. The baPWV was significantly related to somatic symptoms of depression, but not to cognitive symptoms of depression or depression total score after adjusting for covariates.

Table 1. The demographic characteristics and research variables between the mild and the severe arteriosclerosis groups among patients with CAD

Variables	Mild arteriosclerosis group (n = 21)			Severe arteriosclerosis group (n = 21)			t/P/χ^2	p value
	Mean	SD	Range	Mean	SD	Range		
baPWV (cm/s)	1212.50	82.09	997.50-1300.50	1826.31	154.27	1591-2107		
Age	58.48	7.40	46-74	63.19	5.74	53-74	t = -2.31*	0.03
Gender							p = 0.36	1.00
Male	19			20				
Female	2			1				
Height (cm)	167.55	7.23	155-181	166.76	3.87	158-174	t = 0.44	0.66
Body mass index	26.64	3.77		25.82	3.21		t = 0.76	0.45
Numbers of vessel stenosis	2.20	0.94	1-3	2.00	0.96	1-3	t = 0.57	0.58
Numbers of comorbidities	3.29	1.59	1-5	4.24	2.07	2-10	t = -1.67	0.10
Left ventricular ejection fraction	67.61	11.98	42-84.4	51.45	22.45	20-80	t = 2.22*	0.04
Smoking (n)							χ^2 = 1.81	0.61
No smoking	10			6				
Give up smoking	8			11				
Sometimes	0			0				
Less than half package each day	1			2				
1-2 package each day	2			2				
Exercise frequency (n)							χ^2 = 3.71	0.30
Few	2			3				
1-2 times/week	5			1				
3-6 times/week	5			4				
Everyday	9			13				
Exercise duration (n)							χ^2 = 2.83	0.42
None	2			3				
Less than 30 min/time	4			5				
30-60 min/time	9			4				
More than 60 min/time	6			9				
Medication (n)								
Antiplatelet	17			16			χ^2 = 0.00	1.00
α-blocker	2			5			χ^2 = 1.79	0.23
β-blocker	16			9			χ^2 = 4.94*	0.04
Anti-lipid	12			12			χ^2 = 0.05	1.00
Angiotensin converting enzyme inhibitors	15			14			χ^2 = 0.01	1.00
Nitroglycerin	5			7			χ^2 = 0.67	0.50
Diuretic	2			6			χ^2 = 2.84	0.12
Calcium channel blocker	0			1			χ^2 = 1.09	0.49
Laboratory data								
Total cholesterol	160.43	23.13	125.00-212.00	171.38	27.00	136.00-224.00	t = -1.14	0.27
Low density lipoprotein	88.61	20.14	57.60-122.40	92.51	26.62	33.00-136.80	t = -0.44	0.67
High density lipoprotein	45.62	7.10	37.80-64.70	47.69	16.71	26.60-72.80	t = -0.38	0.71
Triglyceride	129.07	68.71	48.00-262.00	133.79	74.70	51.00-303.00	t = -0.17	0.86
Fasting sugar	117.64	21.97	91.00-150.00	124.58	51.43	85.00-265.00	t = -0.46	0.65
HbA1c	6.31	0.62	5.80-7.50	6.55	0.80	5.70-8.00	t = -0.72	0.48

* $p < 0.05$; # $p < 0.001$.

baPWV, brachial-ankle pulse wave velocity; HbA1c, glycated hemoglobin; P, Fisher's exact test; t, two-sample t test; χ^2, chi-square test.

Table 2. The differences between the mild and the severe arteriosclerosis groups in depressive symptoms

