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Original Article

Relationship between the aortic valve calcification and gradient with carotid stenosis severity and plaque's morphology in patients with ischemic stroke

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Abstract

Objectives: The relationship between aortic valve calcification (AVC) and aortic valve outflow gradients with carotid artery stenosis (CAS) has been discussed and debated. The present study aims to investigate the relationship between AVC and CAS with the presence and severity of CAS.

Methods: In this cross-sectional study, we collected carotid artery (CA) Doppler ultrasonography and echocardiography results from 150 patients hospitalized for ischemic stroke. The case group consisted of 75 patients with an atherosclerotic plaque in the carotid artery with >50% stenosis. Seventy-five patients without atherosclerotic plaques in the carotid artery were included in the control group.

Results: AVC and AV peak gradients were significantly higher in the case group compared to the control group (p=0.0001, p=0.015) respectively. In the case group, there was no significant association between AVC and AV peak gradient with the severity of CAS and between AVC and carotid plaque morphology (p=0.88, p=0.14, p=0.089) respectively. The two groups had no significant difference in the rate of aortic regurgitation (AR) (P=0.57).

Conclusions: Aortic valve calcification and aortic valve gradients are significantly related to CAS. AVC and aortic valve gradients could be considered risk factors for CAS and stroke. Contrary to this, the severity of gradients and AVC was not directly related to the severity of CAS and its morphology.

Keywords: Ischemic stroke, Carotid stenosis, Calcinosis, Echocardiography, Doppler

Introduction

Ischemic stroke, including thrombotic and embolic, is the most common cause of morbidity and mortality worldwide (1). Calcified aortic valve disease is the most common valve disease in Western societies today, and assessment serves as a prognostic factor for mortality from cardiovascular diseases (CVD), including stroke. Therefore, many studies are increasingly focused on prevention or treatment to prevent the progression of valve calcification (2, 3). Several studies have shown the relationship between aortic valve calcification and atherosclerotic diseases such as carotid plaques (4-8).The relationship between mitral valve calcification and atherosclerotic diseases was more prominent than that of the aortic valve (9, 10). Thoracic aortic calcification and even abdominal aortic calcification have been associated with an

increased risk of stroke (11-18). The role of the carotid duplex test is to diagnose obstruction of the carotid system. It is of particular importance to accurately diagnose stenosis, which is associated with an increased risk of cerebral infarction.

CAS with a narrowing over 75% is defined as a critical stenosis and is associated with an increased risk of cerebral infarction. Plague composition information helps physicians make decisions regarding medical or invasive therapeutic intervention. Doppler ultrasonography can determine the severity of CAS (19-21). There are no clear recommendations for the routine use of echocardiography in evaluating ischemic stroke. It is usually performed as part of an initial diagnostic work-up, but physicians may limit its value if the suspicion of an embolic source is low. Some studies have demonstrated that in patients with risk factors for embolic stroke, transthoracic echocardiography alone can miss up to 32% of relevant abnormalities, such as intracardiac thrombi that would require anticoagulation or structural lesions like patent foramen ovale that may benefit from invasive intervention (22, 23).

Few studies have been conducted to evaluate the relationship between AVC and CAS based on echocardiography and Doppler ultrasonography of the carotid artery in patients with stroke. Given the importance of the relationship between AVC and CVS in determining the risk of stroke in patients with this valvular heart disease, it is important to evaluate individuals suspected of having this disease and to avoid the development of stroke. We decided to conduct this study to take precautionary measures to prevent stroke and reduce its occurrence. Based on our knowledge, no previously published study compares the relationship between AVC and severity of aortic valve gradients with CAS and carotid plaque morphology in patients with stroke. Therefore, this study was planned and carried out to examine the relationship between the severity of AVC and AV gradients with CAS and plaque morphology in patients with acute ischemic stroke.

Materials and Methods

This prospective cross-sectional study was conducted on 150 hospitalized patients diagnosed with ischemic stroke between 2019 and 2021 at Tabriz University of Medical Sciences. Patients with ischemic stroke consecutively enrolled in the study. The case group consisted of 75 patients with an atherosclerotic plaque in the carotid artery with >50% stenosis. Seventy-five patients without atherosclerotic plaques in the carotid artery were included in the control group. Exclusion criteria were prosthetic aortic valve, rheumatic heart diseases, heart valve surgery, carotid artery surgery, or stenting.

