Bidirectional association between depressive symptoms and carotid atherosclerosis in community-based older adults in China

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ABSTRACT

We explored the bidirectional association between depressive symptoms and measures of carotid atherosclerosis. This study included 1155 participants aged 55 years and older. Depressive symptoms was assessed by 30-item Geriatric Depression Scale (GDS-30) score. Common carotid artery intima-media thickness (CCA-IMT), carotid plaques and carotid stenosis were measured at both common carotid arteries using an edge detection system. In part 1, we explored the risk of CCA-IMT on depressive symptoms. We identified a significantly increased risk of depressive symptoms with the severity of carotid atherosclerosis. ORs (95%CI) of CCA-IMT thickening, carotid plaque and carotid stenosis for depressive symptoms were 1.48(0.72–3.03), 2(1.03–3.85) and 5.29(2.16–12.97) comparing with normal CCA-IMT in adjusting all potential risk factors models. When using carotid atherosclerosis as a continuous variable, the OR for depressive symptoms was 1.32 (95%CI 1.16–1.49) with every 0.1mm elevated in CCA-IMT after adjustment for all potential confounders. In part 2, we explored the risk of depressive symptoms on carotid atherosclerosis. We found elevated depressive symptoms significantly increased the risk of carotid atherosclerosis in multi-factor adjusted models [OR (95%CI): 1.65(1.10–2.47)]. When using depressive symptoms as a continuous variable, the ORs for carotid artery atherosclerosis were 1.32 (95%CI 1.16–1.49) with every 1 GDS-30 score elevated after adjustment for all convenient risk factors. The current study demonstrated the bidirectional links of carotid atherosclerosis measures with depressive symptoms. More cohort study and clinical trial focusing on the issue need to be explored in the future.

1. Introduction

Depressive syndromes, a most common mood disorder, concern affection more than 350 million individuals worldwide and appears to be more challenging in the aged population (Marcus, Yasamy, Ommeren, Chisholm, & Saxena, 2012; Ribeiro, Bauer, & Mcr, 2017). In addition, cardiovascular disease (CVD) has been identified as the leading cause of death worldwide and was the topmost diseases affecting the Chinese population. One hand, accumulating evidence has shown that depressive syndromes significantly elevated risk for incidence and mortality of CVD (Gan, Gong, & Tong, 2014; Capistrant et al., 2013; Wulsin & Singal, 2003). It's reported that comparing with the overall patient population, the prevalence of depression is two to

four times as common in cardiovascular patients (Haas, Davidson, & Schwartz, 2005; Loomba, Aggarwal, & Arora, 2015) and this situation was more seriously in China (Ren, Yang, Browning, Thomas, & Liu, 2014). Another hand, vascular risk factors were confirmed to be leading reason causing depressions. It's widely acceptable that depression was prevalent among post-stroke/myocardial infarction patients and the concept of "vascular depression" has been mentioned for decade years.

Carotid atherosclerosis serves as a subclinical surrogate for the development of CVD. Identifying carotid intima–media thickness (CIMT), carotid plaque and carotid stenosis and evaluating its characteristics by ultrasonography have long been used as indicators of subclinical atherosclerosis in epidemiologic studies (Ali, Khan, & Khosa, 2017).

So far, accumulating publications highlighted the association

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between depressive symptoms and atherosclerosis in bi-direction. However, the results on this issue are far from being uniform and few community-based epidemiologic studies have attempted to explore such a link in one population. Moreover, given the quantity of the published evidence and the controversial results (Almeida, Alfonso, Flicker, Hankey, & Norman, 2012; Nicholson, Kuper, & Hemingway, 2006), we analyzed the data from the Beijing Longitudinal Study of Aging (BLSA) to determine whether there was the presence of associations of depressive syndromes with abnormal CCA-IMT, a measure of subclinical atherosclerosis, in bi-directions.

