Assessment of the value of 3D-DSA combined with neurointerventional thrombolysis in the treatment of senile cerebrovascular occlusion

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Abstract. Assessment of the value of three-dimensional digital subtraction angiography (3D-DSA) combined with neurointerventional thrombolysis in the treatment of senile cerebrovascular occlusion was investigated. A total of 129 patients with senile cerebrovascular occlusion admitted to the Affiliated Hospital of Zunyi Medical University from August 2015 to September 2017 were collected. Among them, 69 patients who underwent neurointerventional catheter thrombolysis under 3D-DSA were included in the study group, and 60 patients treated with neurointerventional thrombolysis were the control group. The levels of inflammatory cytokines IL-6, IL-1β and IL-8 in the two groups were measured by enzyme linked immunosorbent assay (ELISA) before treatment (T0), 7 days (7d) after treatment (T1) and 14 days (14d) after treatment (T2). The score of the National Institute of Health Stroke Scale and the clinical efficacy of patients in the two groups were compared before and after treatment, and Barthel index (BI) was used for investigation before and after treatment. The recurrence rate of disease in the two groups within 1 year was recorded. At T1, IL-6, IL-1β and IL-8 in the study group were significantly lower than those in the control group (P<0.05). The NIHSS score in the study group was lower than that in the control group after treatment (P<0.05). The BI score in the study group was significantly higher than that in the control group after treatment (P<0.05). After the prognostic follow-up, the disease recurrence rate of the study group was significantly lower than that of the control group (P<0.05). In conclusion, 3D-DSA combined with neurointerventional thrombolysis can significantly reduce the expression of inflammatory cytokines and improve the quality of life in patients with cerebrovascular occlusion, which has a high clinical value.

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Introduction

Cerebrovascular occlusion is a common disease of elderly people, which poses a great threat to human life (1) and has a great impact on patients' quality of life (2). Cerebral infarction is caused by cerebral vascular occlusion, which needs timely opening of the blood vessels to make blood vessel flow normal, thus to achieve the purpose of treatment (3,4). Thrombolysis is a common treatment method for cerebrovascular occlusion in clinical practice and an important way of opening occlusive cerebral vessels (5). With the progress of clinical medicine in recent years, interventional therapy has also been widely used in clinical practice, providing a new method for cerebral vascular occlusion (6). This was confirmed in the studies of Tian *et al* (7) and Lei *et al* (8). However, Rao *et al* (9) achieved a better effect than conventional treatment when they applied interventional therapy to the treatment of aneurysms. Therefore, interventional therapy has gradually become the first choice for clinical treatment of cerebrovascular diseases (10). With the wide application of interventional therapy, however, its disadvantages are gradually exposed. For example, improper selection of puncture site may not only result in ineffective treatment, but also cause aggravation of the disease (11), and it is particularly important for the more complex structure of the brain vascularity when selecting puncture site. Therefore, in order to improve the efficacy of interventional therapy, the relevant auxiliary examinations are the key to treatment.

Three-dimensional digital subtraction angiography (3D-DAS) is an extremely effective detection method (12), which digitizes X-ray images taken before and after the contrast agent to obtain a clear vascular image (13). Compared with traditional X-ray examination, 3D-DAS has the characteristics of high resolution, short examination time and less use of contrast agent, which is particularly suitable for the organization of vascular tissues (14). At present, there are few studies on the application of 3D-DAS combined with

interventional therapy in the treatment of cerebral vascular occlusion, and its clinical application prospect cannot be determined. Therefore, this investigation provides a reliable reference for the future clinical treatment of such diseases by comparing the use of 3D-DSA combined with interventional therapy and simple interventional therapy for patients with cerebrovascular occlusion.

Patients and methods

General data. A total of 129 patients with senile cerebrovascular occlusion admitted to the Affiliated Hospital of Zunyi Medical University (Zunyi, China) from August 2015 to September 2017 were collected as the study subjects. Among them, 69 patients who underwent neurointerventional catheter thrombolysis under 3D-DSA were included in the study group, with an average age of 61.6±4.5 years. The 60 patients treated with neurointerventional thrombolysis were included in the control group, with an average age of 62.2±4.8 years.

The study was approved by the Ethics Committee of Affiliated Hospital of Zunyi Medical University. Patients who participated in this research had complete clinical data. Signed informed consents were obtained from the patients or the guardians.

Inclusion and exclusion criteria. Inclusion criteria: patients met the diagnostic criteria for cerebral vascular embolization, patients diagnosed with cerebral vascular embolization after a series of examinations in the hospital, patients treated in the hospital after diagnosis and patients with complete data and who agreed to cooperate with the investigation of medical staff.