Variables including gender, age, CAS severity and carotid plaques echogenicity, history of ischemic heart disease (IHD), diabetes mellitus (DM), renal failure, hyperlipidemia, previous stroke, family history of cardiovascular disease (CVD), hypertension (HTN), and echocardiographic parameters including ejection fraction (EF), left ventricular-aortic pressure gradient (LV-Ao PG), AVC, aortic regurgitation (AR) were collected. CAS was assessed using Doppler ultrasound and stenosis severity was assessed using blood flow velocity using continuous wave Doppler. CAS was defined as a significant atherosclerotic plaque with >50% narrowing of carotid arteries. Carotid artery plaque morphology was reported as hypo-echoic, hyper-echoic, and mixed-echo. AVC in echocardiography was defined as the presence or absence of aortic valve calcification. The aortic valve peak pressure gradient was measured using the continuous wave doppler echocardiography.

Carotid artery stenosis severity by Doppler ultrasound

Peak Systolic Velocity Stenosis (%)	**(ICA)**	**(ICA)**	**ICA/CCA ratio**
0% -49%	<140 cm/s	<40cm/s	<2
50%-74%	>140 cm/s	<125cm/s	>2
75%-94%	>140 cm/s	>125 cm/s	>3
95%-99%	Variable	Variable	Variable
Total occlusion	No flow	No flow	-

ICA; internal carotid artery, CCA; common carotid artery

Data were analyzed using SPSS software version 16. To assess the relationship between qualitative and quantitative variables, a chi-square test, paired t-test, an independent sample t-test, and Pearson's correlation coefficient were used.

Results

A total of 150 patients participated in the study, 75 in the case group and 75 in the control group. The mean ages in the case and control groups were 59.7 and 61.1 years, respectively. 45 patients in the case group and 42 patients (56%) in the control group were male. The distribution of HTN, DM, hyperlipidemia, history of stroke, IHD, family history of CVD, and hyperlipidemia in both groups are shown in the Table1. As Table 1 shows, there was no significant difference between the case and control groups.

Table1: The history of diseases in both case and control groups

Variable	Case group N (%)	Control group N (%)	Significance level
Hypertension	46 (61.3)	38 (50.7)	0.18
Diabetes	19 (25.3)	13 (17.13)	0.23
History of stroke	11 (14.7)	15 (20.0)	0.38
History of IHD	10 (31.3)	4 (5.3)	0.09
Family history of CVD	3 (4.0)	4 (5.3)	0.69
Total Cholesterol	191.03 mg.dl	186.97 mg.dl	0.65
LDL	117.66 mg.dl	109.37 mg.dl	0.25
Triglyceride	168.24 mg.dl	162.14 mg.dl	

IHD; Ischemic heart disease, CVD; Cardiovascular diseases, LDL; Low-density lipoprotein

The prevalence of CAS with 50-70% stenosis, with 70-90%, with greater than 90%stenosis was 54% (41 patients), 23% (17 patients), and 17% (12 patients), respectively. The type of carotid artery plaque's echogenicity in the case group was mixed-echo at 37.3%, hyper-echo at 26.7%, and hypo-echo at 36%. The prevalence of AVC in the case and control groups was 38% (28 patients) and 13% (10 patients), respectively (p value=0.001). It shows that the AVC was significantly higher in the case group compared to the control group. Also, our results showed a significant difference between the AV peak pressure gradient in the case group (11±8.3mmHg) compared to the control group (7.6±3.9 mm Hg) (p value=0.015).

As shown in Table 2, in patients in the case group, there was no significant association between the presence of AVC and the carotid plaque echogenicity type (hypo, hyper, mixed) (p value = 0.89). Moreover, in the case group, none of the AV peak gradients and AVC had a significant association with the severity of CAS (p value = 0.14) (p value = 0.89), respectively Tables 3 and 4.

Table2: The relationship between AVC and carotid plaque echogenicity

AVC	Carotid plaque echo		
	Hypo echo	Hyper echo	Mixed
absence of calcification of the aortic valve	16(21%)	13(17%)	18(24%)
presence of calcification of the aortic valve	11(14%)	7(9%)	10(13%)
Significance level	0.89		

AVC: Aortic valve calcification

Table3: The association of aortic valve peak pressure gradient with the severity of carotid stenosis

Carotid stenosis severity	Peak pressure gradient across the aortic valve(mmHg)	Significance level
50-70%	9.8 ± 4.89	
70-90%	11.89 ± 7.18	0.14
>90%	15.45 ± 6.87	

Table4: The relationship between AVC with carotid artery stenosis severity

AVC	Carotid occlusion		
	>90%	**70-90%**	**50-70%**
Absence of calcification of the aortic valve	6(8%)	12(16%)	24(32%)
Presence of calcification of the aortic valve	6(8%)	5(6%)	17(22%)
Significance level	0.89		

AVC: Aortic valve calcification

The degenerative aortic regurgitation rate was 26% (20 patients) in the case group and 22% (17 patients) in the control group without a significant difference between the two groups (*p* value = 0.57).

