ORIGINAL ARTICLES

The application value of TCD combined with CDUS in the large artery atherosclerosis

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Abstract

Objective: To explore the value of TCD and CDUS on diagnosis of large artery atherosclerosis.
Methods: In our study, 90 patients who had been admitted to our hospital and diagnosed as LAA according to CISS typing were selected as the research object. A retrospective analysis was conducted, using CTA as golden standard for diagnoses of stenoses. Explore the risk factors of LAA, the reliability of TCD and CDUS in diagnosis of the stenosis and distribution of stenosis in each vessel.
Results: Hypertension and type 2 diabetes are risk factors of LAA vascular stenosis. Middle cerebral artery stenosis detection by TCD carries the highest reliability (sensitivity 90.91%, specificity 97.89%, positive predictive value 96.15%, the negative predictive value was 94.9%, the positive likelihood ratio was 43.18, negative likelihood ratio 0.09, Kappa = 0.9). The consistency of TCD is as good as CTA in head and neck part. The negative coincidence rate was higher in the anterior circulation vessels (97.98%), followed by the coincidence rate of severe stenosis (95.23%). However, the detection rate of posterior circulation vessels positive, moderate and severe stenosis, mild stenosis gradually decreased by TCD. CDUS carries general reliability in detecting intracranial extracranial stenosis, the highest reliability in internal carotid artery (kappa 0.82), and the worst consistency in vertebral artery (kappa 0.38). The negative coincidence rate of CDUS in extracranial cerebrovascular stenosis was highest (97.22), followed by the overall compliance rate (91.55%). 242 branches of vascular stenosis were discovered in our study, among which intracranial artery stenosis 61.15% (148/242) is higher than that in extracranial artery 38.85% (90/242), ratio of moderate to severe stenosis is as high as 82.23% (199/242). Intracranial artery stenosis in ICA is extremely common (51.11%, 46/90), and MCA is the common area of intracranial artery stenosis (37.16%, 55/148).
Conclusions: (1) Hypertension, type 2 diabetes are risk factors for LAA stenosis. (2) TCD detection of intracranial vascular stenosis carries the best consistency, and reliability of MCA is the highest. In our search, MCA possesses the highest rate of stenosis, and negative coincidence rate by TCD examination was the highest, which could be used for screening method for stenosis. The reliability of TCD in diagnosis of moderate and severe stenosis was relatively better than mild stenosis. (3) CDUS detection of anterior circulation lesions is better than that of posterior circulation lesions. Evaluate effect on moderate and severe stenosis was better than that of mild one. The ratio of ICA stenosis was the highest, but the effect on VA was poor. (4) The incidence of intracranial vascular stenosis is more common than that of the intracranial vascular stenosis.

Key Words: TCD, CDUS, Large artery atherosclerosis

Large artery atherosclerosis (LAA) is a common cause of ischemic stroke (IS), usually leads to serious adverse events, which seriously affects the social function.[1] Positive prevention and treatment of LAA is particularly important.[2] Therapeutic decision-making, prognosis assessment, and the risk of recurrence of acute LAA largely depends on the etiology of stroke classification. At present, the imaging examination of blood vessels is still one of the most sig-

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nificant auxiliary examination of LAA. The examination of intracranial and cerebrovascular blood vessels is essential to the diagnosis and treatment of ischemic cerebrovascular disease. CTA enables repeated 3D observation of vascular status, intuitively and clearly showing intracranial major arteries and tertiary branches of blood vessels. The significance of CTA lies in the fact that it carries a high coincidence rate of stenosis with regard to its site and degree, (diagnosis rate of carotid artery stenosis > 50%, the sensitivity and specificity were respectively 97% and 90%[3]), and better plaque development than DSA.

