Original Article

Distribution of cerebral artery stenosis and risk factors in ethnic Zhuang and Han patients with ischemic stroke in Guangxi province

Fengkun Zhou, Jingqun Tang, Pingping Li, Bao Liao, Chao Qin

Department of Neurology, The First Affiliated Hospital of Guangxi Medical University, Nanning 5320021, China

Contributions: (I) Conception and design: C Qin; (II) Administrative support: C Qin; (III) Provision of study materials or patients: F Zhou; (IV) Collection and assembly of data: F Zhou, J Tang, B Liao; (V) Data analysis and interpretation: F Zhou, P Li; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

Correspondence to: Chao Qin, MD. Department of Neurology, The First Affiliated Hospital of Guangxi Medical University, No. 22, Shuang Yong Road, Nanning 5320021, China. Email: 252508206@qq.com.

Abstract: Previous studies have demonstrated differences in the distribution of intracranial and/or extracranial atherosclerosis (I-ECAS) by region and race. Despite this, few studies have examined the distribution of arterial stenosis in ischemic stroke patients of the Zhuang population in Guangxi, China. We therefore aimed to investigate the distribution of cerebrovascular stenosis in ischemic stroke patients across different ethnicities in Guangxi province. A total of 1,101 patients were divided into 2 groups according to their ethnicity: the Zhuang group and Han group. All patients underwent 64-slice spiral computed tomographic angiography (CTA) scanning to document the presence of intracranial or extracranial stenosis. Results showed that: (I) intracranial atherosclerosis (ICAS) a higher incidence of ECAS (51.1% *vs.* 48.9%); (II) I-ECAS was the most common lesion type, followed by ICAS; (III) Zhuang patients had a higher rate of ECAS (20.2% *vs.* 15.2%, P=0.047) and a lower rate of I-ECAS (35.8% *vs.* 42.3%, P=0.041) than that of the Han group. Furthermore, Zhuang patients had a higher percentage of stenosis in the posterior circulation (23.0% *vs.* 13.1%, P<0.001) and a lower percentage of stenosis in the anterior circulation (29.3% *vs.* 41.5%, P<0.001) than Han patients; (IV) large artery atherosclerosis (LAA) was the most commonly identified cause of stroke, and the Zhuang group had a lower proportion of LAA than the Han group (47.7% *vs.* 55.4%; P=0.020); (V) smoking and drinking were independent risk factors for ICAS; older age, male gender, and drinking were independent risk factors for ECAS; older age, male gender, hypertension, and drinking were independent risk factors for I-ECAS; age, hypertension, diabetes, hyperlipidemia, smoking, and drinking were independent risk factors for LAA. These outcomes indicate that there are ethnicity differences in the distribution of cerebrovascular stenosis in Guangxi. The variability in the risk factors involved may explain the variation in the distribution of cerebral atherosclerosis between ethnic groups.

Keywords: Cerebrovascular stenosis; intracranial atherosclerosis (ICAS); extracranial atherosclerosis (ECAS); ethnic; risk factors; ischemic stroke

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Introduction

Intracranial and/or extracranial atherosclerosis (I-ECAS) is the primary cause of ischemic stroke worldwide. Past research has established that the distribution of I-ECAS is influenced by regional and ethnic factors. For instance, stroke patients in the west more commonly suffer from ECAS, while intracranial atherosclerosis (ICAS) is more prevalent in the Asian population (1,2). In China, approximately 30–40% of acute ischemic strokes and more than 50% of transient ischemic attacks (TIAs) are caused by ICAS (3,4), with a regional north-to-south gradient in the distribution of strokes (5). Indeed, Pu *et al*. (6) reported that the proportion of patients with ICAS in China is significantly higher in the northern region (50.22%) than in the southern region (41.88%).