Discussion

The results of the current study revealed that there was a significant difference between AVC and the AV pressure gradient in the case group compared to the control group (*p* value=0.0001) (*p* value=0.015), respectively. This relationship suggests that patients with AVC especially with higher aortic valve peak pressure gradients are more likely to have carotid atherosclerotic plaques, which can be regarded as an important indicator in predicting the occurrence of ischemic stroke. Related to aortic valve regurgitation, there was no significant difference between the two groups (*p*=0.57).Several studies have shown an association between AVC and CAS in patients without stroke. This relationship was shown to be associated with cardiovascular disease. Our results were consistent with these findings (27, 28).

Another study has shown that, unlike calcifying mitral valve disease, AVC is a poorly recognized risk factor for stroke (2). Although autopsy studies have found evidence of systemic embolism in one-third of cases with calcified aortic valve disease, data from large clinical trials examining the association between calcified aortic valve disease and stroke are limited and conflicting (2-5).

Another study has found calcified aortic plaques in 26% of patients with stroke, and the presence of aortic plaques was significantly associated with intracranial (IC) or extracranial (EC) atherosclerosis (14). Some studies have revealed a relationship between aortic atherosclerosis and intracranial artery calcifications in ischemic stroke patients (17). The presence of thoracic aorta plaques may be a marker of generalized atherosclerosis, high vascular risk, and advanced vascular disease. (12,13,15,17). In a study to assess the association of thoracic aorta calcification on chest X-ray (CXR) with intracranial artery stenosis in patients with ischemic stroke based on angiographic findings, patients were classified as the normal carotid artery, significant CAS, and carotid artery occlusion. Aortic calcification was observed by CXR in 26.7% of patients. AVC was higher in elderly patients and patients with hypertension. AVC was related to intracranial artery stenosis in patients with stroke (*p*= 0.008). But there was no significant association between AVC and extracranial stenosis in patients with stroke (*p*=0.67).

Our result showed that not only AVC but also aortic valve pressure gradients had significant relation with CAS. This result shows that it could be a logical conclusion that patients with AVC with higher gradient must consider high risk for stroke and require primary prevention for stroke. But our findings couldn't show the relation between the severity of AVC and aortic valve stenosis with severity of the carotid stenosis (*p*= 0.14 and *p*=0.89 respectively).

Conclusion

Aortic valve calcification and aortic valve gradients are significantly related to CAS. Carotid plaque morphology was not related to AVC and aortic valve gradients. AVC and aortic valve gradients could be considered as risk factors for CAS and stroke. Contrary to these cases, the severity of gradients and AVC was not directly related to the severity of CAS and its morphology.

Conflicts of Interest

None

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References

1.Adams Jr HP, Bendixen BH, Kappelle LJ, et al. Classification of subtype of acute ischemic stroke. Definitions for use in a multicenter clinical trial. TOAST.Trial of Org 10172 in Acute Stroke Treatment.*Stroke*.1993; 24(1):35-41.

2.Khetarpal V, Mahajan N, Madhavan R, et al. Calcific aortic valve and spontaneous embolic stroke: a review of literature. *J Neurol Sci*. 2009; 287(1-2):32-5.

3.Oliveira-Filho J , Massaro AR, Yamamoto F, et al.Stroke as the first manifestation of calcific aortic stenosis. *Cerebrovasc Dis*. 2000; 10(5):413-6.

4.Bugnicourt JM, Bonnaire B, Lepage L, et al.Stroke due to spontaneous calcified cerebral embolus as presenting feature of calcified aortic stenosis. *J Mal Vasc*. 2008; 33(2):106-9.

5.Mahajan N, Khetarpal V, Afonso L. Stroke secondary to calcific bicuspid aortic valve: case report and literature review. *J Cardiol*. 2009; 54(1):158-61.

6.Vernhet H, Torres GF, Laharotte JC, et al.Spontaneous calcific cerebral emboli from calcified aortic valve stenosis. *J Neuroradiol*. 1993; 20(1):19-23.

