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Original Article

Efficacy of neurointerventional therapy in patients with ischemic stroke and risk factors affecting cognitive function recovery

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Abstract: Objective: To investigate the efficacy of neurointervention combined with intravenous thrombolysis in ischemic stroke patients and the risk factors affecting cognitive function recovery. Methods: A total of 114 patients with acute ischemic stroke (AIS) treated in Baoji People's Hospital from January 2017 to December 2020 were retrospectively selected and divided into an observation group and a control group according to different treatment methods. The observation group was treated with neurointervention + intravenous thrombolysis (n = 64), and the control group underwent intravenous thrombolysis (n = 50). The efficacy, recanalization rate, incidence of adverse events, National Institutes of Health Stroke Scale (NIHSS) score, Mini-Mental State Examination (MMSE) score and modified Rankin Scale (mRS) score were evaluated and compared between the two groups. Patients were further divided into a cognitive dysfunction group and a non-disorder group according the MMSE score after treatment, and logistics regression was used to analyze the risk factors of cognitive dysfunction. Results: The overall response rate and the total recanalization rate of the observation group were significantly higher than those of the control group (both $P < 0.05$). Compared with those before operation, the NIHSS score at 7 d after operation and the mRS score 3 months after operation decreased, while the MMSE score increased in both groups ($P < 0.05$). The postoperative NIHSS score and mRS score were lower and MMSE score was higher in the observation group than those in the control group ($P < 0.05$). No significant difference was identified in the incidence of adverse events between the two groups ($P > 0.05$). Logistics regression analysis revealed that age, diabetes mellitus, hyperlipidemia and lesions at critical sites were independent risk factors for cognitive impairment in patients with AIS. Conclusion: Interventional thrombectomy combined with intravenous thrombolysis is effective in the treatment of cerebral infarction. This regimen can reduce neurological deficits and improve the recanalization rate. In addition, age, diabetes, hyperlipidemia and lesions at critical sites are independent risk factors for the development of cognitive impairment in AIS patients.

Keywords: Neurointervention, intravenous thrombolysis, ischemic stroke, cognitive function, risk factors

Introduction

The prevalence and incidence of stroke are increasing as reported by the Global Burden of Disease Report 2017, accounting for 4.3% of the total global burden of disease [1, 2]. As one of the major chronic diseases threatening human health and the first cause of death and disability in China, stroke has five major characteristics: high morbidity, high disability rate, high mortality, high recurrence rate and high economic burden [3]. At present, there are more than 13 million stroke patients over 40 years old in China. Surveys have shown [4] that the incidence of cerebrovascular events in China is expected to increase by 50% over the number of patients in 2010 by the year 2030. A positive correlation was observed between the incidence of stroke and the rise of age, especially for people over 50 years old [5]. Underlying diseases including hypertension, diabetes, dyslipidemia and atrial fibrillation are the main risk factors for stroke, and the prevalence of those diseases is also highly relevant to the increase of age. Increased occurrence of cardiovascular disease was inevitable because elderly people tend to have low basal metabolic rate, reduced lean tissue and increased adipose tissue [6].

Patients with ischemic stroke should be given active and effective therapeutic intervention after the onset to avoid further damage on intracranial tissue caused by intracerebral ischemia and hypoxia [7]. At present, the main conventional treatment is intravenous thrombolysis, which can restore the blood supply and microcirculation of intracranial large artery lumen in patients. However, clinical practice has proven that intravenous thrombolysis alone also has shortcomings such as insignificant efficacy, difficulty in restoring blood supply to the intracranial ischemic area in a short period of time, and poor improvement of cognitive and limb motor functions in patients [8, 9]. With the rapid development of modern medicine, interventional therapy has become an important treatment in neurology, and mechanical thrombectomy is regarded as a critical treatment for cerebral infarction [10]. However, there are relatively few reports on the combined use of interventional therapy and intravenous thrombolysis, especially the clinical data on improving the neurological function of patients.

