Correlation Between Carotid Plaque Location And Carotid Blood Flow Dynamics

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Abstract

Purpose: This study was aimed to investigate the influence of carotid hemodynamics in common carotid artery (CCA) and internal carotid artery (ICA) on carotid plaque location.

Methods: A total of 4444 participants from Anhui Maanshan People's Hospital were selected from December 2013 to December 2018. Doppler ultrasound was used to measure the location of carotid plaque. Multiple logistic regression and smooth curve were applied to determine the relationship of carotid plaque location and hemodynamic indexes.

Results: Compared with the none plaque group, the ratio of artery systolic and diastolic blood flow velocity in right internal carotid (RICA S/D) was a risk factor for left side plaque group (OR=1.548) after adjustment. Artery systolic and diastolic blood flow velocity ratio of left common carotid artery (LCCA S/D) was a risk factor for right side plaques (OR=1.250). Resistance index of right internal carotid (RICA RI) was a protective factor for bilateral plaques (OR=0.097), while LCCA S/D and RICA S/D were risk factors for bilateral plaques (OR=1.201, OR=1.457). After age stratification, resistance index of right common carotid artery (RCCA RI) and resistance index of left internal carotid artery (LICA RI) were protective factors for bilateral plaques in groups younger than 52 (OR=0.046, OR=0.042). Artery systolic and diastolic blood flow velocity ratio of right common carotid (RCCA S/D) and RICA S/D were risk factors for bilateral plaques (OR=1.557, OR=1.843). In groups older than 52, RICA S/D was a risk factor for left plaque (OR=1.388). LCCA S/D was a risk factor for right plaque (OR=1.575). LCCA S/D and RICA S/D were risk factors for bilateral plaques (OR=1.348, OR=1.311).

Conclusions: In groups younger than 52, the formation of bilateral carotid plaque is associated with low bilateral carotid RI and increased right carotid artery flow rate. In groups older than 52, plaque formation in one carotid artery is associated with high blood flow velocity on the other artery.

1. Introduction

Atherosclerosis is an important concerned issue to public health worldwide[1, 2]. There is no obvious symptoms in early stages of atherosclerosis while plaque ruptures, the incidence of serious acute cardiovascular and cerebrovascular events is higher[2–5]. In the process of atherosclerosis, with the thickening and stenosis of vascular wall, hemodynamics also changes accordingly[3, 6–8]. In addition, hemodynamic changes will also aggravate vascular lesions and accelerate the development of atherosclerosis[9, 10]. In recent years, with the rapid popularization of carotid color Doppler ultrasound, it is of great significance to monitor the changes of hemodynamics for cardiovascular and cerebrovascular diseases[11, 12].

At present, there are many studies focus on the relationship between hemodynamics and atherosclerosis, but in view of the complex relationship between them, it is still necessary to further explore the law of their interaction. Carotid artery plaque is a direct and vital index of carotid artery disease[13–15], and carotid ultrasound can estimate the degree of carotid atherosclerosis by measuring the characteristics of plaque with the peak systolic velocity (SPV), end diastolic velocity (EDV), resistance index (RI) and other hemodynamics indicators of carotid artery. Studies confirmed that the combined application of PSV and EDV has advantages in studying the pathological characteristics of carotid arteries[16, 17]. Due to the plaque location being one of the important characteristic to carotid artery plaque, the aim of this study is to explore the relationship between carotid artery plaque location and hemodynamic index, and provided evidence for the predictive value of carotid hemodynamics on plaque location.

2. Participants And Methods

2.1 Study design and population

This cross-sectional study was conducted in Maanshan People's Hospital, and the subjects were selected from December 2013 to December 2018. Finally, the study involved a total of 4444 participants made up of 2236 females (50.32%) and 2208 males (49.68%). Inclusion criteria: (1) age between 18 and 80 years; (2) no history of cerebral hemorrhage or cerebral thrombosis; (3) no carotid artery related surgery history. Exclusion criteria: (1) heart disease, (2)cancer, (3)renal insufficiency. This was a continuous series of registered patients. The study protocol conforms to the ethical guidelines of the 1975 Declaration of Helsinki. This study was approved by review board of the hospital (NO.2014001), and all participants in the study signed informed consent[18].