Exclusion criteria: Patients complicated with multiple tumors, patients complicated with other cardiovascular and cerebrovascular diseases, patients complicated with autoimmune diseases, patients suffering from infectious diseases, mental disorders, other organ dysfunction, and physically disabled patients who were unable to take care of themselves.

Therapies. Patients in the control group were punctured in the manner of Seldinger and then placed a guide catheter close to the diseased vessel. The patients were injected with urokinase (Guangdong Techpool Biochemical Medicine Co., Ltd.; H44024032, 10,000 units) 200,000 units + 20 ml normal saline mixture. Fifty milliliters normal saline + 200-500,000 units urokinase was pumped into the patients with a micro-pump catheter at a rate of 1 ml/min. Both groups were re-examined with skull CT 24 h after treatment. If no bleeding changes were found, patients were given aspirin enteric-coated tablets (Shenyang Original Pharmacolabo Co., Ltd.; SFDA approval no. H20065051, 50 mg/tablet) at a dose of 100 mg. Patients in the study group were treated with neurointerventional thrombolysis under 3D-DSA: Local anesthesia was used with the assistance of 3D-DSA (Siemens) to puncture and intubate the femoral artery on the right side of patients, and the artery sheath was inserted. The whole cerebral vascular angiography was performed with a digital subtraction angiography to determine the specific location of the occluded blood vessel, and the subsequent procedure was consistent with the control group.

Detection methods. Enzyme linked immunosorbent assay (ELISA) was used to detect the levels of inflammatory cytokines IL-6, IL-1β and IL-8 in the two groups before treatment (T0), 7 days (7d) after treatment (T1) and 14 days (14d) after treatment (T2). The operation process was strictly in accordance with the kit instructions.

Observational indexes. Main indicators: ELISA was used to detect the levels of inflammatory cytokines IL-6, IL-1β and IL-8 in the two groups before treatment (T0), 7d after treatment (T1) and 14d after treatment (T2). The NIHSS score was used to score the neurological deficits and compare the clinical efficacy of the two groups before and after surgery. The National Institutes of Health Stroke Scale was used for NIHSS score (15). At 14d after treatment, the efficacy assessment standard for stroke was formulated by referring to the '4th national academic conference on cerebrovascular diseases' (16). The incidence of adverse reactions after treatment was compared between the two groups.

Secondary observational indexes: Barthel index (BI) was used for investigation before and after treatment (17). Patients in both groups were followed up for 1 year for prognosis, and the recurrence rate of disease in both groups was recorded within 1 year.

Statistical methods. In this study, SPSS 20.0 (IBM Corp.) medical statistical analyzer was used for statistical analysis of collected data. GraphPad Prism 7 (GraphPad Software Co., Ltd.) was used to image rendering of the collected data. Utilization of enumeration data (%) was qualified by the Chi-square test and represented by χ^2. The measurement data were expressed by mean ± standard deviation (mean ± SD). All the measurement data were in normal distribution. The independent sample t-test was used for comparison between the two groups, and comparison in group was qualified by paired t-test and expressed by t. $P<0.05$ was considered statistically significant.

Results

Comparison of general data. There were no differences in sex, age, BMI, nitric oxide sythase (NOS), endothelin-1 (ET-1) pg/ml, vascular endothelial growth factor (VEGF) pg/ml, 50 sec hemodynamics (SRV) mPa/sec, living environment, smoking history, drinking history, family medical history or ethnicity ($P>0.05$) (Table I).

Levels of inflammatory cytokines IL-6, IL-1β and IL-8 of patients in the two groups before treatment (T0), 7d after treatment (T1) and 14d after treatment (T2). There were no significant differences in levels of inflammatory cytokines IL-6, IL-1β, IL-8 of patients in the two groups ($P>0.05$). After 7d of treatment, levels of IL-6, IL-1β, IL-8 in the study group were all lower than the control group ($P<0.05$). After 14d of treatment, levels of IL-6, IL-1β and IL-8 were all lower than these of 7d after treatment, and levels of IL-6, IL-1β and IL-8 were lower in the study group than the control group after 14d of treatment ($P<0.05$) (Fig. 1).