As the mortality of stroke decreases, the number of stroke survivors with cognitive impairment has increased [11]. Approximately 10% patients had dementia before the first stroke, 10% developed dementia shortly after the first stroke, and about 33% developed dementia after repeated strokes [12]. Cognitive impairment diagnosed during the recovery period seriously affects the life quality and life span of stroke patients and burdens their families psychologically and economically [13]. Due to the uncontrollable risk factors for cognitive impairment after stroke, study of intervening factors of cognitive impairment after stroke has become a hot topic in recent years.

In this study, we aimed to analyze the effect of neurointervention combined with intravenous thrombolysis on ischemic stroke and the risk factors affecting the recovery of cognitive function, so as to provide a reference for the treatment of clinical ischemic stroke patients and the prevention of cognitive dysfunction.

Methods and materials

Clinical data

A total of 114 patients with acute ischemic stroke (AIS) treated in Baoji People's Hospital from January 2017 to December 2020 were retrospectively selected and divided into an observation group and a control group according to different treatment methods. The observation group was treated with neurointervention + intravenous thrombolysis (n = 64), and the control group was treated with intravenous thrombolysis (n = 50). This study was approved by the medical Ethics Committee of Baoji People's Hospital.

Inclusion and exclusion criteria

Inclusion criteria: (1) patients who were diagnosed with acute cerebral infarction according to the *Chinese Guidelines for Early Endovascular Intervention for Acute Ischemic Stroke* [14] and brain CT examination; (2) patients with aged 30 to 75 years; (3) patients admitted within 6 h after onset; (4) patients with complete clinical data; (5) patients who was having the first episode.

Exclusion criteria: (1) patients with surgical history within 1 month; (2) patients with heart, liver, kidney or other organ diseases; (3) patients with cognitive impairment, affective disorders or other mental illness; (4) patients with intracranial hemorrhage or arteriovenous malformations; (5) patients with malignant tumors; (6) pregnant women; (7) patients with allergy or intolerance to anesthetic drugs, contrast agents, anticoagulant drugs or antiplatelet aggregation drugs.

Treatment regimens

Patients in the control group were treated with intravenous thrombolysis. The patients were given aspirin enteric-coated tablets (Diao Group Chengdu Pharmaceutical Co., Ltd., GYZZ H51022603) 100 mg/time, qd, po; Ozagrel sodium (Shandong Luoxin Pharmaceutical Group Co., Ltd., GYZZ H20043953) 75 mg/time, once a day, intravenous injection; alteplase (Boehringer Ingelheim Pharma GmbH & Co. KG, GYZZ SJ20160055) 0.9 mg/KG + 100 ml normal saline, intravenous injection of 10%

dose within 1 minute, and the remaining dose was intravenously infused within 1 h. Head CT was reexamined 24 h after thrombolysis was completed.

Patients in the observation group were treated with additional neurointerventional thrombectomy. First, the patients were generally anaesthetized, and the Rebar-27 microcatheter (EV3, USA) and Solitaire stent (EV3, USA) were used cooperatively to determine the location of emboli. Next, the stent was released to cover the emboli in the proximal third of the stent. Then, with its guide wire fixed, the stent was partially recovered and tightened, along with the microcatheter, to withdraw the guiding catheter. Reflux was formed while the liquid drip in the guiding catheter was stopped during the withdrawal of the stent. Finally, the recanalization of the vessel was observed with angiography. Repeated thrombectomy was performed if necessary.

Outcome measures

Main outcome measures: The National Institutes of Health Stroke Scale (NIHSS) score [15] was compared between the two groups before treatment and after 7 days of treatment, and the score ranged from 0 to 42, with higher scores representing severer neurological deficits. The modified Rankin Scale (mRS) score [16] was compared between the two groups before treatment and after 3 months of treatment, with a score of 0 to 5 points. A mRS score ≤ 2 indicated a good prognosis, and a score > 2 indicated a poor prognosis. Cognitive function was evaluated using the Mini-Mental State Examination (MMSE) score [17], with higher scores indicating milder cognitive dysfunction. According to the MMSE score, patients were divided into a cognitive dysfunction group and non-disorder group with a score of 27 as the cut-off value, and logistics regression was used to analyze the risk factors of cognitive dysfunction.

