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Original Article

Carotid atherosclerosis is associated with hypertension in a hospital-based retrospective cohort

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Abstract: Objective: We aim to investigate the association between carotid artery plaque and blood pressure variation, as well as other cardiovascular risk factors. Materials and methods: We retrospectively analyzed clinical data of inpatients with high blood pressure treated in the Department of Hypertension from April 2009 to June 2010. Results from carotid ultrasonography, demographic characteristics, and other clinical data were obtained from 408 patients. Results: (1) The rate of positive plaque in carotid artery was 55.1%, and there was no difference between men and women. However, this rate was positively correlated with the age of the patients. (2) The rate of positive plaque in carotid artery was associated with the duration of the disease, fasting blood-glucose levels, total cholesterol, and low-density lipoprotein-cholesterol (LDL-C). (3) The prevalence of carotid artery plaque increased in accordance with the coefficient of systolic pressure variation ($X^2 = 15.83$, $P = 0.001$), whereas no correlation existed between prevalence of carotid artery plaque and coefficient of diastolic pressure variation and the plaque prevalence ($X^2 = 0.24$, $P = 0.97$). Mean systolic blood pressure (MSBP) was positively correlated with prevalence of carotid artery plaque ($X^2 = 10.47$, $P = 0.005$). (4) Multivariate regression analysis indicated that carotid plaque was associated with the age, duration of hypertension, high-density lipoprotein-cholesterol (HDL-C), LDL-C, 24 h MSBP, and coefficient of systolic pressure variation, whereas no associations were found with the coefficient of diastolic pressure variation, 24 h average diastolic blood pressure (AvDP), and 24 h mean arterial pressure (MAP) ($P > 0.05$). Conclusion: Carotid atherosclerosis was independently associated with variation of blood pressure, especially with coefficient of systolic blood pressure variation.

Keywords: Carotid artery plaque, variation of blood pressure, ultrasonography

Introduction

During the American College of Cardiology's (ACC) annual meeting in 2010, blood pressure variation (BPV) was emphasized for further discussion about hypertension. *Lancet Hypertension* published a related article, which stated that BPV was the most significant topic in clinical hypertension research in 2010. Although hypertension was the most common remediable cardiovascular risk factor, little is known about the damage on target organs caused by hypertension [1]. The benefits from anti-hypertensive drugs, which are supported by all major clinical guidelines of hypertension treatment, can be accounted for by a decrease in blood pressure into the normal blood pressure range [1]. However, the importance of measurement indices, such as clinical BPV and highest blood pressure, tends to be overlooked. It remains unknown whether anti-hypertensive drugs have an effect on these measurement indices [2]. Although BPV is not a new topic properly understanding and maintaining BPV is essential. Using statistical analyses of patient data on daylong ambulatory blood pressure in the hypertension clinic in our hospital, we aim to evaluate the impact of BPV on the genesis and development of carotid artery atherosclerosis and to underscore the significance of BPV in atherosclerosis for clinical medicine.

Materials and methods

Study population and diagnostic criteria

We randomly selected 706 inpatients from the hypertension clinic in our hospital during the

Table 1. Baseline of clinical data between two groups of patients

Items	Patient with plaque, n = 225	Patient without plaque, n = 183	P
Age (Year)	61.57 ± 11.65	47.56 ± 13.85	< 0.001
Male (n, %)	116 (56.3)	103 (51.3)	0.341
BMI (Kg/M^2)	27.15 ± 7.51	26.86 ± 3.86	0.636
Smoking (n, %)	62 (27.4)	49 (26.8)	0.860
Hypertension duration (Yr)	3.95 ± 2.46	2.43 ± 1.74	< 0.001
FBG (mmol/L)	6.07±1.63	6.03 ± 4.67	0.905
2 hPG (mmol/L)	8.99 ± 2.88	8.69 ± 3.23	0.322
CHO (mmol/L)	4.85 ± 1.22	4.56 ± 1.08	0.012
TG (mmol/L)	1.97 ± 1.44	2.06 ± 1.46	0.533
HDL_ C (mmol/L)	1.15 ± 0.36	1.15 ± 0.61	1.000
LDL_ C (mmol/L)	3.02 ± 0.85	2.93 ± 0.93	0.309
MSBP (mmHg)	128.51 ± 16.67	123.97 ± 19.27	0.011
AvDP (mmHg)	74.32 ± 11.61	80.71 ± 11.04	< 0.001
MAP (mmHg)	80.13 ± 33.33	84.64 ± 31.86	0.166
Variable coefficient (SP)	2.90 ± 0.78	2.60 ± 0.76	< 0.001
Variable coefficient (DP)	2.73 ± 0.75	2.69 ± 0.75	0.592