2.2 Research methods

2.2.1 Questionnaire survey

The questionnaire was developed by radiologists and epidemiologists, reviewed and revised by clinicians and radiologists. All investigators were trained uniformly prior to the study. The contents of the questionnaire included general demographic characteristics (such as age, sex, etc.), behavioral characteristics (such as smoking, alcohol consumption, etc.), and previous disease history (such as hypertension, diabetes, etc.). All the investigations were conducted by face-to-face interviews with the subjects themselves or their accompanying family members.

2.2.2 Physical examination

Physical examination includes blood pressure, height and weight. Data are obtained by professionally trained surveyors who are skilled in operating instruments and equipment in accordance with standardized measurement methods.

Blood pressure measurement: After resting in a quiet environment for 15 minutes, ask the participants to take a sitting position with both legs vertical and both feet flat on the floor with the brachial artery in the right arm flush with the heart. A desktop Hg sphygmomanometer (Fish Jump, Jiangsu, China) was used for measurement. Systolic and diastolic blood pressure were represented by Korotkoff stage I and V readings, respectively. Blood pressure was taken three times and averaged, with rest intervals of 1-2min. It need to measure again if the results of the three measurements differ greatly. The average of the last two records was used for analysis.

Height and weight measurement: Ultrasonic height and weight experience model hGM-800 (Shengyuan, Henan) was used to measure height and weight. When measuring, place the height and weight meter on a flat ground and correct zero point. Ask the participant to take off his coat and shoes, look straight in front of him, and stand at attention on the bottom of the meter with his feet hanging down naturally, with his heels, sacrum and shoulder blades close to the support of the meter, and then read his height and weight. The unit of height is centimeter (cm), and the unit of weight is Kg. Each reading is in one decimal place.

2.2.3 Carotid ultrasound

Participants rest peacefully for 10 minutes before being examined to keep their heart rate and blood pressure stable. Ask the participants to remove the neck pendant, coat and fully expose the neck before examination. 5–13 MHZ linear array probes used by a professional physician (AIOKA-A7 and AIOKA-A10, Tokyo; Philips-IU22, Colombia) the internal and external carotid arteries were measured parallel and forward from the left and right common carotid arteries through the bifurcation of the carotid artery. The intima thickness and hemodynamic indexes (PSV, EDV, RI of common carotid artery and internal and external carotid artery) were recorded and printed by another physician. If the participants has plaque, the site, thickness and size of the plaque should also be measured.

2.2.4 Definition

(1) Hypertension: Taking antihypertensive drugs or systolic blood pressure ≥ 140 mm Hg or diastolic blood pressure ≥ 90 mm Hg[20].

(2) Diabetes: Plasma glucose concentration ≥ 11.1 mmol/L at any time; fasting plasma glucose (FPG) ≥ 7.0 mmol/L or oral glucose tolerance test (OGTT) ≥ 11.1 mmol/L for 2 hours[21].

(3) Smoking: Smokers who have smoked continuously for 6 months or more in their life should smoke one or more cigarettes a day. Smoking for 6 consecutive months, smoking no less than 4 times a week, and smoking no more than once a day on average is occasional[22].

(4) Alcohol consumption: No less than 50mL of 56-proof liquor per day, and drinking more than 5 times per week was considered as regular drinking; drinking less than 50mL a day and less than 5 times a week is considered occasional drinking[23].

(5) Carotid artery disease: $1.0\text{mm} \leq \text{IMT} \leq 1.5\text{mm}$ showed thickening of carotid intima; the $\text{IMT} > 1.5\text{mm}$ was the formation of cervical plaques[24].