2. Participants and methods

2.1. Participants

The study participants came from the BLSA, which was initiated in 1992, and the objectives of the study was to explore the health status in older adults. Briefly, a stratification-random- clustering procedure was designed to ensure the representativeness of the average age, education and economic level in Beijing population older than 55 years in 1992 (Guan, Tang, & Fang, 2016; Jiang, Tang, & Futatsuka, 2002). A structured questionnaire was applied in 1992 and surveys conducted every 3 or 5 years after baseline. All the residents aged 55 years and older in the selected communities / villages were enrolled in every wave of surveys. In 2009, carotid artery was examined using B-mode ultrasonography, as well as blood samples were collected besides questionnaire. The current study is based on the survey in 2009 and 2468 individuals were investigated.

Among the 2468 participants, 1052 did not complete ultrasonography examination or blood test. We excluded 261 participants with a history of stroke or myocardial infarction. Thus, a total of 1155 participants (508 males and 647 Females) were analyzed. All participants provided informed consent regarding the survey, B-ultrasonic and blood data. All procedures and protocols of the research were conducted according to the principles of the Declaration of Helsinki and approved by ethics committees of Xuanwu Hospital, Capital Medical University, Beijing, China.

This research included 2 parts. In part 1, whether carotid atherosclerosis was the risk factor of depressive symptoms was explored. In part 2, whether depressive symptoms could increase the risk of carotid atherosclerosis was investigated.

2.2. Physical examination and laboratory measurements

Blood pressure was measured using a standard mercury sphygmomanometer. Sitting blood pressure (BP) was measured at the right arm twice, with a 2- to 5-minute interval after resting for 20 min, and the mean of 2 measurements was calculated for analysis. Height and body weight were also measured using standard method.

All bold samples were taken from the participants in the morning after an overnight fast. The blood samples were rapidly centrifuged at 1800 g for 10 min and the separated plasma samples were immediately stored in a refrigerator at 2–8 °C and transferred to a central laboratory (IPE Center for Clinical Laboratory, Beijing, China). Blood samples were stored there at −70 °C until analysis. Total cholesterol (TC), triglyceride (TG) and fasting blood glucose (FBG) were performed using Hitachi 7600 automatic analyzer (Hitachi High-Technologies Corporation, Japan). The plasma level of hypersensitive C creative protein (HsCRP) was measured using the Immunoturbidimetric Assay (Orion Diagnostica, Finland).

2.3. Assessment of depressive symptoms and recognize functions

Depressive symptoms was assessed by face-to-face interviews using a validated Chinese version of the 30-item Geriatric Depression Scale (GDS-30), which is a well-validated instrument that has gained wide acceptance for use in research (Radloff, 1977; Stiles & Mcgarrahan, 1998). The GDS-30 form consists of 30 questions relevant to depression, such as motivation, self-image, losses, agitation and mood. A yes/no format was designed for each question. A summary score ranged from 0 to 30 was generated, and a cut-off of 11 or more was used to define the presence of depressive symptoms. Recognize functions were estimated using 30 items Mini-Mental State Examination (MMSE) scales (Folstein, Folstein, & McHugh, 1975).

2.4. Definitions

Hypertension was defined based on the Joint National Committee guideline (JNC VII) (Detection JNCO, 2003) as systolic BP (SBP) ≥ 140 mm Hg or/and diastolic BP (DBP) ≥ 90 mm Hg, a previous diagnosis of hypertension by physician, or taking antihypertensive medication in the past 2 weeks. Diabetes mellitus was defined following American Diabetes Association criteria (Wysham & Sue, 2011) as FBG 7.0 mmol/L (126 mg/dL), having a history of diabetes, or taking hypoglycemic medication. Diagnosis of dyslipidemia should meet at least one of the following criteria according to the Adult Treatment Panel III guidelines: high TC (serum level of TC 6.21 mmol/L [240 mg/dL]) or high TG (serum level of TG 2.26 mmol/L [200 mg/dL]) or current use of anti-lipid agents (Program NCE, 2002). Body mass index (BMI) was calculated as body weight in kilogram divided by the square of height in meter. In present study, we defined smokers/drinkers as those who were current smokers/drinkers or occasionally until the time of the investigation. Active physical was defined as those who had physical activities more than half hour per day. Literatures refer to those who had more than 6 year education. Self-assessment on income was sorted as fair, satisfy and dissatisfy.