One southern area, the Guangxi Zhuang Autonomous Region, is a multi-ethnic province located in southwest China. The Zhuang ethnic group, the largest minority in China, accounts for 31.39% of the total population of Guangxi. However, few studies have investigated the distribution of arterial stenosis in ischemic stroke patients of the Zhuang population in Guangxi, while the differences between stroke distribution in Zhuang and Han ethnicities also remains unclear. The present study aimed to summarize the distribution characteristics of intracranial/extracranial artery stenosis in Guangxi patients of different ethnicities following their first ischemic stroke using 64-slice spiral computed tomographic angiography (CTA) scanning.

Methods

Patient population

The present study was approved by the ethics committee of our institution, and was carried out at the Department of Neurology in the First Affiliated Hospital of Guangxi Medical University (Guangxi, Nanning, China). From January 1 to December 31, 2017, patients who experienced their first ischemic stroke onset within 14 days of admission and were within the age of 18–80 years old, were enrolled into the present study. Patients were excluded when their cerebral infarction was attributable to head trauma, or when their ischemic lesions were attributable to complications from subarachnoid hemorrhage or an angiography procedure.

A total of 1,122 patients, who were diagnosed with ischemic stroke via computed tomography (CT) or magnetic resonance imaging (MRI), were examined. On admission, baseline data including age, gender, ethnicity, medical history, and physical examination results, were collected. All patients underwent a specified clinical evaluation, including laboratory tests, a wide range of blood tests, and electrocardiography. Furthermore, intracranial and extracranial carotid vessels were examined by CTA. Stroke subtypes were classified according to the Chinese ischemic stroke subclassification (CISS) criteria (7). The stroke subtype was assigned to each patient by 2 investigators. In case of discrepancies, these patient records were reviewed by a senior investigator. The final categorization was based on the consensus agreement of all investigators.

Definition of intracranial and extracranial arterial stenosis

The internal carotid artery (ICA) can be separated into 7 segments, as described by Bouthillier *et al*. (8): C1, cervical; C2, petrous; C3, lacerum; C4, cavernous; C5, clinoid; C6, ophthalmic; C7, communicating. C5 is the boundary of the intracranial/extracranial segment. Meanwhile, the vertebral artery can be divided into intracranial/extracranial segments, with the foramen magnum serving as the boundary. The intracranial arteries include the following: the carotid intracranial segment (I-ICA: C5-C7), the middle cerebral artery (MCA), the anterior cerebral artery (ACA), the posterior cerebral artery (PCA), the intracranial segment of the vertebral artery (I-VA), and the basilar artery (BA). The extracranial arteries include the following: the carotid extracranial segment (E-ICA: C1-C4), the extracranial segment of the vertebral artery (E-VA), the common carotid artery (CC), and the subclavian artery (SUBA).

Extracranial artery stenosis was measured according to the North American Symptomatic Carotid Endarterectomy Trial (NASCET) stenosis grading method (9) as follows: stenosis (%) = (1 − N/D) × 100% (N: the diameter of the narrowest lesion; D: the diameter of the distal normal vessel). The categories of stenosis were as follows: no stenosis, 0%; mild stenosis, ≤29%; moderate stenosis, 30–69%; severe stenosis, 70–99%; and complete occlusion.

Intracranial artery stenosis was measured according the method proposed by the Warfarin-Aspirin Symptomatic Intracranial Disease Study (WASID) (10,11) as follows: stenosis (%) = [(Dn − Ds)/Dn) ×100% (Ds, the diameter of the artery at the site of the most severe stenosis; Dn, the diameter of the proximal normal vessel). If the proximal segment was diseased, contingency sites, including the distal artery (second choice), and the feeding artery (third choice), were chosen to measure Dn). The categories of intracranial arterial stenosis and occlusion were as follows: (I) normal, 0–29%; (II) mild, 30–49%; (III) moderate, 50–79%; (IV) severe, 80–99%; (V) occlusion, 100%.

Definition of vascular risk factors

Hypertension (12), diabetes (13), hyperlipidemia (14), heart disease, and Hyperhomocysteinemia (15) were defined based on the personal history of these diagnoses, and on the present diet or medical treatment for these disorders. Smoking habit was qualified as smoking >5 cigarettes per day, while alcohol consumption was qualified as the consumption of >50 mL of alcohol/day.