3. Method

Continuous variables are represented by mean and standard deviation and categorical variables by percentage. Differences in demographic characteristics, laboratory indicators and hemodynamic characteristics were analyzed by analysis of variance and Chi-square test. Subjects were divided into four groups according to cervical plaque location: left, right, both and none. Multiple logistic regression was used to analyze the relationship between carotid plaque location and hemodynamics. Plaque location (left, right, both, none) is selected as the independent variable, hemodynamic indexes as dependents, and age, gender, coronary heart disease (CHD), hypertension (HBP), diabetes mellitus, dyslipidemia, smoking and alcohol consumption were included in the model as correction factors. The relationship

between carotid artery S/D and age was tested using generalized smoothing splines, and the knot locations was generated automatically in generalized additive models with R package MGCV. All p values were two-tailed, with a significance level of 0.05.

3. Result

3.1 Clinical characteristics of different carotid plaque position

The basic characteristics of participants are shown in Table 1. The average age of the subjects was 61.88 ± 11.72 years, 49.6% were male, and 63.95% had carotid plaque. There were significant different in age, sex, CHD, HBP, dyslipidemia, alcohol and smoking among four carotid plaque location groups ($p < 0.05$).

Table 1
Clinical features of carotid plaque location

Variable	Left (n = 186)	Right (n = 188)	Both (n = 2468)	None (n = 1602)	F/χ^2	P
Age(year)	63.97 ± 8.86	64.54 ± 9.49	64.40 ± 11.34	57.42 ± 11.50	3.773	< 0.001
BMI(kg/m ²)	24.03 ± 3.60	23.88 ± 3.18	24.27 ± 5.62	24.36 ± 3.46	0.684	0.562
Gender, male(%)	90(48.39)	94(50.00)	1275(51.62)	749(46.67)	9.674	0.022
CHD(%)	16(8.60)	21(11.17)	324(13.12)	102(6.36)	48.490	< 0.001
Hypertension (%)	130(69.89)	143(76.06)	1597(64.66)	894(55.70)	55.167	< 0.001
Dyslipidemia(%)	64(34.41)	54(28.72)	630(25.51)	570(35.51)	48.913	< 0.001
Diabetes(%)	86(46.24)	89(47.34)	1122(45.43)	702(43.74)	1.736	0.629
Smoking(%)	69(37.10)	74(39.36)	793(32.11)	488(30.40)	8.791	0.032
Alcohol(%)	65(34.95)	66(35.11)	620(25.14)	441(27.55)	16.793	0.001
Note: CHD coronary heart disease						

3.2 Comparison of hemodynamic indexes

The characteristics of hemodynamic indexes are shown in Table 2. There RCCA PSV, RCCA EDV, RICA PSV, LCCA PSV, LCCA EDV, LICA PSV, RCCA RI, RICA RI, LCCA RI, RCCA S/D, RICA S/D, LCCA S/D and LICA S/D were statistically significant among four CP location groups($p < 0.05$).

Table 2
Comparison of hemodynamic indexes among the four groups.