Variables	Mild arteriosclerosis group (n = 21)			Severe arteriosclerosis group (n = 21)			F [a]	p value
BDI-II	Mean	SD	Range	Mean	SD	Range		
Depression total score	6.69	10.18	0-31	13.75	13.05	0-39	4.72#	0.04
Cognitive symptoms of depression	4.46	8.09	0-23	8.83	9.77	0-28	3.26	0.09
1. Sadness	0.23	0.60		0.08	0.29		0.01	0.94
2. Pessimism	0.31	0.75		1.25	1.55		5.30#	0.03
3. Past failure	0.31	0.86		0.83	0.94		3.88†	0.06
4. Loss of pleasure	0.46	0.97		0.58	1.00		0.45	0.51
5. Guilty feelings	0.15	0.56		0.25	0.62		0.44	0.51
6. Punishment feelings	0.38	0.87		0.83	1.34		1.08	0.31
7. Self-dislike	0.15	0.38		0.50	0.67		3.82†	0.07
8. Self-criticalness	0.23	0.60		0.50	0.80		2.25	0.15
9. Suicidal thoughts or wishes	0.08	0.27		0.08	0.29		0.61	0.44
10. Crying	0.08	0.28		0.42	0.90		2.50	0.13
11. Agitation	0.23	0.60		0.33	0.89		1.77	0.20
12. Loss of interest	0.54	1.13		0.75	1.22		0.29	0.60
13. Indecisiveness	0.38	0.96		0.33	0.65		0.37	0.55
14. Worthlessness	0.15	0.38		0.92	1.08		8.73*	0.008
17. Irritability	0.46	0.88		0.17	0.39		0.82	0.38
21. Loss of interest in sex	0.31	0.63		1.00	1.21		3.44	0.08
Somatic symptoms of depression	2.23	2.49	0-8	4.92	4.12	0-11	7.09#	0.02
15. Loss of energy	0.77	0.83		1.00	1.04		3.17	0.09
16. Changes in sleeping pattern	0.54	0.66		1.00	1.13		2.59	0.12
18. Changes in appetite	0.08	0.28		0.67	1.07		3.75†	0.07
19. Concentration difficulty	0.15	0.38		1.00	1.13		6.53#	0.02
20. Fatigue	0.69	0.95		1.25	1.06		3.83†	0.07

* p < 0.01; # p < 0.05; † p < 0.07. [a] ANCOVA analysis for adjusting the age, taking the beta blocker, and left ventricular ejection fraction. BDI-II, Beck Depressive Inventory II; SD, standard deviation.

Table 3. The multiple linear regression for relationship between baPWV and depression (n = 86)

	Somatic symptoms of depression			Cognitive symptoms of depression			Depression total score		
R^2	0.40			0.25			0.31		
	β	Standard error	p value	β	Standard error	p value	β	Standard error	p value
(Constant)	6.813	4.256	0.12	24.674	12.426	0.05	31.487	15.729	0.05
Age	-0.204†	0.051	< 0.001	-0.438	0.148#	0.005	-0.642#	0.187	0.001
Gender	1.119	1.273	0.38	4.513	3.716	0.23	5.632	4.703	0.24
Numbers of vessel stenosis	-0.120	0.414	0.77	-1.097	1.207	0.37	-1.217	1.528	0.43
Left ventricular ejection fraction	-0.007	0.023	0.76	-0.056	0.066	0.40	-0.063	0.084	0.45
Number of comorbidities	0.688#	0.201	0.001	1.402	0.586*	0.02	2.090#	0.742	0.007
baPWV	0.004*	0.002	0.01	0.003	0.005	0.49	0.008	0.006	0.22

* p < 0.05; # p < 0.01; † p < 0.001.

Some studies have found both cognitive and somatic symptoms as predictors of adverse cardiac outcomes,[21] whereas others have found somatic but not cognitive symptom as a predictor of adverse cardiac outcomes.[17,18] Previous studies observed that cerebrovascular disease occurred 2 to 3 years prior to development

of depression. Therefore, vascular depression hypothesis was addressed in this study that depression was one of outcomes of CAD.[22,23] To our knowledge, this is the first study to suggest that more severe arterial stiffness (baPWV) was related to somatic symptoms of depression. Atherosclerosis is a progressive process in CAD, and patients with CAD may cause work and social function impairments, and comorbidity of anxiety and depression problems along with the increasing disease severity.[24] Therefore, depression may be involved in CAD prognosis and cause adverse cardiac events and premature mortality.

In addition, this study found a cut-off point for baPWV is 1826 cm/s (1.826 m/s) for severe arteriosclerosis group among patients with CAD. This cut-off point was very similar to 1.83 m/s for arteriosclerotic ischemic stroke, and previous study also found baPWV was significantly higher in large artery atherosclerosis and small artery disease than in the healthy control group.[25] Therefore, 1.8 m/s might be an important cut-off point for pathologic or clinical condition, and more studies and increased sample size are needed to examine the reliability and validity in the future study.

The present study has several limitations. First, CAD was diagnosed several days to several years prior to baPWV measurement in most patients. Although baPWV and depression were measured at the same time, several factors may be involved in this correlation during the prognosis process of CAD. Second, all somatic symptoms of depression were worse in the severe arteriosclerosis group than in the mild arteriosclerosis group. However, the small sample size may have limited the statistical power. Therefore, future large-scale studies are necessary to investigate the relationship between baPWV and depressive symptoms.

In conclusion, baPWV is a simple and noninvasive predictor of CAD, and depressive symptoms were risk factors in CAD prognosis and related to adverse cardiac events and mortality. Furthermore, reduced depressive symptoms may be an important psychological intervention in cardiac rehabilitation.

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CONFLICTS OF INTEREST

All the authors declare no conflicts of interest.

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