Statistical analysis

All analyses were performed using SPSS version 19.0 (SPSS Inc., Chicago, IL, USA). Categorical variables are presented as percentages. The chi-square test or Fisher's exact test were used to compare categorical variables. Continuous variables are presented as mean [standard deviation (SD)]. The independent samples *t*-test or Wilcoxon test were used to compare continuous variables. Multinomial logistic regression analyses were performed to identify vascular risk factors that were independently associated with each type of atherosclerosis using the non-atherosclerotic group as the reference for all analyses. For traditional vascular risk factors, all risk factors significantly associated with any type of atherosclerosis were included in the model for the univariate analyses (P<0.05). All tests were two-sided, and P<0.05 was considered to be statistically significant.

Results

Overall baseline characteristics of the study groups

Table 1 shows the baseline characteristics of the cohort as a whole and within the categories determined by participant ethnicity. A total of 1,122 patients met the inclusion criteria. Furthermore, among these patients, 749 patients were of Han ethnicity, 352 patients were of Zhuang ethnicity, while 21 patients were of another ethnicity. Since the number of patients of other ethnicities was too small to be analyzed, only 1,101 patients of the Han and Zhuang ethnicities were included in the study. Overall, the mean age at admission and onset of stroke was 63.28±11.84 years (range, 18–80 years). Among all patients, 68.1% were male, 71.7% had a history of hypertension, 34.9% had a history of diabetes mellitus, 40.4% had a history of hyperlipidemia, 15.8% had a history of heart disease, 44.1% had a history of hyperhomocysteinemia, 35.9% were current smokers, and 29.3% were heavy drinkers.

Patients in the Zhuang group were younger on average than patients in the Han group. Zhuang patients were more likely to consume alcohol and cigarettes, and had a significantly higher rate of hypertension and a lower rate of diabetes mellitus.

Differences in the distribution of cerebral artery stenosis between ethnic groups

The distribution of cerebral artery stenosis is shown in *Tables 1* and *2*. In total, there were 885 (80.4%) patients with atherosclerosis. Furthermore, a total of 3,099 stenotic vessels were detected in 597 patients with arterial stenosis in the Han group and in 288 patients in the Zhuang group. Among these, 1,583 (51.1%) were cases of ICAS, while 1,516 (48.9%) were cases of ECAS. The trend in the distribution was consistent between these two ethnic groups, with I-ECAS being the most common lesion type, followed by ICAS. However, in the Zhuang group, the percentage of ECAS was notably higher than that in the Han group, while the percentage of I-ECAS was significantly lower than that in the Han group. The percentage of stenosis in the anterior circulation in the Zhuang group was significantly lower than that in the Han group. Conversely, the percentage of stenosis in the posterior circulation in the Zhuang group was significantly higher than that in the Han group. In the Zhuang group, the proportion of I-ICA, MCA, and E-VA were notably lower than those in the Han group, while the proportion of PCA, I-VA, and E-ICA were notably higher than those in the Han group.

Differences in stroke etiology between groups

The stroke etiology is shown in *Table 1*. Large artery atherosclerosis (LAA) was the most commonly identified cause of stroke, followed by penetrating artery disease (PAD). In the Zhuang group, the proportion of LAA was significantly lower than that of the Han group, while the proportion of cardiogenic stroke (CS) was higher than that in the Han group.

Differences in risk factors between groups

When the non-atherosclerosis group was used as a reference

Table 1 Demographic data, vascular territories, and etiology by ethnic group [n (%)]