Variable	Left (n = 186)	Right (n = 188)	Both (n = 2468)	None (n = 1602)	F	p
RCCA PSV	61.08 ± 16.070	58.28 ± 16.16	63.21 ± 22.69 ^b	64.12 ± 18.38 ^b	5.225	0.001
RCCA EDV	16.96 ± 5.58	16.10 ± 5.39	17.29 ± 7.53 ^b	18.45 ± 6.18 ^{abc}	13.267	< 0.001
RICA PSV	52.86 ± 35.43	50.79 ± 20.61	53.00 ± 25.43	50.41 ± 15.86 ^c	4.442	0.004
RICA EDV	19.06 ± 7.41	19.18 ± 8.05	19.46 ± 9.34	19.69 ± 6.95	0.537	0.657
LCCA PSV	63.90 ± 17.20	61.29 ± 17.58	65.92 ± 20.84 ^b	67.08 ± 19.35 ^{ab}	5.704	0.001
LCCA EDV	18.47 ± 5.92	17.52 ± 6.42	18.51 ± 7.53	20.37 ± 7.13 ^{abc}	25.094	< 0.001
LICA PSV	51.22 ± 17.54	48.13 ± 15.95	53.27 ± 20.73 ^b	51.01 ± 18.56 ^c	7.200	< 0.001
LICA EDV	19.60 ± 7.58	18.70 ± 7.09	20.02 ± 8.43 ^b	20.16 ± 7.02 ^b	2.093	0.099
RCCA RI	0.72 ± 0.06	0.72 ± 0.06	0.72 ± 0.06	0.71 ± 0.06 ^{abc}	16.389	< 0.001
RICA RI	0.62 ± 0.06	0.62 ± 0.07	0.63 ± 0.08	0.61 ± 0.07 ^{ac}	23.046	< 0.001
LCCA RI	0.71 ± 0.06	0.71 ± 0.07	0.72 ± 0.07	0.70 ± 0.06 ^{abc}	38.590	< 0.001
LICA RI	0.62 ± 0.07	0.61 ± 0.08	0.62 ± 0.08	0.66 ± 1.79	0.608	0.609
RCCA S/D	3.75 ± 0.80	3.80 ± 1.00	3.85 ± 1.04	3.63 ± 0.88 ^{bc}	18.455	< 0.001
RICA S/D	2.89 ± 2.07	2.714 ± 0.61	2.84 ± 1.06	2.64 ± 0.52 ^{ac}	16.030	< 0.001
LCCA S/D	3.60 ± 0.81	3.709 ± 1.00	3.77 ± 1.12 ^a	3.44 ± 0.86 ^{abc}	34.101	< 0.001
LICA S/D	2.68 ± 0.48	2.690 ± 0.62	2.78 ± 1.08	2.61 ± 0.69 ^c	12.243	< 0.001
Note: the letter a indicates comparison with the left group, p < 0.05; the letter b indicates comparison with right group, p < 0.05; the letter c indicates comparison with both group; p < 0.05.						

3.3 Relationship between hemodynamics and carotid plaque location

The analysis results of relationship between hemodynamics and carotid plaque location are shown in Table 4. The VIF of hemodynamic indexes were all less than 10, and there was no obvious collinearity between them, thus hemodynamic indexes could be included in the regression analysis(Table 3). Results showed that RICA S/D was higher in the left group than in the none group (OR = 1.564, 95%CI: 1.202–2.036). RICA RI, LCCA S/D, and RICA S/D in bilateral plaques were 0.833 times (95%CI: 0.713–0.974), 1.199 times (95%CI: 1.019–1.410), and 1.467 times (95%CI: 1.144–1.881) higher than those without plaques, respectively.

Table 3
Colinear diagnosis of hemodynamic

Variable	β	S.E.	t	p	Tolerance	VIF
intercep	3.449	0.116	29.761	< 0.001		
LCCA S/D	-0.016	0.017	-0.945	0.345	0.367	2.723
RCCA S/D	-0.01	0.026	-0.382	0.703	0.185	5.395
RICA S/D	-0.03	0.014	-2.143	0.032	0.635	1.574
LICA S/D	-0.013	0.012	-1.013	0.311	0.882	1.134
RCCA RI	0.01	0.026	0.404	0.686	0.174	5.737
RICA RI	-0.018	0.015	-1.232	0.218	0.544	1.837
LCCA RI	-0.05	0.019	-2.62	0.009	0.325	3.081
LICA RI	0.014	0.011	1.288	0.198	0.999	1.001

Table 4
Relationship between carotid plaque and hemodynamics

Unadjusted						Adjusted ^a			
Location	Variable	β	S.E.	p	OR(95%CI)	β	S.E.	p	OR(95%CI)
Left	RICA S/D	0.366	0.124	0.003	1.442(1.131,1.840)	0.448	0.135	0.001	1.564(1.202,2.036)
Right	LCCA S/D	0.219	0.112	0.05	1.245(1.001,1.550)	0.212	0.125	0.091	1.236(0.967,1.581)
Both	LCCA S/D	0.197	0.081	0.016	1.217(1.038,1.428)	0.181	0.083	0.029	1.199(1.019,1.410)
	RICA S/D	0.308	0.116	0.008	1.361(1.085,1.708)	0.383	0.127	0.003	1.467(1.144,1.881)
	RICA RI	-0.031	0.072	0.667	0.970(0.842,1.116)	-0.182	0.080	0.022	0.833(0.713,0.974)
Note: compared with none group.95% CI 95% confidence interval. a Adjusted for age, gender, BMI. CHD, HBP, diabetes mellitus, dyslipidemia, smoking and alcohol.									