2.5. Carotid ultrasonography

Carotid atherosclerosis, including intima-media thickness, the presence of plaques and carotid stenosis were measured Using B-mode ultrasonography. The way of measurements and definition of the atherosclerosis statement were introduced elsewhere (Gu, Fang, & Hua, 2016). In brief, mean Common carotid artery intima-media thickness (CCA-IMT) was defined as the mean IMT value of the left and right CCA. The CCA-IMT thickening was defined as mean CCA-IMT ≥ 1.0 mm (Roman et al., 2006). Carotid plaque was defined as a focal structure that encroaches into the arterial lumen of at least 0.5 mm or 50% of the surrounding IMT value or demonstrates a thickness > 1.5 mm as measured from the media-adventitia interface to the intima-lumen interface (3rd AUoBotABot, 2012). Carotid stenosis measurements were performed according to the guideline of the Society of Radiologists in Ultrasound Consensus Conference (Grant, Benson, & Moneta, 2003).

2.6. Statistical analysis

Descriptive statistics are expressed as mean ± standard deviation for continuous variables and percentages for categorical variables. Chi-square test was used for categorical variables and analysis of variance was used for continuous variables. Binary logistic regression was performed to estimate odds ratios (ORs) to compare the magnitude of the association between depressive symptoms and carotid atherosclerosis. Statistical significance was considered as a p value < 0.05. All analyses were performed using SPSS 17.0 software (SPSS Inc, Chicago, Illinois, USA).

Table 1a
General Characteristics of the Participants According to Depressive Symptoms.

Variables	Total (N = 1155)	Depress-free (N = 988)	Depression (N = 167)	X^2/F value	*p* value
Age, years	68.89 ± 7.94	68.9 ± 7.77	68.81 ± 8.9	8.412	0.895
Female, n (%)	647(56)	554(56.1)	93(55.7)	0.009	0.933
Urban, n (%)	760(65.8)	636(64.4)	124(74.3)	6.195	0.013
Education, ≥6ys, n (%)	438(37.9)	381(38.6)	57(34.1)	1.191	0.301
No partner, n (%)	279(24.2)	232(23.5)	47(28.1)	1.695	0.204
Smoker, n (%)	269(23.3)	226(22.9)	43(25.7)	0.649	0.429
Drinker, n (%)	318(27.6)	272(27.6)	46(27.5)	< 0.001	1
Exercise, n (%)	962(83.3)	837(84.7)	125(74.9)	9.992	0.002
Income self-assessment, n (%)					
Fair	166(14.4)	129(13.1)	37(22.3)	68.945	< 0.001
Satisfy	860(74.6)	776(78.6)	84(50.6)		
Dis-satisfy	127(11)	82(8.3)	45(27.1)		
Hypertension, n (%)	712(61.6)	597(60.4)	115(68.9)	4.301	0.039
Diabetes, n (%)	183(15.8)	162(16.4)	21(12.6)	1.565	0.252
Dyslipidemia, n (%)	432(37.4)	369(37.3)	63(37.7)	0.009	0.931
BMI, kg/m²	24.12 ± 4.05	24.23 ± 4.07	23.47 ± 3.88	0.168	0.023
HsCRP, mg/L	0.37 ± 0.48	0.38 ± 0.49	0.34 ± 0.42	0.869	0.415
MMSE	25.97 ± 4.43	26.15 ± 4.24	24.93 ± 5.31	24.255	0.005
ADL, n (%)	18(1.6)	7(0.7)	11(6.6)	32.172	< 0.001
Grade of CIMT	1 ± 0.15	0.99 ± 0.15	1.05 ± 0.15		< 0.001
Normal CCA-IMT	145(12.6)	133(13.5)	12(7.2)	16.348	0.001
CCA-IMT thickening	262(22.7)	230(23.3)	32(19.2)		
Carotid Plaque	690(59.7)	584(59.1)	106(63.5)		
Carotid Stenosis	58(5)	41(4.1)	17(10.2)		

Abbreviations: CCA-IMTCommon carotid artery intima-media thickness; BMIbody mass index; MMSE, Mini-Mental State Examination; ADL, Activities of daily living.