Variable	All (n=1,101)	Han (n=749)	Zhuang (n=352)	P
Age (mean)	63.28±11.84	64.16±11.78	61.47±11.75	<0.001
Males	750 (68.1)	500 (66.8)	250 (71.0)	0.166
Hypertension	789 (71.7)	518 (69.2)	271 (77.0)	0.008
Diabetes	384 (34.9)	289 (38.6)	95 (27.0)	<0.001
Hyperlipidemia	445 (40.4)	310 (41.4)	135 (38.4)	0.357
Heart disease	174 (15.8)	118 (15.8)	56 (15.9)	1.000
Hyperhomocysteinemia	486 (44.1)	338 (45.1)	148 (42.0)	0.362
Smoking	395 (35.9)	253 (33.8)	142 (40.3)	0.037
Drinking	323 (29.3)	202 (27.0)	121 (34.4)	0.013
Distribution of atherosclerosis 1				0.047
Non- atherosclerosis	216 (19.6)	152 (20.3)	64 (18.2)	0.464
ICAS	257 (23.3)	166 (22.2)	91 (25.9)	0.194
ECAS	185 (16.8)	114 (15.2)	71 (20.2)	0.047
I-ECAS	443 (40.2)	317 (42.3)	126 (35.8)	0.041
Distribution of atherosclerosis 2				<0.001
Non-atherosclerosis	216 (19.6)	152 (20.3)	64 (18.2)	0.464
Anterior	414 (37.6)	311 (41.5)	103 (29.3)	<0.001
Posterior	179 (16.3)	98 (13.1)	81 (23.0)	<0.001
Anterior and posterior	292 (26.5)	188 (25.1)	104 (29.5)	0.125
Subtype of CISS				0.066
LAA	583 (53.0)	415 (55.4)	168 (47.7)	0.020
CS	84 (7.6)	48 (6.4)	36 (10.2)	0.029
PAD	266 (24.2)	172 (23.0)	94 (26.7)	0.199
OE	31 (2.8)	22 (2.9)	9 (2.6)	0.846
UE	137 (12.4)	92 (12.3)	45 (12.8)	0.845

Data are expressed as mean (± SD) or n (%). ICAS, intracranial atherosclerosis; ECAS, extracranial atherosclerosis; I-ECAS, intracranial and extracranial atherosclerosis; anterior, stenosis in anterior circulation; posterior, stenosis in posterior circulation; anterior and posterior, stenosis in both anterior and posterior circulation; CISS, Chinese Ischemic Stroke Subclassification; LAA, large artery atherosclerosis; CS, cardiogenic stroke; PAD, penetrating artery disease; OE, other etiology; UE, undetermined etiology.

group, the multiple logistic regression analysis (*Table 3*) indicated that smoking and drinking were independent risk factors for ICAS; older age, male gender, and drinking were independent risk factors for ECAS, while older age, male gender, hypertension and drinking were independent risk factors for I-ECAS.

The multiple logistic regression analysis indicated that older age, hypertension, diabetes mellitus, hyperlipidemia, smoking, and drinking were significantly associated with an increased risk of LAA stroke (*Table 4*).

Discussion

The present study demonstrated that the incidence of ICAS was higher than the incidence of ECAS (51.1% *vs.* 48.9%) in the Guangxi population. Furthermore, the rate of cerebral artery stenosis was higher than that reported in previous studies, which was 46.6% in the CICAS study (3)

Table 2 The distribution of atherosclerosis in the Han and Zhuang ethnicity groups [n (%)]

Variable	Total	Han	Zhuang	P
ICAS	1,583	1,084	499	<0.001
I-ICA	430 (27.2)	313 (28.9)	117 (23.4)	0.025
ACA	123 (7.8)	85 (7.8)	38 (7.6)	0.920
MCA	530 (33.5)	389 (35.9)	141 (28.3)	0.003
PCA	202 (12.8)	110 (10.1)	92 (18.4)	<0.001
I-VA	212 (13.4)	131 (12.1)	81 (16.2)	0.026
BA	86 (5.4)	56 (5.2)	30 (6.0)	0.477
ECAS	1,516	1,013	503	0.035
E-ICA	549 (36.2)	390 (38.5)	159 (31.6)	0.009
E-VA	446 (29.4)	278 (27.4)	168 (33.4)	0.020
CC	370 (24.4)	244 (24.1)	126 (25.0)	0.703
SUBA	151 (10.0)	101 (10.0)	50 (9.9)	0.985

Data are expressed as n (%). ICAS, intracranial atherosclerosis stenosis; ECAS, extracranial atherosclerosis stenosis; I-ICA, carotid intracranial segment; ACA, anterior cerebral artery; MCA, middle cerebral artery; PCA, posterior cerebral artery; I-IVA, intracranial segment of the vertebral artery; BA, basilar artery; E-ICA, carotid extracranial segment; E-VA, extracranial segment of the vertebral artery; CC, common carotid artery; SUBA, subclavian artery.