3.4 Association between carotid plaque location and hemodynamics in different ages

Table 5 shows that through age stratification(Supplement Fig. 1–8) and before and after adjustment for gender, BMI, CHD, HBP, diabetes mellitus, dyslipidemia, smoking and alcohol. In groups less than 52, RCCA S/D, RICA S/D in bilateral plaques were higher than none group (OR = 1.561, 95%CI: 1.001–2.434; OR = 1.745, 95%CI: 1.011–3.013). RCCA RI and in bilateral plaques were lower than none group (OR = 0.706, 95%CI: 0.498-1.000). In groups older than 52, RICA S/D on the left side of plaques were higher than none plaques (OR = 1.425, 95%CI: 1.069–1.899). LCCA S/D in the right plaque was higher than none group (OR = 1.562, 95%CI: 1.080–2.258). The LCCA S/D and RICA S/D levels in bilateral plaques were 1.379 and 1.342 times higher than those in the none group, respectively (95%CI: 1.123,1.695; 95%CI (1.020,1.764).

Table 5
Association between carotid plaque location and hemodynamics in different ages

		Unadjusted					Adjusted ^a			
	Location	Variable	β	S.E.	p	OR(95%CI)	β	S.E.	p	OR(95%CI)
≤ 52 year	Left	LCCA S/D	-0.939	0.465	0.043	0.391(0.157,0.972)	-0.901	0.492	0.067	0.406(0.155,1.066)
	Both	RCCA S/D	0.388	0.220	0.077	1.474(0.958,2.267)	0.445	0.227	0.050	1.561(1.001,2.434)
		RICA S/D	0.600	0.269	0.026	1.822(1.076,3.086)	0.557	0.279	0.046	1.745(1.011,3.013)
		RCCA RI	-0.308	0.171	0.071	0.735(0.525,1.027)	-0.348	0.178	0.050	0.706(0.498,1.000)
> 52year	Left	RICA S/D	0.336	0.138	0.015	1.400(1.068,1.835)	0.354	0.147	0.016	1.425(1.069,1.899)
	Right	LCCA S/D	0.436	0.171	0.011	1.546(1.105,2.163)	0.446	0.188	0.018	1.562(1.080,2.258)
	Both	LCCA S/D	0.290	0.100	0.004	1.336(1.097,1.626)	0.322	0.105	0.002	1.379(1.123,1.695)
		RICA S/D	0.277	0.131	0.034	1.319(1.021,1.705)	0.294	0.140	0.035	1.342(1.020,1.764)
Note: compared with none group. a Adjusted for age, gender, BMI. CHD, HBP, diabetes mellitus, dyslipidemia, smoking and alcohol.										

4. Discussion

In the process of atherosclerotic plaque formation, atherosclerotic plaque also has unbalancedness, for instance, the growth of bilateral carotid artery plaque is asymmetrical. It presents as plaque on one side of the carotid artery, but not the other[25–27]. Based on previous research, carotid atherosclerotic plaque was found to be a clear correlation with the risk factors of carotid atherosclerosis[28, 29]. We intend to further explore the relationship between the growth site of carotid atherosclerotic plaque and the change of hemodynamic indexes by detecting the hemodynamic change indexes of atherosclerotic vessels and observing the different growth sites of their respective plaques. Therefore, the influence of carotid hemodynamics on atherosclerotic plaque can be objectively judged[3, 30].