TCD[4–8] has been widely used in clinical screening for clinical monitoring in recent years due to the characteristics of economy, non-invasiveness, repeatable check and so on. CDUS,[9–11] as one of the most popular vascular ultrasound techniques, has an irreplaceable advantage in the evaluation of the vascular wall, plaque morphology and stenosis of the extra cranial segment. CTA, TCD, CDUS and other kinds of tests have their advantages and disadvantages, while combined examination provides a more complete information of vascular morphology and hemodynamics. In our study, LAA patients with intracranial and extracranial vascular stenosis were selected as our research objects since CTA and DSA possesses a higher consistency in vascular stenosis, and capacities of TCD, CDUS and CTA in detecting vascular stenosis and related information were collected to analyze reliability and consistency of diagnosis method of TCD and CDUS, which provides help for clinical medical students with a reasonable optimization vessel inspection programs and treatment.

1 materials and methods

1.1 Research objects

The patients, who were admitted to the department of internal neurology at Baogang Hospital for cerebral infarction from 2011 and the first 5 months of 2012, were selected as the objects. On the basis of complete basic data, a total of 90 cases were finally diagnosed as LAA according to CISS classification after the patients underwent TCD, neck vascular ultrasound,and CTA examination of head and neck. It is divided into stenosis group and non-stenosis group, among which 15 cases were without intracranial and external stenosis, 75 patients were with stenosis.

1.2 Inclusion and exclusion criteria

The objects should meet the following requirements: (1) Conform to diagnostic criteria of ischemic stroke that was revised at 4th National cerebral vascular disease conference, among which the NIHSS scores should be less than 22 points, responsible lesion was confirmed by CT/MRI examination, another round examination is required until the responsible lesion was not figured out after admission within one week, the candidates were diagnosed as LAA according CISS criteria, and aortic arch atherosclerosis cerebral infarction was excluded. (2) The incidence of the population (40-79 years old) was admitted to hospital within 1 week since the onset of the disease. (3) Blood vessels were demonstrated to be fine over the examination of TCD, neck vascular ultrasound, head and neck CTA. (4) Candidates with vascular occlusion were excluded.

1.3 Methods

1.3.1 Diagnostic criteria for risk factors

Internal Medicine by Zaiying Lu and Nanshan Zhong, published in 2008, was regarded as the reference for the diagnosis of hypertension, diabetes, coronary heart disease and lipid abnormality.[12] Lung cancer and cigarette smoking in Europe by Simonato L et al.[13]was the reference for smoking history. Cerebrovascular Disease Control Guide (trial version) by editing committee of Chinese guidelines for prevention and treatment of cerebrovascular disease.[14]

1.3.2 Determination of Stenosis

Assessment method of detecting the percentage of carotid artery stenosis are using measurement of the internal diameter stenosis. Normal data reference for determination of TCD is Ultrasonic diagnostics of carotid artery and cerebral vascular supplementary Table 1 by Prof. Yang. The diagnosis standard of TCD stenosis refers to Skull neck and peripheral blood vessel ultrasound.[15] CTA measurement of the degree of vascular stenosis is in accordance with the NASCET method.[16]

1.3.3 Instruments and inspection methods

TCD inspection method is DWL-box detector. Each segment of intracranial vascular was observed through temporal window, ocular window and sub-occipital window, and recorded various related parameters. The detector TCD uses blind detection method, which could not look directly into the blood vessels,so that its comprehensive assessment is based on a variety of indicators. For example, blood flow velocity and (or) pulsation index in TCD change unequally in response to partial abnormal blood vessels. Blood changes and collateral circulation and a variety of parameters are required to reach a comprehensive evaluation. Since anatomic site adjacent to initial segment stenosis in TICA and MCA, it remains difficulties to make the distinctions. Carotid artery test is advisable if necessary to improve the detection rate. Light Speed VCT 64 layer spiral CTA by GE company was adopted in our research.

