Scientific Research Publishing

International Journal of Clinical Medicine, 2023, 14, 282-289
https://www.scirp.org/journal/ijcm
ISSN Online: 2158-2882
ISSN Print: 2158-284X

Association between Fundus Atherosclerosis and Carotid Arterial Atherosclerosis

Ting Wang*, Xiaoqian Xu, Ruifang Xiang, Juan Wang, Xiaoqin Liu

Health Management Center, Deyang People's Hospital, Deyang, China
Email: *277292477@qq.com

How to cite this paper: Wang, T., Xu, X.Q., Xiang, R.F., Wang, J. and Liu, X.Q. (2023) Association between Fundus Atherosclerosis and Carotid Arterial Atherosclerosis. *International Journal of Clinical Medicine*, **14**, 282-289.
https://doi.org/10.4236/ijcm.2023.145024

Received: April 28, 2023
Accepted: May 27, 2023
Published: May 30, 2023

Abstract

Objective: To investigate the correlation between fundus atherosclerosis and carotid arterial atherosclerosis. **Methods:** A total of 516 people undergoing physical examination in Deyang People's Hospital between June 2020 and December 2022 were randomly selected. Fundus atherosclerosis and carotid arterial atherosclerosis were evaluated by fundus photography and carotid artery ultrasonography, respectively. **Results:** Among the 516 physical examination patients, 198 (38.4%) had normal fundus examination, and 318 (61.6%) had fundus arteriosclerosis. Among them, 166 cases were of grade I (32.2%), 86 cases were of grade II (16.7%), and 66 cases were of grade III (12.8%). There were 286 cases (55.4%) without carotid atherosclerosis, 201 cases (38.9%) with carotid atherosclerotic plaque, and 33 cases (6.4%) with carotid stenosis. Fundus arteriosclerosis is independently associated with carotid artery intima-media thickness, vulnerable plaques, plaque scores, and carotid artery stenosis ($P < 0.05$). **Conclusion:** In summary, there is a close relationship between carotid artery disease and the degree of arteriosclerosis in the eyeground. Fundus photography is a simple, non-invasive, and easily acceptable method of inspection. The results obtained from it are useful in determining the severity of carotid atherosclerosis and guiding early detection and intervention in clinical cases. This can help reduce the incidence of cardiovascular and cerebrovascular diseases.

Keywords

Carotid Arterial Atherosclerosis, Fundus, Carotid Plaque, Carotid Stenosis, Ultrasonography

1. Introduction

Atherosclerosis, especially carotid atherosclerosis, is closely related to the occur-

rence, development and recurrence of cerebral infarction, and is the most important cause and risk factor of cerebral infarction [1]. Insufficient perfusion of the carotid artery will inevitably cause blood supply disorders to the retina, retrobulbar artery, and posterior ciliary artery, resulting in impaired circulation within the optic disc. The eyeground artery is the only artery that can be directly observed from the body surface through an ophthalmoscope or fundus camera. The degree of its atherosclerotic lesions can be used as a window to reflect systemic arteriosclerosis and is closely related to the onset of cardiovascular and cerebrovascular diseases [2] [3]. The carotid artery is an important branch of the human aorta, while the ophthalmic artery mostly originates from the internal carotid artery. Plaque-like lesions in the carotid artery can cause thickening of the intima-media, leading to arterial stenosis, hemodynamic changes, and blood microcirculation disorders, leading to ischemic eye diseases [4]. In addition, an increasing number of studies have confirmed that patients with carotid artery stenosis often have ischemic eye lesions, which often appear as the first symptom of internal carotid artery stenosis [5]. This study is intended to help clinical patients objectively evaluate the presence and severity of atherosclerosis in different individuals through non-invasive examinations such as ophthalmoscope or fundus camera by observing the correlation between eyeground arteriosclerosis and carotid atherosclerosis, and guide clinical patients to better prevent stroke at the first level.

2. Research Object and Method

2.1. Research Subjects

516 individuals aged ≥ 40 years who underwent neck vascular ultrasound and color fundus photography simultaneously at the physical examination center of Deyang People's Hospital in Sichuan Province from June 2020 to December 2022 using a random sampling method. Among them, there are 257 males and 259 females, aged 40 - 80 years, with an average age of 54.6 ± 16.3 years.

2.2. Method

1) Evaluate the traditional risk factors of the enrolled patients, including age, gender, hypertension, diabetes, coronary heart disease and other medical history; Fasting venous blood was collected to measure blood glucose, total cholesterol, triglyceride, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol and homocysteine.