3. Results

3.1. General characteristics of the participants in two parts of current study

3.1.1. Part1. General characteristics of the participants according to depressive symptoms

The distributions of demographic characteristics and risk factor profiles according to depressive syndromes is shown in part 1 (Table 1a). Among the 1155 participants (average age: 68.89 ± 7.94 years), 167 (14.5%) had depressive syndromes. Compared with individuals without depressive syndromes, those with depressive syndromes were less exercise habits, less BMI level, less MMSE score or dissatisfied on incomes, more urban residents, more properties of hypertension and disabilities (according to ADL) (all *ps* < .05). The proportion of depressive symptoms increased significantly with the severity of carotid artery atherosclerosis. The proportion of depressive symptoms in carotid stenosis individuals is 2.5 times than in free-carotid stenosis (*p* = .001). However, no significant difference was found between depressive symptoms groups on age, gender, education level, smoke and drink habits, marriage status, diabetes, hyperlipidemia, and HsCRP (all *ps* > .05).

3.1.2. Part2. General characteristics of the participants according to types of carotid artery atherosclerosis

The distributions of demographic characteristics and risk factor profiles according to types of carotid artery atherosclerosis is shown in part 2 (Table 1b). Among the 1155 participants, age and proportion of smoke habits, hypertension, diabetes and depressive symptoms significantly elevated with the severity of carotid artery atherosclerosis (*all ps* < .05). On the contrary, education level, MMSE scores and proportion of female significantly decreased with the severity of carotid artery atherosclerosis (*all ps* < .05). Also, dis-satisfied on incomes and no partners were significant different between types of carotid artery atherosclerosis (*all ps* < .05). No significant difference on living area, smoke habits, exercise, Hs-CRP, BMI and ADL was shown between carotid artery atherosclerosis groups (*all ps* > .05).

3.2. Bidirectional association between carotid atherosclerosis and depressive symptoms

3.2.1. Part1. Association of depressive symptoms with carotid atherosclerosis by binary logistic regression

Table 2a lists the ORs for depressive syndromes according to grade of carotid artery atherosclerosis. Compared with normal CCA-IMT, the risk of depressive symptoms increased greatly with severity of carotid artery atherosclerosis [CCA-IMT thickening (OR: 1.54, 95% confidence interval [CI] 0.77–3.1), presence of carotid plaque (OR: 2.01, 95%CI 1.08–3.76) and carotid stenosis (OR: 4.6, 95%CI 2.03–10.41)]. This association persisted after multivariate adjustment (OR: 1.48; 95%CI 0.72–3.03 for CCA-IMT thickening; OR: 2; 95%CI 1.03–3.85 for carotid plaque; OR: 5.29, 95%CI 2.16–12.97 for carotid stenosis). We couldn't find a significant association of depressive symptoms with CCA-IMT thickening (both in single factor or multi-factor analysis). When using carotid atherosclerosis as a continuous variable, the OR for depressive symptoms was 1.32 (95%CI 1.16–1.49) with every 0.1 mm elevated in CCA-IMT after adjustment for all potential confounders. We demonstrated that elevated CCA-IMT measurement increased significantly the risk of depressive symptoms (both as a categorical or continuous variable) in part1.

3.2.2. Part2. Association of carotid atherosclerosis with depressive symptoms by binary logistic regression

Table 2b lists the ORs for carotid artery atherosclerosis according to depressive symptoms. Here we divided carotid artery atherosclerosis into two groups in order to show the results clearly and conveniently. One was normal CCA-IMT group, another one was carotid artery atherosclerosis group (including CCA-IMT thickening, presence of carotid plaque, and carotid stenosis). The risk of depressive symptoms for carotid artery atherosclerosis were moderate (OR: 1.65; 95% CI: 1.10–2.47) after adjustment for all potential confounders. When using depressive symptoms as a continuous variable, the ORs for carotid artery atherosclerosis were 1.32 (95%CI 1.16–1.49) with every 1 GDS-30 score elevated after adjustment for all convenient risk factors. So a significant association between carotid artery atherosclerosis and depressive symptoms (both as a categorical or continuous variable) was confirmed in Part 2.