Secondary outcome measures: The clinical data of patients were recorded and compared between the two groups, as along with the incidence of intracranial hemorrhage and reperfusion injury within 14 days and death within 90 days. The recanalization rate (complete recanalization rate + partial recanalization rate) was accessed by reexamination of brain CT 48 h after operation. (1) Complete recanalization: after treatment, hemoperfusion was restored in ≥ 50% of ischemic lesions; (2) Partial recanalization: after treatment, hemoperfusion was restored in < 50% of ischemic lesions; (3) No recanalization: no significant change was observed in thrombus, or movement of thrombus was found.

Statistical analysis

Data were processed using SPSS 20.0 software. Normality test was performed first by Shapiro-Wilk method, and measurement data in accordance with normal distribution were expressed as mean ± standard deviation (Mean ± SD). Inter-group and intra-group comparisons were conducted with independent sample t-test and paired t-test, respectively. χ^2 test was used for comparison of enumeration data. Logistics regression was applied to determine prognostic factors affecting cognitive function, and receiver operating characteristic (ROC) curve was used to analyze the efficacy of risk factors in affecting the cognitive function in patients. $P < 0.05$ indicated statistical significance.

Results

Comparison of baseline data

Comparison of the clinical data showed that there was no statistical difference in age, sex, body mass index, time from onset to admission, medical history and lesions at critical sites between the two groups ($P > 0.05$, **Table 1**).

Comparison of postoperative recanalization rate

By comparing the recanalization rate between the two groups, it was found that the observation group held a higher rate of recanalization than the control group did ($P < 0.05$, **Table 2**).

Comparison of NIHSS and mRS scores between the two groups

The NIHSS and mRS scores of the two groups were both identified to be reduced evidently after treatment ($P < 0.001$, **Figure 1**). Further comparison showed that the deceases in the observation group were more significant than those in the control group ($P < 0.01$, **Figure 1**).

Table 1. Comparison of baseline data

Variable	Control Group (n = 50)	Observation group (n = 64)	x^2 value	*P* value
Age			0.269	0.603
≥ 60 years	29	34		
< 60 years	21	30		
Sex			0.837	0.360
Male	27	40		
Female	23	24		
BMI			0.381	0.536
≥ 25 kg/m^2	20	22		
< 25 kg/m^2	30	42		
Time from onset to admission			1.790	0.181
≥ 6 h	25	24		
< 6 h	25	40		
Medical history				
Diabetes	24	27	0.383	0.535
Hyperlipidemia	18	20	0.285	0.593
Lesions at critical sites			0.080	0.776
Critical site	19	26		
Non-critical site	31	38		

Note: Body Mass Index (BMI), frontal lobe, temporal lobe, base and thalamus are critical sites, while parietal lobe, occipital lobe, brainstem and cerebellum are non-critical sites.

Table 2. Comparison of postoperative recanalization rate

Group	Complete recanalization	Partial recanalization	No recanalization	Recanalization rate
Control Group (n = 50)	10 (20.00%)	28 (56.00%)	12 (24.00%)	38 (76.00%)
Observation Group (n = 64)	24 (37.50%)	34 (53.13%)	6 (9.37)	58 (90.63%)
x^2 value				4.515
P value				0.036