Comparison of NIHSS scores of the two groups before and after treatment. NIHSS score was used to score neurological

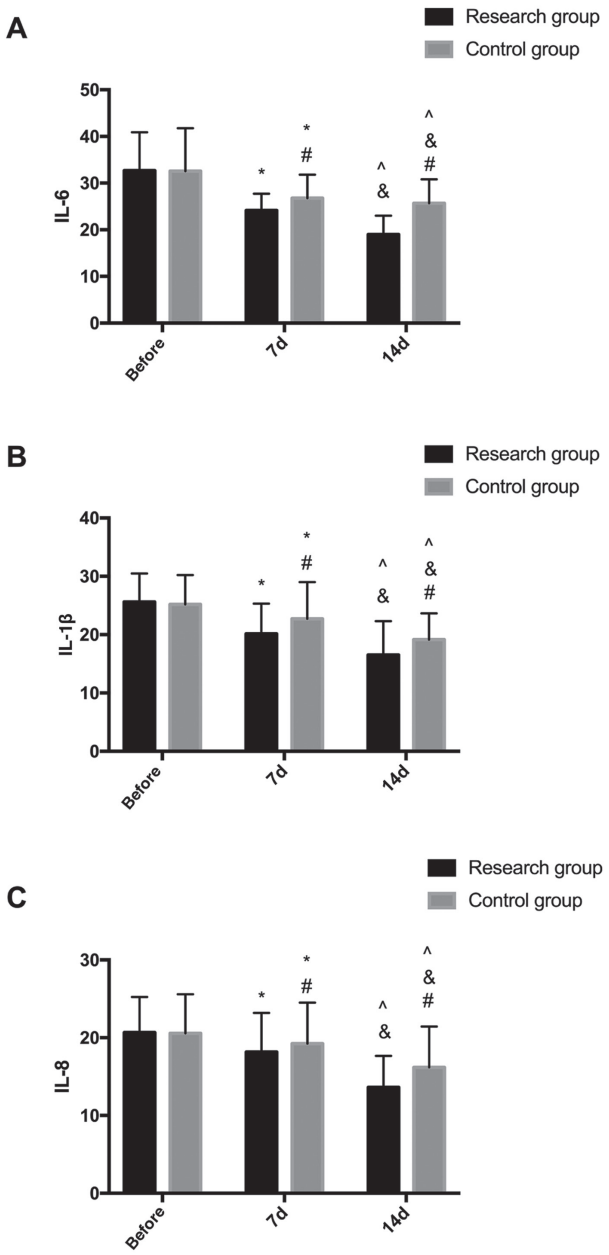

Figure 1. (A) Changes of inflammatory cytokine IL-6 level before treatment (T0), 7d after treatment (T1) and 14d after treatment of patients in the two groups. (B) Changes of inflammatory cytokine IL-1β level before treatment (T0), 7d after treatment (T1) and 14d after treatment of patients in the two groups. (C) Changes of inflammatory cytokine IL-8 level before treatment (T0), 7d after treatment (T1) and 14d after treatment of patients in the two groups. *P<0.05 compared with before treatment; #P<0.05 compared with study group; ^P<0.05, 14d after treatment compared with 7d after treatment; &P<0.05 14d after treatment compared with before treatment.

defects before and after surgery. The results showed that there was no significant difference in NIHSS score between the two groups before treatment (P>0.05). After treatment, NIHSS scores of the two groups at the four time periods (2 h, 1d, 7d and 14d after treatment) were significantly lower than those before treatment, with statistically significant differences (P<0.05). The improvement of NIHSS score in the study group was significantly better than that in the control group, and the difference was statistically significant (P<0.05) (Fig. 2).

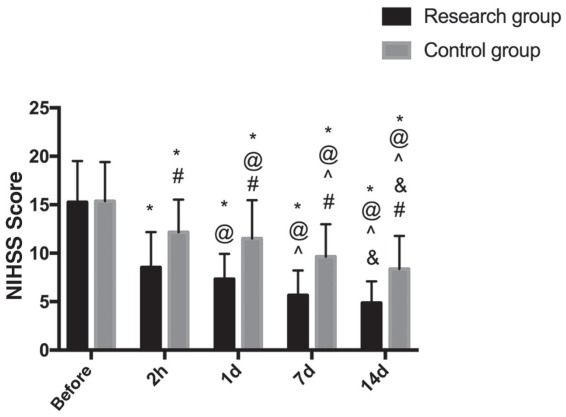

Figure 2. The NIHSS scores before treatment in four time periods (2 h, 1d, 7d and 14d) after treatment in the two groups were compared. *P<0.05 compared with before treatment; @P<0.05 compared with 2 h after treatment; ^P<0.05 compared with 1d after treatment; &P<0.05 compared with 7d after treatment; #P<0.05 compared with the study group of the same time.