Table 1b

General Characteristics of the Participants According to Grade of CCA_IMT.

Variables	Normal CCA-IMT (N = 145)	CCA-IMT Thickening (N = 262)	Carotid Plaque (N = 690)	Carotid Stenosis (N = 58)	X^2/F value	p value
Age, years	64.96 ± 6.87	65.89 ± 7.41	70.48 ± 7.75	73.34 ± 7.03	44.077	< 0.001
Female, n (%)	108(74.5)	146(55.7)	372(53.9)	21(36.2)	30.555	< 0.001
Urban, n (%)	106(73.1)	164(62.6)	453(65.7)	37(63.8)	4.743	0.192
Education, n (%)	61(42.1)	114(43.5)	249(36.1)	14(24.1)	10.204	0.017
No partner, n (%)	26(17.9)	51(19.5)	194(28.1)	8(13.8)	15.519	0.001
Smoker, n (%)	17(11.8)	64(24.4)	167(24.2)	21(36.2)	16.549	0.001
Drinker, n (%)	37(25.5)	78(29.8)	182(26.4)	21(36.8)	3.855	0.278
Exercise, n (%)	125(86.2)	217(82.8)	572(82.9)	48(82.8)	1.015	0.798
Income self-assessment, n (%)						
Fair	25(17.2)	37(14.2)	95(13.8)	9(15.8)	14.35	0.026
Satisfy	115(79.3)	184(70.5)	518(75.1)	43(75.4)		
Dis-satisfy	5(3.4)	40(15.3)	77(11.2)	5(8.8)		
Hypertension, n (%)	78(53.8)	145(55.3)	447(64.8)	42(72.4)	13.899	0.003
Diabetes, n (%)	11(7.6)	36(13.7)	125(18.1)	11(19)	11.38	0.01
Dyslipidemia, n (%)	54(37.2)	104(39.7)	253(36.7)	21(36.2)	0.785	0.853
BMI, kg/m^2	24 ± 4.35	24.29 ± 4.42	24.14 ± 3.86	23.51 ± 3.83	0.648	0.584
HsCRP, mg/L	0.19 ± 0.41	0.17 ± 0.38	0.22 ± 0.5	0.31 ± 0.91	1.801	0.145
MMSE	26.84 ± 3.17	26.32 ± 4.16	25.74 ± 4.73	24.99 ± 4.19	3.984	0.008
ADL, n (%)	0(0)	1(0.4)	16(2.3)	1(1.7)	7.271	0.064
Depressive Symptoms, n (%)	12(8.3)	32(12.2)	106(15.4)	17(29.3)	16.348	0.001

Abbreviations: CCA-IMT, Common carotid artery intima-media thickness; BMI, body mass index; MMSE, Mini-Mental State Examination; ADL, Activities of daily living.

4. Discussion

In current study, we found that bidirectional association between carotid artery atherosclerosis and depressive symptoms in a community-based aged population. Numerous of literature have highlighted the issue. However, bidirectional association between the two conditions was seldom explored in one population.