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1.3.4 Data processing and statistical methods

Collate the original data, using SPSS 17.0 statistical software for statistical analysis. It is divided into stenosis group (75 cases of LAA) and non-stenosis group (15 patients with LAA), based on the selection criteria of the occurrence of vascular stenosis, and the role of gender, age, hypertension, diabetes, abnormal lipid metabolism, coronary heart disease, smoking, drinking as risk factors of cerebral infarction are observed. After the single factor analysis of each risk factor, the risk factors of cerebral infarction stenosis were finally determined by two categories of Logistic regression analysis. To figure out the value of TCD in detecting the existence of stenosis in intracranial segment of major vascular (SCA, MCA, ACA, VA and Ba, PCA) of 75 LAA patients by statistical methods, detection information by CDUS on extracranial segments into intracranial major artery (CCA, ICA, VA). The positive predictive value, negative predictive value, sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, Kappa value, were calculated by using statistical method and the reliability analysis was made. X2 test was performed in each group with the narrow blood vessels as matched data, and the results were obtained. Analyze distribution of vascular stenosis in the intracranial and vascular blood vessels, and make sure the common stenosis areas.

Table 1: TCD detection of intracranial vascular stenosis

TCD	CTA(internal carotid artery system)				Total	CTA（posterior cerebral circulation）				Total
	Without stenosis	Mild stenosis	Moderate stenosis	Severe stenosis		Without stenosis	Mild stenosis	Moderate stenosis	Severe stenosis	
Without	341	10	4	2	357	321	9	5	3	338
Mild	4	8	0	0	12	5	7	0	0	12
Moderate	2	0	38	0	40	2	0	10	0	12
Severe	1	0	0	40	41	1	0	0	12	13
total	348	18	42	42	450	329	16	15	15	375
Coincidence rate of TCD and CTA (%)	97.98	44.44	90.47	95.23	94.88	97.57	43.75	66.67	80	93.33

2 Results

2.1 Risk factor analysis of LAA

Analysis of the four risk factors of age, hypertension, type 2 diabetes and smoking was conducted and their correlation analysis was also made by exloring one single factor. The logistic model: $P = exp(1.559X1 + 1.778X2)/\{1 + exp1.559X1 + 1.778X2\}$. X represents the return of the independent variables in the model, X1 for hypertension, X2 for the type 2 diabetes, the dependent variable Y s for stenosis, P for the stenosis probability. Based on comprehensive analysis, risk factors of type 2 diabetes and hypertension were statistically significant (p<0.05). It is included that the two indicators are correlated with vascular stenosis, and remained as risk factors which stimulated stenosis in LAA patients.

2.2 TCD detection of intracranial blood vessels

The occurrence of internal carotid artery stenosis is very common in MCA of the internal carotid artery vascular system, accounting for 53.92% vessels (55/102). The number of blood vessels that were with stenosis is equivalent in SCA and ACA. 37 vertebral-basilar artery blood vessels were found with stenosis by TCD, and 46 by CTA, among which stenosis in 37 vertebral-basilar artery blood vessels consistent with detection result by CTA. Stenosis in vertebral basilar artery system is less than that of internal carotid artery system (see Table 1). The consistency of TCD in cerebral artery was the best, followed by the internal carotid artery system. The consistency of TCD in vertebral basilar artery system was fair, while it is the worst in BA (see Table 2). The results of paired comparisons X2 test indicated that the difference between the two methods was not significant (p>0.05). By comparing TCD and CTA in detecting stenosis rating results, TCD detection of circulating vascular negative coincidence rate can reach as high as 97.98%, pre vascular mild stenosis detection rate is minimum, and medium and severe vascular stenosis with higher positive rate. Two patients with severe stenosis were misrecognized. The value of TCD and CTA in detecting stenosis in vertebral

basilar artery blood vessels was compared. The coincidence rate of mild stenosis was 43.75%, moderate stenosis coincidence rate was 66.67%, severe stenosis coincidence rate was 80.00%, and the negative coincidence rate was the highest. However the missed diagnosis of moderate stenosis and severe stenosis by TCD were 5 and 3 respectively.