Table 3 Comparison of vascular risk factors between the ICAS, ECAS, or I-ECAS groups and the non-atherosclerotic group by multiple logistic regression models

Variable	ICAS			ECAS			I-ECAS		
	OR	95% CI	P	OR	95% CI	P	OR	95% CI	P
Age	0.999	0.983–1.015	0.869	1.023	1.005–1.042	0.012	1.028	1.012–1.044	<0.001
Male	1.447	0.950–2.203	0.085	1.727	1.113–2.682	0.015	2.400	1.648–3.495	<0.001
Ethnicity (Han)	0.898	0.591–1.366	0.616	0.653	0.413–1.018	0.060	1.066	0.727–1.565	0.743
Hypertension	1.454	0.961–2.200	0.076	1.254	0.807–1.948	0.314	1.603	1.107–2.320	0.012
Diabetes mellitus	1.095	0.728–1.647	0.772	1.130	0.729–1.751	0.585	1.168	0.811–1.683	0.404
Hyperlipidemia	1.140	0.771–1.686	0.511	0.955	0.626–1.457	0.829	1.109	0.781–1.576	0.563
Hyperhomocysteinemia	1.038	0.694–1.551	0.857	1.225	0.803–1.867	0.346	1.270	0.889–1.816	0.189
Smoking	1.800	1.184–2.737	0.006	0.915	0.574–1.457	0.708	1.080	0.726–1.606	0.705
Drinking	1.834	1.183–2.843	0.007	1.729	1.065–2.808	0.027	1.743	1.153–2.635	0.008

For P values, patients of the none-atherosclerosis group served as the reference group; OR, odds ratio; ICAS, intracranial atherosclerosis; ECAS, extracranial atherosclerosis; I-ECAS, intracranial and extracranial atherosclerosis.

and 49.8% in Shi's study (16). This change in prevalence may be explained by the following: (I) the subjects were selected using a method that differed from the previous studies, as the CICAS study (3) excluded patients with heart disease, while the present study enrolled patients with heart disease. Thus, the present inclusion criteria were broader; (II) the definition of arterial stenosis was different to that used in previous studies: in the CICAS study, ICAS was defined as a ≥50% diameter reduction of the MRA, while in the study conducted by Shi *et al.*, a

Table 4 Comparison of the vascular risk factors between LAA stroke and non-LAA stroke by multiple logistic regression models [n (%)]

Variable	LAA (n=583)	Non-LAA (n=518)	OR	95% CI	P
Age	64.51±11.43	61.93±12.14	1.023	1.012–1.035	<0.001
Males	407 (69.8)	343 (66.2)	1.034	0.779–1.373	0.817
Ethnic (Han)	415 (71.2)	334 (64.5)	1.288	0.984–1.686	0.065
Hypertension	451 (77.4)	338 (65.3)	1.657	1.257–2.183	<0.001
Diabetes mellitus	228 (39.1)	156 (30.1)	1.440	1.106–1.875	0.007
Hyperlipidemia	275 (47.2)	170 (32.8)	1.804	1.399–2.327	<0.001
Hyperhomocysteinemia	279 (47.9)	207 (40.0)	1.174	0.907–1.519	0.222
Smoking	241 (41.3)	154 (29.7)	1.612	1.217–2.136	0.001
Drinking	197 (33.8)	126 (24.3)	1.556	1.163–2.081	0.003

Data are expressed as mean (±SD) or n (%). LAA, large artery atherosclerosis; OR, odds ratio.