In part1 of the present study, we confirmed that a significant, moderate positive association between elevated CCA-IMT measurement and prevalent depressive symptoms. The results kept stable after adjustment for age and gender and persisted in multivariate adjusted models. It's accordant with previous studies. In three City Study, it's reported that presence of carotid plaque, not carotid artery intima-media thickness is associated with the progression of depressive symptoms in elderly persons and the occurrence of high level of depressive symptoms in elderly men (Prugger, Godin, & Perier, 2015). In Korean, they observed a significant association between depressive symptoms and CIMT in middle-aged and older females (Lee, Shin, & Choi, 2014). In a nationwide retrospective cohort study developed in Taiwan, it showed that using statins in patients with hyperlipidemia is associated with a decreased risk of depression (Chuang et al., 2014). However, in the Rotterdam Study, which was a prospective, population-based study, it revealed atherosclerosis does not appear to increase the risk of incident depression in older adults (Newson et al., 2010). In Parruti, as well as in Jorge's studies, they demonstrated negative connection between depressive symptoms and carotid plaque (Jorge, Lertratanakul, & Lee, 2017; Parruti, Vadini, & Sozio, 2013). The

inconsistent results from the research may be partly due to several factors, including the diversity in study design, demographic characteristics, depression assessment tools and cut-off values.

Based on the limitation of observational studies, clinical trials were developed to test the link of atherosclerosis with depressive symptoms. Mlekusch et al. found that depressive symptoms had a significant reduction after undergoing carotid artery stenosis placement compared with controls (Mlekusch, Mlekusch, & Minar, 2006). In Huang and Chen's study, the therapeutic effect of carotid angioplasty stent was revealed to be superior to that of antidepressants for those post-stroke depression patients with high-grade carotid artery stenosis (Huang, Chen, & Guo, 2012). Gressier et al. identified drug-resistant major depression was associated with carotid artery stenosis (Gressier et al., 2011). All these evidence supported the link of atherosclerosis with depression.

Based on the accumulating evidence, the association of atherosclerosis with depression has received more attention. It lead to a concise monitoring protocol published by several authorities (De et al., 2009; Lichtman, Froelicher, & Blumenthal, 2014). The guidelines on cardiovascular disease prevention identify depression as risk factors offering guidance on their clinical assessment and management, although it was queried for lacking of sufficient evidences.

In part2 of the present study, results show that depressive symptoms was associated with carotid artery atherosclerosis in fully adjusted models. For decade years, an increasing number of clinical, epidemiological studies and meta-analysis had proved the link between depression and atherosclerosis, although the results was still in controversy.

Table 2a

ORs for Depressive Symptoms According to Carotid Atherosclerosis by Binary Logistic Regression.

	Model I OR(95%CI)	Model II OR(95%CI)	Model III OR(95%CI)
CCA-IMT as series variables	14.84(4.76-42.24)	18.41(5.72-59.25)	1.32(1.16-1.49)[c#]
CCA-IMT as sorts variables			
Normal CIMT	1.00(reference)	1.00(reference)	1.00(reference)
CIMT-thickening	1.542(0.768-3.096)	1.587(0.788-3.197)	1.48(0.72-3.03)
Carotid Plaque	2.012(1.076-3.762)[a]	2.216(1.167-4.209)[a]	2(1.03-3.85)
Carotid Stenosis	4.596(2.029-10.41)[c]	5.368(2.293-12.565)[c]	5.29(2.16-12.97)

Note: [a] $p < 0.05$, [c] $p < 0.001$. [#] 1standard Deviation = 1 mm.

Abbreviations: CCA-IMT, Common carotid artery intima-media thickness. OR, odds ratio; CI, confidence interval. Model I, unadjusted model; Model II, adjusted for age, sex; Model III, adjusted for age, sex, living area, education level, marriage status, smoking, drinking status, exercise habit, hypertension, diabetes, BMI, dyslipidemia, hsCRP, MMSE score, incomes self-assessment and ADL.

Table 2b

ORs for Carotid Atherosclerosis According to Depressive Symptoms by Binary Logistic Regression.

	Model I OR(95%CI)	Model II OR(95%CI)	Model III OR(95%CI)
Depressive Symptoms as series variables	1.035(1.012-1.059)[b]	1.036(1.012-1.062)[b]	1.03(1.01-1.06)[a]
Depressive Symptoms as sorts variables	1.624(1.124-2.345)[b]	1.785(1.208-2.637)[b]	1.65(1.10-2.47)[a]

Note: [a] $p < 0.05$, [b] $p < 0.01$.