Table 2: Analysis of TCD reliability

Blood vessel	Sensitivity	Specificity	positive predictive values	negative predictive values	Positive likelihood ratio	Negative likelihood ratio	Kappa values
SCA	82.35	97.64	85.00	95.38	31.29	0.27	0.76
MCA	90.91	97.89	96.15	94.90	43.18	0.09	0.90
ACA	79.17	98.41	90.48	96.12	49.88	0.21	0.82
VA	71.43	97.67	83.33	95.45	30.71	0.29	0.74
BA	54.55	96.88	75.00	92.54	17.45	0.47	0.58
PCA	57.14	97.79	72.73	95.68	25.90	0.11	0.61

2.3 CDUS detection of extracranial vessels

A total of 450 extracranial vascular stenosis (CCA, ICA, VA) was found in 75 LAA patients. CDUS found 72, CTA found 90, consistent with the CTA 62, see table 3.Detector consistency of ICA by CDUS was the highest, on the basis of statistical method. The sensitivity of CDUS in VA the worst,and Kappa value is the lowest, suggesting that detection effect of CDUS on the circulation of blood vessel is poor. Therefore, there is less chance of getting reliable positive results (see Table 4). X2 values of matched pairs of enumeration data (CCA, ICA, VA) were 0.44, 0.36, 6.72, respectively, indicating that the reliability of CDUS in detecting stenosis in CTA is general and consistency of CDUS in vertebral artery check is poor. (p-value 0.008<0.05) Coincidence rate the negative coincidence rate of 97.22% is acceptable, moderate stenosis detection is 72.41% and severe stenosis detection is 85.71%,a relatively high rate. 4 cases in 28 patients with severe stenosis was misdiagnosed as non-stenosis by CDUS.

2.4 The distribution of blood vessels in the lesions of intracranial external artery stenosis

In 90 cases of LAA, 75 cases of vascular stenosis were found by CTA, 15 cases were found normal, so the total abnormal rate was 78.94% (75/90). A total of 1275 blood vessels were examined in 75 patients with LAA, among them, 450 extracracranial vessels, 825 intracranial vessels, and cerebrovascular stenosis was discovered in 242 vessels. However, subclavian artery stenosis detected in four branches by ultrasound was not included in our study as CTA did not enclose the subclavian artery. Intracranial artery stenosis rate is 148, accounting for 61.15% of all the 242 vessels with lesions, which is higher than that in extracranial artery vessels (90/242). Extracranial stenosis which was found in ICA branches was up to 46, accounting for 51.11% of extracranial artery stenosis, and the amount of vessels affected with stenosis in CCA and VA was the same. Intracranial stenosis which had been found in ICA branches was as high as 55, accounting for 37.16%(55/148) of intracranial artery stenosis, followed by SCA and ACA. The middle cerebral artery was found to be with moderate and severe stenosis in the cerebral artery (see Table 5).

3 Discussion

This paper takes CTA as the diagnostic standard. The examination results indicate that TCD and CTA have good consistency in the detection of intracranial stenosis, especially in the case of MCA, and the results are consistent with those in Guan Jingxia's research.[17] In this paper, the statistical analysis results show that the rate of compliance is lower than that of the anterior circulation, which is related to the anatomical structure of vertebral artery and basilar artery. All the cases in our research were diagnosed as LAA, which

carries higher incidence rate of vascular stenosis as well as detection rate. Most CTA patients received CTA examination to consummate the TCD and CDUS examination, only to increase the detection rate of stenosis.