7. Boon A, Lodder J, Cheriex E, et al. Risk of stroke in a cohort of 815 patients with calcification of the aortic valve with or without stenosis. *Stroke*.1996; 27(5):847-851.

8. Wilson JH, JJ Cranley. Recurrent calcium emboli in a patient with aortic stenosis.*Chest*.1989; 96(6): 1433-1434.

9.Aronow WS. Mitral annular Calcification: Significant and worth acting upon. *Geriatrics*.1991; 46(4):73-5, 79-80, 85-6.

10.Jassal DS, Tam JW, Bhagirath KM, et al. Association of mitral annular calcification and aortic valve morphology: a substudy of the aortic stenosis progression observation measuring effects of rosuvastatin (ASTRONOMER) study. *Eur Heart J*. 2008; 29(12):1542-7.

11.Kim YS, Park HY, Yun KH, et al. Association of Aortic Knob Calcification with Intracranial Stenosis in Ischemic Stroke Patients. *J Stroke*.2013; 15(2):122-5.

12.Nam HS, Han SW, Lee JY, et al. Association of aortic plaque with intracranial atherosclerosis in patients with stroke.*Neurology*. 2006; 67(7):1184-8.

13.Tanne D, Tenenbaum A, Shemesh J, et al. Calcification of the thoracic aorta by spiral computed tomography among hypertensive patients: Associations and risk of ischemic cerebrovascular events. *Int J Cardiol*.2007; 120(1):32–37.

14.Kronzon I, Tunick PA. Aortic atherosclerotic disease and stroke.*Circulation*.2006; 114(1):63–75.

15.Nam HS, Han SW, Lee JY, et al. Association of aortic plaque with intracranial atherosclerosis in patients with stroke. *Neurology*.2006; 67(7):1184–1188.

16.Bugnicourt JM, Chillon JM, Tribouilloy C, et al. Relation between intracranial artery calcifications and aortic atherosclerosis in ischemic stroke patients. *J Neurol*. 2010; 257(8):1338-43.

17.Katsanos AH, Giannopoulos S, Kosmidou M, et al.Complex atheromatous plaques in the descending aorta and the risk of stroke: a systematic review and meta-analysis.*Stroke*. 2014; 45(6): 1764-70.

18. Heidrich j, Heuschmann PU, Kolominsky-Rabas P, et al. Variations in the use of diagnostic procedures after acute stroke in Europe: results from the BIOMED II study of stroke care. *Eur J Neurol*. 2007; 14(3):255-61.

19.Fernandes M, Keerthiraj B, Mahale AR, et al. Evaluation of carotid arteries in stroke patients using color Doppler sonography: A prospective study conducted in a tertiary care hospital in South India. *Int J Appl Basic Med Res*. 2016; 6(1):38-44.

20.Fragata I, Galo S, Manita M, et al. Prevalence of carotid artery disease in an ischemic stroke population: role of Doppler ultrasonography. *Acta Med Port*.2006; 19(6):446-50.

21.Molisse T, Tunick PA, Kronzon I. Role of echocardiography in aortic atherosclerotic disease and stroke. *Minerva Cardioangiol*.2007; 55(2):267-74.

22.Kasner SE, Lynn MJ, Jackson BP, et al. Echocardiography in patients with symptomatic intracranial stenosis. *J Stroke Cerebrovasc Dis*. 2007; 16(5):216-9.

23.Daniel WG, Mugge A. Transesophageal echocardiography. *N Engl J Med*.1995; 332(19):1268-79.

24.Chlumsky J,Charvat J. Echocardiography and carotid solography in diabetic patients after cerebrovascular attacks. *J Int Med Res*. 2006; 34(6):689-94.

25.Walpot J, Pasteuning WH, Hoevenaar M, et al. Transesophageal echocardiography in patients with cryptogenic stroke: does it alter their management?A 3-year retrospective study in a single non- referral center. *Acta Clin Belg*. 2006; 61(5):243-8.

26.Abreu TT, Mateus S, Correia J. Therapy implications of transthoracic echocardiography in acute ischemic stroke patients.*Stroke*.2005; 36(7):1565-6.

27.Masoumi S, Separham A, Parizad R, et al. Dual Left Anterior Descending Artery: Clinical Overview and Interventional Management. *J Tehran Heart Cent*. 2023;18(2):146–50.

28.Soylu M, Demir AD , Ozdemir O, et al. Relationship Between Plaque Morphology of Carotid artery and aortic valve calcification. *Angiology*.2003; 54(6):637-40.