Abbreviations: CCA-IMT, Common carotid artery intima-media thickness. OR, odds ratio; CI, confidence interval. Model I, unadjusted model; Model II, adjusted for age, sex; Model III, adjusted for age, sex, living area, education level, marriage status, smoking, drinking status, exercise habit, hypertension, diabetes, BMI, dyslipidemia, hsCRP, MMSE score, incomes self-assessment and ADL.

Wu, Sun, Wang, Li, and Ma, (2018) performed a meta-analysis recently, in which 5947 patients with depressive symptoms and 34,423 controls without depressive symptoms were included. They examined the link of depressive syndromes with increased CCA-IMT in all individuals, and confirmed depressive symptoms contributed toward subclinical atherosclerosis. Results from the Namwon Study, in which a total of 7554 Korean males and females aged 45–74 with free cardiovascular diseases were included, also revealed the fully adjusted risk of females with depressive symptoms for abnormal CCA-IMT (≥ 1.0 mm) was significant (OR, 1.63; 95% CI, 1.16–2.30) (Lee et al., 2014). Furthermore, the association was supported by a large randomized clinical trial, which 26,828 patients were included. The results show anti-depressants reduced the hazard of major adverse cardiovascular events in individuals with moderate to severe depressive symptoms (May, Bair, & Reiss-Brennan, 2015). Unfortunately, the results from the Multi-Ethnic Study of Atherosclerosis didn't reveal the link between antidepressants and subclinical atherosclerosis (Camacho, Mcclelland, & Delaney, 2016), which was also identified in an animal test (Silverstein-Metzler, Justice, & Appt, 2017). A systematic review focusing on clinical trial also demonstrated the treatment or prevention of depressive symptoms didn't significantly improve post-event cardiovascular prognosis (Hackett, Anderson, House, & Xia, 2009). All these inconsistent results promote us to develop more good-designed cohort or clinical trial to test the association between depression and atherosclerosis. Besides, it's proposed that socio-demographic factors, as well as clinical characteristics of depression, such as history of depression, age of depression onset, severity of depression, or even lasting depression, may moderate the relationship between depression and atherosclerosis (Beutel, Wiltink, & Kirschner, 2014; Paranthaman et al., 2012; (Seldenrijk, van Hout, & van Marwijk, 2011; Baune et al., 2012).

The mechanisms underlying the association between depressive symptoms and subclinical atherosclerosis are yet to be fully understood. Ample evidence identifies the hypothalamic–pituitary–adrenal (HPA) axis and the sympathetic nervous system (SNS) act as key factors in the relationships (Carney, Freedland, & Veith, 2005; Lok, Mocking, & Ruhé, 2012; Lombard, 2010). Prior research has identified SNS and the HPA axis can be activated by depressive symptoms and various hormones, such as catecholamines, corticosteroids, glucagon and growth hormone are released subsequently. Besides, pro-inflammatory cytokines, increased sympathetic tone, platelet dysfunction, changes in arterial vessel elasticity and endothelial function were supported mediating the relationship between the two conditions (Baune et al., 2012; Moran et al., 2013).

In present study, bi-directional associations between depressive symptoms and carotid atherosclerosis were determined, which was seldom explored in one population before. Our sample size is relatively large, and the individuals in current study were well representative to the local residents. Besides, recognize function, inflammation, economy factor, and functional disability were included in models analysis, which was seldom to put these variables in past research. However, some limitations of present study should be mentioned. First, the cross-sectional design limits the strength of evidence. Second, those who didn't undergo ultrasonography measurements were excluded in analysis, which might decrease the power of current study. Finally, since

nonparticipants more often had lifetime diagnoses of depressive disorders than participants, selection bias could have occurred.

5. Conclusions

In conclusion, we found that bidirectional association between carotid artery atherosclerosis and depressive symptoms in aged persons. It suggested that depressive symptoms and sub-clinical arteriosclerosis are intertwined. Our findings may provide evidence for assisting with clinical decision-making processes and it's urgent to develop high quality clinical trial or cohort study in coming days.

Conflict of interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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