Table 3: CDUS detection of stenosis in 75 cases of LAA

CDUS	CTA								
	CCA		Total	ICA		Total	VA		Total
	Positive	Negative		Positive	Negative		Positive	Negative	
Positive	16	3	19	39	4	43	7	3	10
Negative	6	125	131	7	100	107	15	125	140
Total	22	128	150	46	104	150	22	128	150

Table 4: Analysis of the reliability of CDUS in the detection of intracranial vascular

Blood vessel	Sensitivity	Specificity	positive predictive values	Negative predictive values	Negative likelihood ratio	Positive likelihood ratio	Kappa values
CCA	97.66	72.73	95.42	84.21	0.28	31.03	0.75
ICA	96.15	84.78	93.46	90.7	0.16	22.04	0.82
VA	98.48	38.89	92.2	77.78	0.62	25.67	0.38

Table 5: The distribution of intracranial-external artery stenosis in different degrees

Degree of stenosis	External artery stenosis				Intracranial artery stenosis						
	CCA	ICA	VA	Total	SCA	MCA	ACA	VA	BA	PCA	Total
Mild	12	16	5	33	4	6	8	8	5	3	34
Moderate	8	10	11	29	12	21	9	4	6	5	57
Severe	2	19	7	28	7	28	7	9	0	6	57
Total	22	46	22	90	23	55	24	21	11	14	148

This study made a comparative analysis of CDUS and CTA. The consistency of CDUS is generally consistent with Ben Lin.[18] The results also showed that the rate of misdiagnosis in CDUS was higher in VA, and the detection effect of CDUS on the posterior circulation was less than that of CTA, which was consistent with the conclusion of Zhang Chen.[19] CCA are reportedly more likely to be narrow, and a larger further study results are advisable to verify the result. In our research, CDUS, with high negative coincidence rate, could serve as a good screening method.

Vascular ultrasound in diagnosis of arterial stenosis is influenced by multi factors. In addition to instruments factors, it still happens for the chances of recanalization for occluded blood vessel within 2-7 days since the onset of cerebral infarction. TCD and CDUS will be affected by human factors. TCD detection was performed by the technician with many years of experience in our department. Compared with CTA, we could get a better consistency. CDUS detection is completed by the Department of ultrasound, and neck vascular ultrasound examination is performed by many technicians. Therefore, it is difficult to determine the consistency of detection level, imposing impact on the result of CDUS as well. Smoking has been demonstrated as arterial risk factors in a number of studies, while this study did not achieve good results regarding their relationship. It may be correlated with sample bias due to differences in population and region.

The distribution of intracranial vascular stenosis was not consistent with the study[20,21] in Tan group, but consistent with the research by Wang Puqing, et al,[22] which may be associated with geographical, risk factors, detection means and objects of the study.

In summary, hypertension, type 2 diabetes are risk factors for the occurrence of stenosis in LAA. The consistency of TCD in detecting intracranial vascular stenosis is fair, but MCA provides the highest reliability. In our experiment, blood vessels in MCA part are the most common place for the incidence of stenosis. Negative coincidence rate of TCD detection was higher, which could be used for narrow screen. The reliability of TCD was slightly higher than that of moderate and severe stenosis. The detection of anterior circulation lesions by CDUS is better than circular lesions. Evaluation effect on severe stenosis in examination is better than that on mild stenosis. Extracranial ICA stenosis ratio was the highest, but it carried poor value in detecting stenosis in VA. Our study indicated that intracranial segment of vascular was a more common area for the incidence of stenosis than that in the outer segment of the artery.

Conflicts of Interest Disclosure

The authors have no conflict of interest related to this article.

References

[1] Bousser MG. Stroke prevention: an update [J]. Front Med, 2012, 6(1): 22-34.

[2] Liu L, Wang D, Wong KS, et al. Stroke and stroke care in China: huge burden, significant workload, and a national priority [J]. Stroke, 2011, 42(12): 3651-3654.

[3] Skutta B, FurstG, E ilers J, et al. Intracranial steno-Occlusive disease: double detector helical CTA versus digital subtraction angiography [J].A- JNR Am JN eurorad io.l 1999, 20(5): 791-799.

[4] Zhao L, Barlinn K, Sharma VK, et al. Velocity criteria for intracranial stenosis revisited: an international multicenter study of transcranial Doppler and digital subtraction angiography [J]. Stroke, 2011, 42(12): 3429-3434.