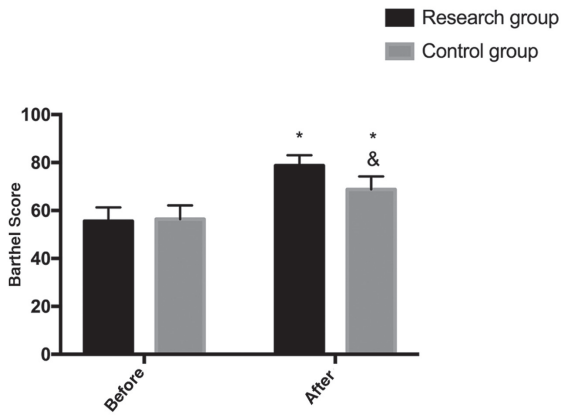

Figure 3. Comparison of Barthel index score between the two groups. *P<0.05 compared with before treatment; &P<0.05 compared with study group.

Clinical efficacy of two groups of patients. The clinical efficacy of the two groups of patients was compared, and the results showed that the marked efficiency rate of the study group was significantly higher than that of the control group on 14d after treatment (P<0.05), and the difference in the total efficiency of the two groups was not statistically significant (P>0.05) (Table II).

Comparison of Barthel index score between the two groups. There was no significant difference in Barthel index score between the two groups before treatment (P>0.05), while Barthel index score after treatment was higher than that of the control group (P<0.05) (Fig. 3).

Disease recurrence rate within 1 year in the two groups. Patients in the two groups were followed up for one year, and 120 patients were successfully followed up, with a follow-up success rate of 93.02%. Among them, there were 3 patients lost to follow-up in the study group and 6 patients in the control group. The one-year disease recurrence rate of the two groups was compared, and it was lower in the study group than the control group (P<0.05) (Table III).

Table I. Comparison of general data of patients in the two groups (%).

	Research group (n=69)	Control group (n=60)	t or χ^2	P-value
Age (years)	61.6±4.5	62.2±4.8	0.732	0.465
Sex			0.305	0.581
Male	48 (69.57)	39 (65.00)		
Female	21 (30.43)	21 (35.00)		
BMI (kg/cm^2)	31.52±5.05	30.86±4.72	0.763	0.447
Nitric oxide synthase (NOS) U/ml	0.821	0.413		
	24.16±3.58	23.62±3.89		
Endothelin-1 (ET-1) pg/ml	0.751	0.454		
	92.04±3.54	91.57±3.55		
Vascular endothelial growth factor (VEGF) pg/ml	0.572	0.569		
	306.65±32.87	309.87±30.75		
50 sec hemodynamics (SRV) mPa/sec	0.919	0.360		
	6.23±0.32	6.17±0.42		
Living environment			0.688	0.407
City	59 (85.51)	48 (80.00)		
Countryside	10 (14.49)	12 (20.00)		
Smoking history			0.011	0.915
With	34 (49.28)	29 (48.33)		
Without	35 (50.72)	31 (51.67)		
Drinking history			1.805	0.179
With	38 (55.07)	40 (66.67)		
Without	31 (44.93)	20 (33.33)		
Family medical history			0.736	0.391
With	9 (13.04)	5 (8.33)		
Without	60 (86.96)	55 (91.67)		
Ethnicity			2.956	0.086
Han	59 (85.51)	66 (94.29)		
Minority	10 (14.49)	4 (5.71)		

Discussion

Cerebrovascular occlusion is the main cause of cerebral infarction (18), its disability rate and death rate remain high (19). At present, the main clinical treatment for elder cerebral vascular occlusion is neurointerventional thrombolysis. Although neurointerventional thrombolysis has a significant therapeutic effect on vascular diseases (20), deficiencies of this method are also very significant. For example, if the puncture point and the puncture path are artificially selected, there may be deviations which have certain risks for the complicated tissue of the blood vessel. It not only causes secondary injury to the patient, but also causes more serious vascular occlusion (21). Therefore, how to accurately implement neurointerventional thrombolysis is the key and difficult point of treatment of cerebrovascular diseases. As shown in this study, treatment with 3D-DSA assisted neurointerventional thrombolysis is of great significance for future clinical practice.