time period from April 2009 to June 2010. 408 patients who underwent carotid B ultrasound examination were finally collected. There were 219 men and 189 women, whose ages ranged from 18 to 97 years (53.3 ± 14.98 (mean ± standard deviation)). Patients who had systolic pressure of 140 mmHg or higher on three successive measurements in different days or diastolic blood pressure (DBP) equal to 90 mmHg or higher were diagnosed with hypertension [3]. Patients with secondary hypertension and patients younger than 18 years old were excluded from this study.

Data collection

Ambulatory blood pressure monitoring (ABPM) was performed once every 15 minutes in the daytime and every 30 minutes at night using a noninvasive, portable blood pressure monitor (Space Labs 90217, the United States). The MSBP, the 24-hour mean DBP (MDBP), the three successive daytime blood pressures in different days (dSBP), the daytime DBP (dDBP), the night SBP (nSBP), the night DBP (nDBP), the 24-hour pulse pressure (24h PP), the 24-hour SBP variable coefficient (24 h SBPV), and the 24-hour DBP variable coefficient (24 h DBPV) were recorded. Color Doppler Ultrasonic Diagnosis Apparatus (ALOKA-a10, Japan) was used for carotid artery duplex Doppler ultrasonography. Patients with carotid plaques were divided into positive plaque group and negative carotid plaque group.

Statistical analysis

Statistical analyses were performed using SPSS13.0 (USA). Measured values following a normal distribution were represented as Mean ± standard deviation. Comparisons between two groups were examined using t-test. The enumeration data was represented as a rate, and comparisons were examined by chi-square test. Logistic regression analysis was used to study the relationship between risk factors and carotid atherosclerosis. *P*-values less than 0.05 were considered statistically significant.

Results

Demographic and baseline characteristics

Analyzing the general demographic characteristics of the chosen patients, shown in **Table 1**, revealed that all factors, except for Body Mass Index (BMI), mean arterial pressure (MAP), fasting blood-glucose (FBG), 2 h plasma glucose (2 h PG) and variable coefficient (DP), were significantly different between the carotid artery plaque group and without carotid artery plaque group ($P < 0.01$). As was shown in the **Table 2**, the prevalence of carotid artery plaque was 55.3%, and there was no gender difference in the anatomic distribution. The prevalence rate for men was 53.7% while for women it was 46.3% ($X^2 = 0.91$, $P = 0.34$).

Association of carotid artery plaques with cardiovascular risk factors

Prevalence rates of carotid artery plaque in patients based on hypertension duration, FBG, total cholesterol (CHO), HDL-C and LDL-C are shown in **Table 2**. The rate of positive plaque in carotid artery was associated with the duration of the disease, FBG, total cholesterol, HDL-C, and LDL-C.

Table 2. Comparison on positive rate of carotid artery plaque according to demographic characteristic and biochemical item

Variables	Patient with plaque		Patient without plaque		X^2	*P*
	N = 225	%	N = 183	%		
Gender					0.908	0.341
Male	116	53.0	103	47.0		
Female	109	57.7	80	42.3		
Age (year)					93.697	< 0.001
< 40	8	13.6	51	86.4		
40-50	29	35.4	53	64.6		
50-60	59	56.2	46	43.8		
60-70	64	78.0	18	22.0		
≥ 70	65	81.3	15	18.7		
Hypertension duration (year)					46.724	< 0.001
< 5	22	34.4	42	65.6		
5-10	41	41.0	59	59.0		
10-20	74	55.2	60	44.8		
> 20	88	80.0	22	20.0		
Weight					0.533	0.766
Normal	52	56.5	40	43.5		
Overweight	96	56.5	74	43.5		
Obese	77	52.7	69	47.3		
Smoking					0.005	0.940
Yes	164	55.0	134	45.0		
No	61	55.9	49	44.1		
FBG (mmol/L)					9.728	0.008
3.9-6.0	144	50.3	142	49.7		
6.1-6.9	38	62.3	23	37.7		
≥ 7.0	43	70.5	18	29.5		
2hPG (mmol/L)					2.385	0.303
< 7.7	86	50.9	83	49.1		
7.8-11.0	101	57.7	74	42.3		
≥ 11.1	38	60.3	25	39.7		
TG (mmol/L)					0.235	0.627
< 1.70	121	56.3	94	43.7		
≥ 1.70	104	53.9	89	46.1		
CHO (mmol/L)					5.833	0.054
< 5.18	153	51.9	142	48.1		
5.18-6.1	51	60.7	33	39.3		
≥ 6.22	21	72.4	8	27.6		
HDL (mmol/L)					9.164	0.003
< 1.04	119	53.3	104	46.7		
≥ 1.04	126	68.3	59	31.7		
LDL (mmol/L)					5.167	0.076
< 3.37	155	51.8	144	48.2		
3.37-4.12	49	62.8	29	37.2		
≥ 4.14	21	67.7	10	32.3		