2) Fundus examination: Using the CR-2 fundus camera from CANON Company in Japan, the examination is completed in a dark room. According to Keith Wagner's classification of the presence and severity of retinal arteriosclerosis [6] [7]: 0 level: no retinal arteriosclerosis; Grade I: Mild extensive thinning of retinal arteries with enhanced reflective bands; Grade II: Retinal artery stenosis and widened reflective band, arteriovenous compression; Level III: On the basis of the above level II, accompanied by retinal hemorrhage or exudation; Grade IV: On

the basis of Grade III retinal fundus changes, optic nerve papillary edema appears. The above examinations and results are determined by two qualified clinical physicians. If the grading of the fundus examination of both eyes is inconsistent, the one with higher grading will be counted.

3) Carotid artery examination method and observation indicators: The Philips EPIQ7 color ultrasound diagnostic instrument and 7.5 MHz linear array probe were used to detect the bilateral carotid arteries of the subject. Sampling location: Common carotid artery (1.0 - 1.5 cm from the bifurcation); the bifurcation of the common carotid artery and the internal carotid artery (1.0 to 1.5 cm from the bifurcation). Observation indicators: a) Intima media thickness (IMT) of the common carotid artery, defined as IMT thickening when IMT ≥ 1.0 mm; b) presence or absence of carotid plaques, whether carotid plaques are vulnerable or stable. Carotid artery plaques are defined as those with IMT ≥ 1.5 mm. For patients with carotid artery plaques, the plaques can be further divided into: (i) hypoechoic lipid soft plaques; (ii) Fibrous flat plaques with moderate echogenicity and rich collagen tissue; (iii) Ulcerative mixed type plaques with varying echogenicity; (iv) A calcified hard plaque with strong echoes and echogenic shadows. Define types (i), (ii), and (iii) of plaques as vulnerable plaques, and type (iv) of plaques as stable plaques. The plaque score method was used to score the plaque [8], that is, without calculating the length of each plaque, only the maximum thickness (mm) of each isolated carotid atherosclerotic plaque on the same side was added to obtain the carotid plaque score on that side, and the sum of the carotid plaque scores on both sides was the total plaque score of the patient. The total plaque score of 1.1 - 5.0 is mild carotid atherosclerosis; 5.1 - 10.0 are moderate carotid atherosclerosis 10.0 is severe carotid atherosclerosis; c) The presence and severity of carotid artery stenosis: The location of the largest plaque is evaluated based on the ultrasound blood velocity of the carotid artery and the cross-sectional area of the residual cavity to determine the presence and severity of carotid artery stenosis. Based on this, the research subjects were divided into: normal or carotid artery stenosis group (vascular stenosis degree < 50%), moderate carotid artery stenosis group (stenosis degree 50% - 69%), and severe carotid artery stenosis group (stenosis degree 70% - 99%) [8] [9].

2.3. Statistical Analysis

Statistical analysis was conducted using SPSS 23.0 statistical software. Counting data is expressed in terms of rate, and inter group comparisons are made using X^2. The measurement data are expressed as mean ± standard deviation. The comparison of measurement data of normal distribution is performed by analysis of variance or t-test, otherwise, the rank sum test is used. Spearman rank correlation analysis of the correlation between fundus arteriosclerosis and age. Use logistic regression to analyze the risk factors of fundus arteriosclerosis and carotid arteriosclerosis. $P < 0.05$ indicates a statistically significant difference.

3. Results

3.1. Comparison of General Conditions and Risk Factors among Different Grades of Fundus Arteriosclerosis

Among the 516 physical examination patients, 198 (38.4%) had normal fundus examination, and 318 (61.6%) had fundus arteriosclerosis. Among them, 166 cases were of grade I (32.2%), 86 cases were of grade II (16.7%), and 66 cases were of grade III (12.8%). No grade IV lesions were found in this group of data. Compared with those with normal fundus examination, those with grade II and III fundus arteriosclerosis were older, had a history of hypertension and diabetes, and other general conditions and risk factors were not statistically significant between the two groups (see Table 1). Spearman correlation analysis found a correlation between the degree of fundus arteriosclerosis and age ($r = 0.422$).