lesion of extracranial artery stenosis <30% was defined as "atherosclerotic change", and not ECAS (16). In contrast, the present study evaluated the different degrees of stenosis, including mild stenosis, through CTA. According to the literature and digital subtraction angiography data, the sensitivity and specificity of CTA in the diagnosis of intra-extracranial artery stenosis was significantly higher than that of MRA (17,18); (III) in recent years, several studies have demonstrated that the proportion of ECAS is increasing in the Asian population. Katsumata *et al*. (19) revealed that carotid plaques could be identified in 76.2% of Japanese patients, while bilateral plaques can be found in 58.2% of patients. These lesions are more frequently observed at present when compared to the rate observed in the last century. Furthermore, a Korean study reported that the incidence of I-ECAS (39%) was significantly higher in the Korean population, when compared to the incidence of ICAS and ECAS. These present results are consistent with the above findings. The reasons for these changes may be the adoption of a Western life style by the Asian population. In addition, Asian dietary habits have changed with an increase in the intake of animal fats and proteins, and the reduction in the intake of carbohydrates and rice.

The present data demonstrate that the trend in the distribution of atherosclerosis is consistent between the Zhuang and Han ethnicities, with I-ECAS being the most common lesion type, followed by ICAS. However, ethnic variations were observed between these groups, with a higher rate of ECAS and a lower rate of I-ECAS in the Zhuang group, when compared to the Han group. Furthermore, Zhuang patients had a higher percentage of stenosis in the posterior circulation and a lower percentage of stenosis in the anterior circulation, when compared to Han patients. These differences were considered to be the result of comprehensive factors. Environmental factors, lifestyle, age, susceptibility genes, and the anatomy of the intra-/extracranial artery may be involved in the progression of cerebral arterial stenosis. It was found that patients of male gender and older age were more likely to suffer from ECAS, and hypertension was only associated with ECAS, while smoking was an independent risk factor of ICAS, which is consistent with previous findings (20,21). Zhuang patients were more likely to consume cigarettes and alcohol, and this may increase the risk of hypertension. The difference in risk factors between groups may explain the observed difference in the distribution of cerebral artery stenosis. Moreover, many studies (22-25) have shown that having a genetic polymorphism is another influential factor for these differences. The difference in genetic polymorphisms between the Zhuang and Han ethnicities should be further investigated.

CISS is a new sub-classification of ischemic stroke that takes into consideration both etiological and pathophysiological information. In CISS, the atherosclerosis of the aortic and intra-/extracranial large arteries belong to LAA (7,26). The present study revealed that LAA was the most frequent subtype of stroke in the populations studied, which is supported by previous studies (27,28). The logistic regression models revealed that among the uncontrollable factors (such as age, gender, and ethnicity), only age was associated with LAA stroke. It is known that age is a non-negligible primary risk factor that contributes to atherosclerosis, because of the exposure time to risk factors is longer in the older population (20,29). After multinomial regression analysis, diabetes mellitus, hyperlipidemia, smoking, and drinking were independent risk factors of LAA stroke. The results of the present study are similar with the report of Tan *et al*. (28).

Some limitations of this study should also be addressed. First, the study was hospital-based, and the participating hospital was in the upper range of first-class hospitals. Thus, some degree of sampling bias existed. Secondly, the selected cases were all patients with ischemic stroke, and did not include patients with asymptomatic cerebral artery stenosis or healthy people. Thus, these results may not be representative the whole population. In addition, not all influential factors of atherosclerosis were tested, and thus further studies are necessary.

Conclusions

The present study contributes to the understanding of the distribution of cerebral artery stenosis and risk factors in Zhuang and Han Patients with ischemic stroke in Guangxi Province. There is an ethnicity-dependent difference in the distribution of cerebral artery stenosis in Guangxi. The proportion of ECAS was higher and the proportion of I-ECAS was lower in Zhuang patients. These observed differences in risk factors between groups can help to explain the variation in the distribution of cerebral atherosclerosis. This observation may have practical implications for the design of specific prevention strategies in stroke. In order to decrease the risk of stroke, public health measures should be strengthened and social determinants of health and risk factor prevention/control should be improved for those at high risk of artery atherosclerosis.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The present study was approved by the ethics committee of the First Affiliated Hospital of Guangxi Medical University.

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