Correlation analyses of carotid artery plaque and blood pressure variation

As shown in **Table 3**, there was a significant correlation between the coefficient of systolic pressure variation (SP) and the prevalence rate of carotid artery plaque (X^2 = 15.83, P = 0.001). On the other hand, there was no significant correlation between the coefficient of diastolic pressure variation (DP) and the prevalence rate (X^2 = 0.24, P = 0.97). The prevalence rate was positively correlated with MSBP (X^2 = 10.47, P = 0.005). The prevalence rate was negatively associated with average diastolic blood pressure (AvDP) when AvDP was less than 80 mmHg. The prevalence rate was consistent when AvDP was more than 80 mmHg (X^2 = 26.63, P < 0.001) Moreover, prevalence rate was negatively associated with 24 h mean arterial pressure (MAP) when MAP was less than 100 mmHg, and the prevalence rate was consistent when MAP was more than 100 mmHg (X^2 = 5.16, P = 0.12).

Multivariate analysis between carotid artery plaque and cardiovascular risk factors

Multivariate analysis was performed between carotid artery plaque as the dependent variable and cardiovascular risk factors as the independent variables with specific plotting parame-

Table 3. Comparison on positive rate of carotid artery plaque according to 24 hambulatory blood pressure

Ambulatory blood pressure	Patient with plaque		Patient without plaque		X^2	*P*
	N = 225	%	N = 183	%		
Variable coefficient (SP)					15.83	0.001
< 5	14	50.0	14	50.0		
6-9	46	42.1	63	57.9		
10-15	121	58.5	86	41.5		
> 15	46	72.1	18	27.9		
Variable coefficient (DP)					0.240	0.971
< 5	14	54.2	11	45.8		
6-9	63	53.9	53	46.1		
10-15	123	56.2	96	43.8		
> 15	28	57.4	20	42.6		
MSBP (mmHg)					10.47	0.005
≤ 120	52	44.8	64	55.2		
121-139	120	57.4	89	42.6		
≥ 140	56	67.5	27	32.5		
AvDP (mmHg)					26.63	< 0.001
≤ 60	32	69.6	14	30.4		
61-69	65	73.9	23	26.1		
70-79	75	52.1	69	47.9		
80-89	29	40.8	41	59.2		
≥ 90	25	41.7	35	58.3		
MAP (mmHg)					5.781	0.123
≤ 90	122	60.4	80	39.6		
91-99	61	54.5	51	45.5		
100-109	27	43.5	34	56.5		
≥ 110	16	48.5	17	51.5		

ters including MSBP, AvDP, MAP, SP, and DP for multifactor regression analysis (**Table 4**). There was no significant correlation between carotid artery plaque and coefficient of diastolic pressure variation, 24 h AvDP, and 24 h MAP ($P > 0.05$). However, carotid artery plaque had significant correlation with age, hypertension duration, HDL-C, LDL-C, 24 h MSBP, and coefficient of variation of systolic pressure variation ($P < 0.001$ or $P < 0.05$) (**Table 4**).

Discussion

Atherosclerosis is the outstanding feature of carotid artery plaque that can lead to cardiovascular and cerebral vascular events. In order to discover early atherosclerotic lesions, atherosclerosis can be examined and found using a B ultrasound. Moreover, detection is an important tool in diagnosing early atherosclerotic lesions, choosing control measures, and evaluating the effectiveness of intervention [4]. Blood pressure is a powerful predictor of cardiovascular events [5]. In order to adapt to the body's physiological function, blood pressure may fluctuate continuously with change in physiological state or environment. Excitement, fear, anxiety and exercise, especially during the contraction period, cause a significant rise in blood pressure while blood pressure falls during sleep. This fluctuation of blood pressure for a certain period of time can be defined as blood pressure variability (BPV) [6]. In recent years, with the wider application of ambulatory blood pressure monitoring in clinical treatment, there has been remarkable progress in BPV research. BPV was represented as the standard deviation or variable coefficient (standard deviation/mean) of blood pressure over a period of time. In addition, variable coefficient has the changed propensity in which higher mean blood pressure led to larger standard deviation [7]. By obtaining short-term (several seconds to sever-