[5] Sebastian J, Derksen C, Khan K, et al. The role of transcranial Doppler embolic monitoring in the management of intracranial arterial stenosis [J]. J Neuroimaging, 2011, 21(2): e166-168.

[6] Uzunca I, Asil T, Balci K, et al. Evaluation of vasomotor reactivity by transcranial Doppler sonography in patients with acute stroke who have symptomatic intracranial and extracranial stenosis[J]. J Ultrasound Med, 2007, 26(2): 179-185.

[7] Reinsfelt B, Westerlind A, Ioanes D, et al. Transcranial Doppler microembolic signals and serum marker evidence of brain injury during transcatheter aortic valve implantation [J]. Acta Anaesthesiol Scand, 2012, 56(2): 240-247.

[8] Itoh S, Suda K, Kishimoto S, et al. Microembolic signals measured by transcranial Doppler during transcatheter closure of atrial septal defect using the Amplatzer septal occlude [J]. Cardiol Young, 2011, 21(2): 182-186.

[9] Nemoto S. [Diagnostic imaging of carotid stenosis: ultrasound, magnetic resonance imaging, and computed tomography angiography [J]. Nihon Geka Gakkai Zasshi, 2011, 112(6): 371-376.

[10] Rodriguez G, Arnaldi D, Campus C, et al. Correlation between Doppler velocities and duplex ultrasound carotid cross-sectional percent stenosis [J]. Acad Radiol, 2011, 18(12): 1485-1491.

[11] Kyriacou EC, Pattichis C, Pattichis M, et al. A review of noninvasive ultrasound image processing methods in the analysis of carotid plaque morphology for the assessment of stroke risk [J]. IEEE Trans Inf Technol Biomed, 2010, 14(4): 1027-1038.

[12] Zaiying Lu, Nanshan Zhong. Internal Medicine [M]. Beijing: People's Medical Publishing House, 2008: 812.

[13] Simonato L,Agudo A,Ahrens W, et al. Lung cancer and cigarette smoking in Europe: an update of risk estimates and an assessment of inter-country heterogeneity [J]. Int J Cancer, 2001, 91(6): 876-887.

[14] Cerebrovascular Disease Control Guide (trial version) by editing committee of Chinese guidelines for prevention and treatment of cerebrovascular disease. Beijing: People's Medical Publishing House, 2007: 12-13.

[15] Yang Hua. Ultrasound of the neck and peripheral blood vessels [M]. Beijing: People's Military Medical Press, 2010: 20-21.

[16] The North American Symptomatic Carotid Endarterectomy Trial Steering Committee (NASCET).North American Symptomatic Carotid Endarterectomy Tria:1 methods, patients' characteristics and progress. Stroke, 1991, 22(6):711-20.

[17] Jingxia Guan, Shaofeng Zhang, Qin Zhou, Xinghan Huang, Zuneng Lu. A study on the diagnostic accuracy of TCD for intracranial arterial stenosis in patients with acute ischaemic stroke. Stroke and Nervous Diseases, 2013, (03): 141-145.

[18] Ben Lin, Guoguang Liu. Comparison between color Doppler Ultrasound and digital subtraction angiography in detecting extracranial carotid artery stenosis. South China Journal of Cardiovascular Diseases, 2014, (04): 508-511.

[19] Chen Zhang, Min Zhang. The clinical application in the diagnosis of cervical artery vascular lesions [J]. China Medical Engineering, 2014, (01):153.

[20] Yuan Liu. Characteristics and risk factors of intracranial atherosclerotic stenosis and occlusion. Neurology, 2011.

[21] Qun Tan. Study of distributing of cerebrovascular stenosis and its risk factor based on DSA in patients with ischemic cerebrovascular Disease. Kangning Chen, Neurology, 2014.

[22] Puqing Wang, Anping Wang, Zhihua Cao, et al. Study on the distribution of cerebral artery stenosis in patients with ischemic cerebrovascular disease by 64 slice CT [J]. Chinese Journal of Geriatric Heart Brain and Vessel, 2011, (11): 1004-1007.