3.2. Single Factor Analysis of the Correlation between the Grading of Eyeground Arteriosclerosis and Carotid Atherosclerosis

Among 516 physical examinees, 286 (55.4%) had no carotid atherosclerotic plaque, 201 (38.9%) had carotid atherosclerotic plaque, of which 58 (11.2%) were vulnerable plaque, 172 (33.3%) were stable plaque; There were 33 cases (6.4%) with carotid artery stenosis, including 23 cases (4.5%) with <50% stenosis and 10 cases (1.9%) with 50% - 69% stenosis. No stenosis ≥ 70% was found in this group of data. The IMT thickness of bilateral common carotid arteries, the incidence of carotid plaques and vulnerable plaques, the score of carotid plaques, and the presence of carotid stenosis in patients with fundus arteriosclerosis were significantly higher than those with normal fundus examination, with statistical significance ($P < 0.05$, see Table 1). Vascular elastic function is related to the degree of arteriolar wall sclerosis, expandability and lumen size, which are all affected by atherosclerosis. The first affected part of arteriosclerosis is the intima

Table 1. Correlation factors of different grades of eyeground arteriosclerosis and their relationship with carotid atherosclerosis.

	normal (198)	Grade I (166)	Class II (86)	Level III (66)	P-value
Age (years)	48.9 ± 13.6	53.3 ± 14.5	61.8 ± 20.6	62.2 ± 19.2	<0.001
Male [number of cases (%)]	96 (48.5)	83 (50.0)	44 (51.2)	34 (51.5)	0.996
Diabetes [cases (%)]	8 (4.0)	10 (6.6)	13 (15.1)	12 (18.2)	<0.001
Hypertension [cases (%)]	17 (8.6)	26 (15.7)	35 (40.7)	35 (53.0)	<0.001
Coronary heart disease [number of cases (%)]	3 (1.5)	3 (1.8)	3 (3.5)	2 (3.0)	0.958
Hyperlipidemia [% of cases]	76 (38.4)	82 (49.4)	53 (61.6)	44 (66.7)	<0.001
Bilateral common carotid artery IMT and (mm)	1.28 ± 0.33	1.46 ± 0.36	1.98 ± 0.38	2.01 ± 0.37	<0.001
Carotid artery plaques [% of cases]	40 (20.2)	65 (39.2)	51 (59.3)	45 (68.2)	<0.001
Vulnerable plaques [% of cases]	10 (5.1)	11 (6.6)	19 (22.1)	18 (27.3)	<0.001
Carotid artery plaque score (points)	1.77 ± 0.54	2.11 ± 0.62	3.98 ± 0.72	4.02 ± 0.81	<0.001
Carotid artery stenosis [% of cases]	4 (2.0)	6 (3.6)	12 (13.9)	11 (16.7)	<0.001

and media, and vascular elastic function is mainly maintained by the elastic fibers of the media. When hardening occurs, the media is damaged, and then the arterial elastic function decreases, thereby affecting the vascular volume, resulting in hemodynamic changes [10].

3.3. Multifactor Analysis of the Correlation between the Grading of Eyeground Arteriosclerosis and Carotid atherosclerosis

With eyeground arteriosclerosis II and III as dependent variables, the parameters with statistical significance between different grades of eyeground arteriosclerosis in the above univariate analysis as independent variables, including age, hypertension, diabetes, carotid atherosclerotic plaque, vulnerable carotid atherosclerotic plaque, carotid stenosis, bilateral common carotid artery IMT thickness and carotid plaque score, etc., Fundus arteriosclerosis was independently correlated with age, hypertension, vulnerable plaque of carotid atherosclerosis, carotid stenosis, IMT of common carotid artery, and carotid plaque score, with statistical significance ($P < 0.05$, see Table 2). Evidence-based medicine confirms that the occurrence of arteriosclerosis is influenced by age, blood pressure, blood lipids, diabetes, uric acid, obesity, smoking and diet habits, and the influence of various risk factors such as genetics. Fundus arteriosclerosis is a type of slow Sexual vascular disease that is one of the indications for target organ and peripheral arterial sclerosis, which is Aging manifestations of the vascular system around the body; Fundus artery microvascular abnormalities and heart. The occurrence, development, and prognosis of cerebrovascular diseases are closely related; Vascular lesions. It is systemic and can predict systemic arterial stiffness simultaneously with an increase in pulse pressure [11].