Table 4. Potential risk factors of carotid artery plaque derived from multivariate logistic regression analysis

Variables	OR	95% *CI* of OR		*P*
		Lower limit	Upper limit	
Male	0.706	0.38	1.311	0.270
Age, unit = 1	1.093	1.067	1.119	0.001
BMI, unit = 1	1.031	0.986	1.077	0.182
Smoking	1.538	0.817	2.894	0.182
Hypertension duration, unit = 1	1.248	1.094	1.424	0.001
FBG, unit = 1	1.026	0.957	1.099	0.478
HDL-C, unit = 1	0.566	0.349	0.919	0.021
LDL-C, unit = 1	1.383	1.053	1.817	0.020
Variable coefficient (SP), unit = 1	1.527	1.066	2.186	0.021

Unit = 1 means the according odds ratio when the continuous variable increases one unit.

al minutes) and long-term (24 hours) data for BPV, the variation range can be reflected by the time-domain analysis (standard deviation), while the coefficient of variability can be reflected by the frequency-domain analysis. In the short time, the frequency-domain method when the blood pressure of an upper arm measured by cuff method was less than 256 times cannot be used. Therefore, at present, the short-term BPV adopted the mean of the standard deviations of blood pressure collected every 30 minutes for the entire day, and the long-term BPV adopted the 24-hour standard deviation of blood pressure [8]. The BPV consists of SBPV and DBPV. However, Sander et al. [9] found that SBP variation was the best predictive index of carotid artery intima-media thickness (IMT) development. Higher BPV led to higher occurrence rate of ischemic heart disease (IHD) and increased development of IMT. Each 1 mmHg increase in BPV was associated with 0.005-0.012 mm greater IMT per year. The variation of SBP in the daytime was positively correlated with the relative risk of early carotid atherosclerosis.

This study indicates that carotid atherosclerosis prevailed among patients with hypertension prevalence rate of 78% in the group above 60 years old and of 86.3% in the group above 70 years old. This rate was higher than that in developed western countries [10]. These results suggest that, based on the age, BPV can be developed, resulting in atherosclerosis becoming more serious. The results were consistent with earlier reports [11]. Therefore, the risk of stroke mainly was increased in China, Japan and other eastern Asian countries; while the risk of coronary artery disease events was increased in Europe [11]. The noteworthy part was that the prevalence rate of carotid artery plaque increased in correlation with the growth of SP and MSBP. However, AvDP and MAP had a separation value (80 mmHg, 100 mmHg). With anything lower than the separation value, the prevalence rate of carotid artery plaque would increase, and blood pressure would decrease. On the other hand, with anything higher than the separation value, the prevalence rate of carotid artery plaque was the same, which may have relationship with the J point of DBP. Because there was no data suggesting the importance of ABPM on prevalence rate of carotid artery plaque, it is important to investigate the clinical significance of ABPM. Some research indicated that, among the patients older than 50 years old, higher SBP tended to increase cardiovascular risk more than higher DBP [12, 13].

Further analyses suggest that age, hypertension duration, HDL-C, LDL-C, SP, and MSBP were the significant factors related to carotid artery plaque, and the variation of SBP was especially one of the main predictive indices of carotid artery plaque. There was an important interaction between mean blood pressure, the instability of blood pressure, and BPV [14]. The baroreceptor should be reset as time went by, and can cushion the fluctuation of blood pressure. However, it was damaged by age variance and peripheral arterial disease, which was mediated by endothelial dysfunction [15]. Vascular events could be predicted by ambulatory blood pressure [16]. The guideline suggested that patients with blood pressure variability should perform 24-hour ABPM, home blood pressure monitoring, or both at the same time to assess blood pressure [17, 18]. Moreover, it was important to monitor blood pressure to identify BPV [19].

In our current study, atherosclerosis of the carotid artery was related to multiple cardiovascular risk factors. Compared with no risk factors, the prevalence rate of hypertension duration, FBG, total cholesterol, and LDL increased atherosclerosis of the carotid artery with statistical significance. Moreover, 24-hour ABPM, SP, MSBP, AvDP, and MAP were closely related to carotid artery plaque. In conclusion, our current study indicates that carotid atherosclerosis was independently associated with variation of blood pressure, especially with coefficient of variation of systolic blood pressure. Therefore, by monitoring blood pressure, carotid artery plaque may be effectively prevented, and the prognosis of cardiovascular disease could be improved.