The results of this study reveal that S/D and RI of common carotid artery and internal carotid artery had an impact on plaque location when comparing the relationship between hemodynamic indexes and carotid plaque location. The ratio of PSV to EDV was used as an indicator of carotid blood flow velocity[31, 32]. RICA S/D is a high risk factor for left side plaque. LCCA S/D, RICA S/D is a risk factor for bilateral plaques, and RICA RI is a protective factor for bilateral plaques. The carotid system is a entirety in which slowing down of blood flow on one side inevitably leads to increased blood flow on the other side[33]. The increased speed of blood flow will cause blood to attack intima of blood vessels, which will damage the intima of blood vessels, resulting in increased friction of the intima of blood vessels. Concurrently, cholesterol and lipid deposits in the blood promote the formation of plaque. As a result when blood velocity decreases on one side, plaques tend to form on the other[34]. However, the left carotid artery arises from the aortic arch which is used to lower blood pressure. Therefore, abnormal blood flow in the left carotid artery cannot cause plaque on the right side. When abnormal blood flow on both sides, the aortic arch is beyond its regulatory range and plaques form.

We confirmed that age is an important factor in atherosclerosis ($p < 0.001$)[35]. Stratified by age (52 years), we found that people over 52 years old accounted for a large proportion, affecting the analysis results of the overall population. When age ≤ 52 years old, the blood velocity of the right cervical and internal carotid arteries slowed down, resulting in a large number of bilateral plaques. The possible reason is that we found most of the subjects under the age of 52 have hypertension, and hypertension is a high risk factor for carotid plaque, therefore both side of carotid arteries are more prone to plaque. In addition, the aortic arch allows normal blood flow to the left carotid artery. Therefore, double blood flow is required to compensate for the plaque on the right side, causing abnormal blood flow in the carotid and internal carotid arteries.

In groups older than 52, as age increase, blood vessels harden and the arch of the aorta becomes less able to regulate. When blood flow decreases on one side, it increases on the other, leading to plaque formation. When blood flow is abnormal on both sides, plaques are more likely to form on both sides.

5. Conclusion

Plaque location is strongly related to hemodynamics at different ages. In people younger than 52 years of age, only right-sided abnormal blood flow was closely associated with bilateral carotid plaque formation. In people older than 52 years, abnormal blood flow in one side of the neck is more likely to form plaques on the contralateral. Carotid hemodynamics is a crucial factor in assessing carotid plaque location.

Abbreviations

RCCA PSV: artery systolic blood flow velocity ratio of right common carotid

RCCA EDV: diastolic blood flow velocity ratio of right common carotid

RICA PSV: artery systolic blood flow velocity in right internal carotid

RICA EDV: diastolic blood flow velocity in right internal carotid

LCCA PSV: artery systolic blood flow velocity ratio of left common carotid artery

LCCA EDV: diastolic blood flow velocity ratio of left common carotid artery

LICA PSV: artery systolic blood flow velocity ratio of left internal carotid artery

LICA EDV: diastolic blood flow velocity ratio of left internal carotid artery

RCCA S/D: artery systolic and diastolic blood flow velocity ratio of right common carotid

RICA S/D: the ratio of artery systolic and diastolic blood flow velocity in right internal carotid

LCCA S/D: artery systolic and diastolic blood flow velocity ratio of left common carotid artery

LICA S/D: artery systolic and diastolic blood flow velocity ratio of left internal carotid artery

RICA RI: resistance index of right internal carotid

RCCA RI: resistance index of right common carotid artery

LICA RI: resistance index of left internal carotid artery

LCCA RI: resistance index of left common carotid artery

Declarations

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Author contributions

Yufeng Wen: Data curation, Formal analysis, Supervision, Project administration. Xia Ren: Conceptualization, Data curation, Formal analysis, Software, Writing—original draft. Mingfei Jiang, Huan Wu: Data curation, Formal analysis, Investigation. Yumei Zhou, Yuhang Fu: Methodology, Software. Fan Su, Lei Cao, Jian Hu: Methodology, Data collection. Grace Tatenda: Review.

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Availability of data and materials

The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

All protocols are carried out in accordance with relevant guidelines and regulations. Ethical approval was received from the Medical Ethics Committee of Wannan Medical College. This study was based on data from Ultrasonic Department at Maanshan People's Hospital in Anhui, China. This study has obtained the participants' written informed consent.

Consent for publication

Not applicable.

Conflict of interest

The authors declare that they have no competing interests.

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