4. Discussion

Atherosclerosis is a chronic and progressive systemic arterial disease, which is characterized by the accumulation of lipids and complex sugars, bleeding and

Table 2. Multiple analyses of the main risk factors for vulnerable plaques.

risk factor	*OR*	95%CI	*P value*
Age	1.13	1.01-3.86	0.036
Hypertension	2.01	1.13-5.36	0.007
diabetes	0.91	0.78-1.36	0.523
carotid atherosclerotic plaque	0.93	0.71-1.68	0.327
Vulnerable plaque of carotid atherosclerosis	1.96	1.09-4.11	0.032
Carotid Stenosis	1.98	1.21-4.87	0.016
Bilateral common carotid artery IMT	1.85	1.16-3.98	0.029
Carotid artery plaque score	1.96	1.23-4.46	0.013

OR: Odds ratio; CI: Confidence interval.

thrombosis, followed by fibrous tissue hyperplasia and calcification, and the gradual degeneration and calcification of the middle layer of the artery, leading to thickening and hardening of the arterial wall and narrowing of the vascular lumen, which are the main reasons for clinical cardiovascular and cerebrovascular events [2] [8] [12]. Carotid atherosclerosis is closely related to the occurrence, development and recurrence of cerebral infarction, and is the most important cause and risk factor of cerebral infarction [1]. Atherosclerosis screening is beneficial for early detection of atherosclerosis patients and early intervention of atherosclerosis, which is of great significance in preventing cardiovascular and cerebrovascular diseases [13].

Carotid atherosclerosis inspection methods include carotid color Doppler ultrasound, CT angiography (CTA), magnetic resonance angiography (MRA) and cerebral angiography [14], but these inspection methods are expensive, some are invasive inspection methods, which is not conducive to carotid atherosclerosis screening. The retinal artery of the fundus is a branch of the internal carotid artery and is one of the few small arteries in clinical practice that can be directly observed in morphology in vivo. With the popularization of digital technology, fundus digital photography technology can provide objective and standardized manifestations of retinal arteriole abnormalities [6] [7], which is a simple, easy-to-implement, low-cost, non-invasive, and easily accepted examination method for patients. Multiple studies have found that the degree of fundus arteriosclerosis is related to cerebral small vessel disease, suggesting that fundus arteriosclerosis can serve as a clinical observation window for cerebral small vessel disease [15]. The correlation between fundus retinal angiopathy and cervical atherosclerosis has been confirmed by some studies. Studies have found that carotid artery IMT is associated with retinal arteriovenous diameter and arterial/venous ratio [16]. In addition, the severity of retinal microvascular lesions is related to the degree of extracranial carotid artery stenosis and the area of carotid artery plaques [17]. The results of this study found that eyeground arteriosclerosis was independently related to vulnerable carotid atherosclerotic plaque, carotid stenosis, common carotid artery IMT, and carotid plaque score, which was consistent with the above results. The results suggest that eyeground atherosclerosis can be used as one of the indicators to judge the presence and severity of carotid atherosclerosis.

This study found that eyeground arteriosclerosis is related to age, hypertension and diabetes, and age and hypertension are independently related to the severity of eyeground arteriosclerosis, which is consistent with previous research results [2] [7]. Therefore, for patients with these risk factors, timely change of bad lifestyle and active intervention of hypertension and diabetes may reduce the incidence of atherosclerosis, and thus reduce the incidence of cardiovascular and cerebrovascular diseases.

To sum up, carotid artery disease is closely related to the degree of eyeground arteriosclerosis. Fundus photography is a simple, easy, non-invasive and easy-to-accept inspection method. Its results are helpful to judge whether carotid athe-

rosclerosis is present and serious, guide clinical early detection and intervention of atherosclerosis, and reduce the incidence of cardiovascular and cerebrovascular diseases.

5. Limitations and Future Directions

This study is a cross-sectional study and cannot explain the sequence of occurrence of fundus arteriosclerosis and carotid arteriosclerosis. However, existing studies have shown that carotid arteriosclerosis occurs earlier than fundus arteriosclerosis. In the future, further experiments on improving arteriosclerosis can be conducted to improve the accuracy of predicting changes in the carotid artery in the fundus arteries.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Yi, X., Lin, J., Wang, C. and Liu, Y. (2017) Genetic Variants of PTGS2, TXA2R and TXAS1 Are Associated with Carotid Plaque Vulnerability, Platelet Activation and TXA2 Levels in Ischemic Stroke Patients. *PLOS ONE*, **12**, e0180704. https://doi.org/10.1371/journal.pone.0180704

[2] Gao, Z. (2018) Study on Hemodynamic Factors Related to Retinal Arteriosclerosis and Its Complications in Cardiovascular and Cerebrovascular Diseases. Master's Thesis, Beijing University of Chinese Medicine, Beijing.