Disclosure of conflict of interest

None.

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References

[1] Kaplan NM. Kaplan's clinical hypertension. Lippincott Williams & Wilkins, 2010.

[2] Rothwell PM. Limitations of the usual blood-pressure hypothesis and importance of variability, instability, and episodic hypertension. Lancet 2010; 375: 938-948.

[3] Hypertension WGoCGftMo. 2004 update: Chinese guideline for prevention and treatment of patients with hypertension (practical edition). Chinese Journal of Cardiology 2004; 32: 1060-1064.

[4] Wang W, Wu YF, Zhao D, Yang Y, Liang LR, Wang M, Xie WX, Sun JY, Zhou GH, Shi P, Ren FX and Huo Y. Distribution characteristics and risk factors of carotid atherosclerosis in middle-aged and elderly Chinese. Chinese Journal of Cardiology 2010; 38: 553-557.

[5] Lawes CM, Vander Hoorn S, Rodgers A and Hypertension ISo. Global burden of blood-pressure-related disease, 2001. Lancet 2008; 371: 1513-1518.

[6] Mancia G and Grassi G. Mechanisms and clinical implications of blood pressure variability. J Cardiovasc Pharmacol 2000; 35: S15-19.

[7] Kikuya M, Hozawa A, Ohokubo T, Tsuji I, Michimata M, Matsubara M, Ota M, Nagai K, Araki T, Satoh H, Ito S, Hisamichi S and Imai Y. Prognostic significance of blood pressure and heart rate variabilities: the Ohasama study. Hypertension 2000; 36: 901-906.

[8] Liu LS. 2010 Chinese guidelines for the management of hypertension. Zhonghua Xin Xue Guan Bing Za Zhi 2011; 701-743.

[9] Sander D, Kukla C, Klingelhöfer J, Winbeck K and Conrad B. Relationship between circadian blood pressure patterns and progression of early carotid atherosclerosis A 3-year follow-up study. Circulation 2000; 102: 1536-1541.

[10] Johnsen SH, Mathiesen EB, Joakimsen O, Stensland E, Wilsgaard T, Løchen ML, Njølstad I and Arnesen E. Carotid atherosclerosis is a stronger predictor of myocardial infarction in women than in men a 6-year follow-up study of 6226 persons: the Tromsø study. Stroke 2007; 38: 2873-2880.

[11] Wang JG. The Choice of blood pressure variability and antihypertensive drugs. Chinese Journal of Hypertension 2010; 716-717.

[12] Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr, Jones DW, Materson BJ, Oparil S and Wright JT Jr. The seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure: the JNC 7 report. JAMA 2003; 289: 2560-2571.

[13] Moser M. Clinical management of hypertension. Professional Communications 2008.

[14] Rothwell PM, Howard SC, Dolan E, O'Brien E, Dobson JE, Dahlöf B, Sever PS and Poulter NR. Prognostic significance of visit-to-visit variability, maximum systolic blood pressure, and episodic hypertension. Lancet 2010; 375: 895-905.

[15] Schlaich MP, Parnell MM, Ahlers BA, Finch S, Marshall T, Zhang WZ and Kaye DM. Impaired L-arginine transport and endothelial function in hypertensive and genetically predisposed normotensive subjects. Circulation 2004; 110: 3680-3686.

[16] Pickering TG, Shimbo D and Haas D. Ambulatory blood-pressure monitoring. N Engl J Med 2006; 354: 2368-2374.

[17] Parati G and Ibsen H. Twenty-four-hour ambulatory blood pressure profiles of high-risk patients in general practice: data from an ambulatory blood pressure monitoring registry. J Hypertens 2007; 25: 929-933.

[18] Parati G, Stergiou GS, Asmar R, Bilo G, de Leeuw P, Imai Y, Kario K, Lurbe E, Manolis A and Mengden T. European Society of Hypertension guidelines for blood pressure monitoring at home: a summary report of the Second International Consensus Conference on Home

Blood Pressure Monitoring. J Hypertens 2008; 26: 1505-1526.
[19] O'Brien E, Asmar R, Beilin L, Imai Y, Mallion JM, Mancia G, Mengden T, Myers M, Padfield P and Palatini P. on behalf of the European Society of Hypertension Working Group on Blood Pressure Monitoring European Society of Hypertension recommendations for conventional, ambulatory and home blood pressure measurement. J Hypertens 2003; 21: 821-848.