The results showed that the levels of inflammatory cytokines IL-6, IL-1β and IL-8 in the patients after 3D-DSA combined with neurointerventional thrombolysis were significantly lower than those in the patients treated with neurointerventional thrombolysis alone. This suggests that 3D-DSA combined with neurointerventional thrombolysis can reduce the inflammation caused by vascular occlusion in patients more effectively. Suzuki *et al* (22) aiming at the application of reconstruction techniques in the diagnosis and treatment of cerebral aneurysms have shown that 3D-DSA images are excellent for cerebral aneurysms, and the levels of inflammatory cytokines are well controlled after treatment. Therefore, it is speculated that 3D-DSA can make the puncture more accurate and the intervention channel better when performing cerebral vascular occlusion surgery, bringing less stress injury and, thus to reduce inflammatory cytokines. The NIHSS scores of the two groups of patients before and after treatment were compared, and the results showed that the improvement of NIHSS scores of the patients treated with 3D-DSA combined with neurointerventional thrombolysis was significantly better than that of the patients treated with neurointerventional thrombolysis alone. This suggests that the use of 3D-DSA assisted neurointerventional thrombolysis is more beneficial to the protection of neurological function and improvement of

Table II. Comparison of clinical efficacy between the two groups.

Groups	No. of cases	Cure	Significant effect	Effective	Invalid	Deterioration	Marked efficiency rate	Total effective rate
Research group	69	17 (24.64)	20 (28.99)	15 (21.97)	10 (14.49)	7 (10.14)	24.64%	75.36%
Control group	60	6 (10.00)	21 (35.00)	15 (25.00)	10 (16.67)	8 (13.33)	10.00%	70.00%
χ^2							4.694	0.467
P-value							0.030	0.495

Table III. Comparison of disease recurrence rate within 1 year in two groups.

	Research group (n=66)	Control group (n=54)	χ^2	P-value
Recurrence	7 (10.61)	14 (25.93)	4.828	0.028
Without recurrence	59 (89.39)	40 (74.07)		

prognosis of patients. Then the therapeutic effect of the two groups of patients was observed, and the marked effective rate of using 3D-DSA as an adjuvant therapy was significantly higher than that of the patients treated with neurointerventional thrombolysis alone, indicating that the use of 3D-DSA as an adjuvant therapy has good clinical value and is worthy of popularization. In assessing the accuracy and practicability of 3D-DSA and 3D-CT angiography for cerebral aneurysms Ishida *et al* (23) revealed that 3D-DSA has a higher diagnostic accuracy, which was conducive to carry out more effective follow-up treatment for the disease, with better therapeutic effect. This supports our experimental results. We speculate that in the treatment of senile cerebrovascular occlusion, it is precisely because 3D-DSA is detected at any angle in the brain, which greatly improves the detection efficiency, so that the neurointerventional thrombolysis can be performed more effectively and accurately, and the therapeutic effect can be improved. The study of Muruet *et al* (24) investigating neurointerventional thrombolytic therapy for ischemic stroke shows that thrombolytic therapy can improve long-term survival rate and functional status after ischemic stroke, its Barthel index is also consistent with this study. Whereas, in the present study, the curative effect of 3D-DSA- assisted neurointerventional thrombolysis is better than that of neurointerventional thrombolysis, so the Barthel index of patients under 3D-DSA-assisted therapy is also higher. The patients were followed up for one year, and the one-year disease recurrence rate of patients after 3D-DSA was significantly lower than that of patients treated with neurointerventional thrombolysis. This suggests that 3D-DSA adjuvant therapy has a good prognosis for senile cerebrovascular occlusion. In future clinical practice, patients with senile cerebrovascular occlusion can be treated by 3D-DSA combined with neurointerventional thrombolysis.

However, we did not make a comparative study on 3D-DSA combined with other therapeutic methods, and it is still unclear whether 3D-DSA combined with other therapeutic methods have the same efficacy in treating senile cerebrovascular occlusion. As the number of subjects in this study is small and the research period is short further study is required.

In conclusion, 3D-DSA combined with neurointerventional thrombolysis in patients with cerebrovascular occlusion can significantly reduce the expression of inflammatory cytokines, improve quality of life, and has a high clinical value.

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Availability of data and materials

The datasets used and/or analyzed during the present study are available from the corresponding author on reasonable request.

Authors' contributions

SJ observed and compared the levels of inflammatory cytokines and wrote the manuscript. LG and ZW conceived and designed the study. LZ and JH were responsible for the collection and analysis of the experimental data. BT and SY interpreted the data and drafted the manuscript. SJ and ZW revised the manuscript critically for important intellectual content. All the authors read and approved the final manuscript.

Ethics approval and consent to participate

The study was approved by the Ethics Committee of Affiliated Hospital of Zunyi Medical University (Zunyi, China). Patients who participated in this research had complete clinical data. Signed informed consents were obtained from the patients or the guardians.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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