[3] Andrawes, N.G., Ismail, E.A., Roshdy, M.M., *et al.* (2019) Angiopoietin-2 as a Marker of Retinopathy in Children and Adolescents with Sickle Cell Disease: Relation to Subclinical Atherosclerosis. *Journal of Pediatric Hematology/Oncology*, **41**, 361-370. https://doi.org/10.1097/MPH.0000000000001486

[4] Feng, Y., Zhao, X. and Jia, X. (2012) Study on the Correlation between Blood Vessel and Internal Carotid Artery Hemodynamic Changes after Bulging in Non Arteritic Anterior Ischemic Optic Neuropathy. *Chinese Clinical Study*, **25**, 268-269.

[5] Li, Q. and Zhang, S. (2017) A Study on the Correlation between Non Arteritic Anterior Ischemic Optic Neuropathy and Ischemic Stroke. *Chinese Journal of Practical Neurology*, **20**, 38-40. (In Chinese)

[6] Walsh, J.B. (1982) Hypertensive Retinopathy. Description, Classification and Prognosis. *Ophthalmology*, **89**, 1127-1131. https://doi.org/10.1016/S0161-6420(82)34664-3

[7] Yildırım, T., Özkan, S., Yılmaz, Ö.Ç. and Yavuz, B. (2020) Increased Rate of Any Retinopathy Risk in Patients with Masked Hypertension. *Clinical and Experimental Hypertension*, **42**, 479-482. https://doi.org/10.1080/10641963.2019.1705320

[8] (2020) Expert Consensus on Several Issues of Head and Neck Vascular Ultrasound (Carotid Artery Part). *Chinese Journal of Cerebrovascular Disease*, **17**, 346-353. (In Chinese)

[9] Yi, X., Liao, D., Wu, L., Chen, H., Li, J. and Wang, C. (2016) CYP Genetic Variants, CYP Metabolite Levels and Symptomatic Carotid Stenosis in Ischemic Stroke Patients. *Journal of Atherosclerosis and Thrombosis*, **23**, 621-631.

https://doi.org/10.5551/jat.32714

[10] Qin, F., Feng, Y. and Zhu, W. (2015) Study on Correlation between Hemodynamic Changes of Internal Carotid Artery and Blood Flow after Bulging in Anterior Ischemic Optic Neuropathy. *New Progress in Ophthalmology*, **35**, 276-278.

[11] Wang, H., Hu, D., Ma, Z., *et al.* (2003) A Study on the Relationship between Pulse Pressure and the Severity of Coronary Artery Disease. *Chinese Journal of Cardiovascular Disease*, **31**, 83-86. (In Chinese)

[12] Borden, W.B., Maddox, T.M., Tang, F., *et al.* (2014) Impact of the 2014 Expert Panel Recommendations for Management of High Blood Pressure on Contemporary Cardiovascular Practice: Insights from the NCDR PINNACLE Registry. *Journal of the American College of Cardiology*, **64**, 2196-2203. https://doi.org/10.1016/j.jacc.2014.09.022

[13] Tian, W., Zhang, X. and He, Y. (2022) Serum NOS3 and GDNF Levels in Patients with Atherosclerotic Cerebral Infarction and Their Clinical Significance. *Journal of Apoplexy and Nervous Diseases*, **39**, 909-912. (In Chinese)

[14] Fitzpatrick, L.A., Berkovitz, N., Dos Santos, M.P., Majeed, N., *et al.* (2017) Vulnerable Carotid Plaque Imaging and Histopathology without a Dedicated MRI Receiver Coil. *The Neuroradiology Journal*, **30**, 120-128. https://doi.org/10.1177/1971400916678244

[15] Qu, M., Kwapong, W.R., *et al.* (2020) Retinal Sublayer Defect Is Independently Associated with the Severity of Hypertensive White Matter Hyperintensity. *Brain and Behavior*, **10**, e01521. https://doi.org/10.1002/brb3.1521

[16] Machalińska, A., *et al.* (2019) Retinal Vessel Dynamic Functionality in the Eyes of Asymptomatic Patients with Significant Internal Carotid Artery Stenosis. *International Angiology*, **38**, 230-238.

[17] Cao, M. and Wu, J. (2021) The Guiding Role of Carotid Artery Color Doppler Flow Information in the Diagnosis and Treatment of Fundus Vascular Obstruction Diseases. *Heilongjiang Medicine*, **34**,192-194.