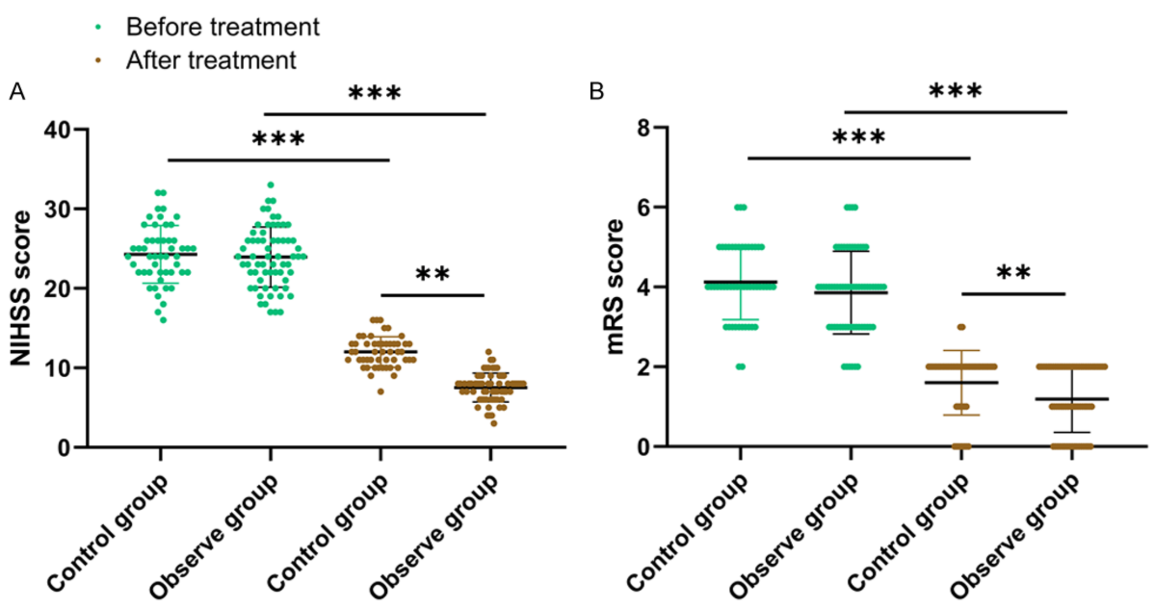

Figure 1. Comparison of NIHSS score and mRS score before and after treatment. A. Comparison of NIHSS score before and after treatment between the two groups. B. Comparison of mRS scores before and after treatment between the two groups. Note: ** indicates P < 0.01, *** indicates P < 0.001, National Institutes of Health Stroke Scale (NIHSS) score, modified Rankin Scale (mRS) score.

Table 3. Comparison of adverse reactions in patients

Group	Intracranial hemorrhage	Reperfusion injury	Death	Total incidence
Control Group (n = 50)	3 (6.00%)	3 (6.00%)	1 (2.00%)	7 (14.00%)
Observation Group (n = 64)	1 (1.56%)	1 (1.56%)	0 (0.00%)	2 (3.12%)
x^2 value				4.565
P value				0.032

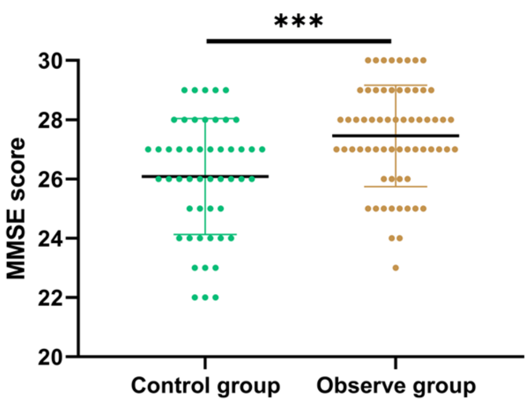

Figure 2. MMSE score after treatment was compared between the two groups. Note: *** means P < 0.001, Mini-Mental State Examination (MMSE).

Comparison of incidence of adverse events between the two groups

The control group had markedly higher incidence of adverse events than the observation group, with specific data presented in **Table 3** (P < 0.05).

Patient cognitive function comparison

By comparing the recovery of cognitive function between the two groups, it was found that the MMSE score after treatment was markedly higher in the observation group than that in the control group (P < 0.01, **Figure 2**).

Risk factors affecting cognitive function recovery

We divided patients into a cognitive dysfunction group and a non-disorder group according to MMSE score, with a score of 27 as the cut-off value. Univariate analysis revealed that age, time from onset to admission, diabetes, hyperlipidemia and lesions at critical sites were risk factors affecting cognitive function in patients (P < 0.05, **Table 4**). Subsequently, we performed multivariate logistics regression analysis after assigning values to the data (**Table 5**). It was found that age, diabetes, hyperlipidemia and lesions at critical sites were independent risk factors affecting cognitive function (P < 0.05, **Table 6**). In addition, we constructed a risk assessment score based on a logistics regression model (risk formula = -3.714 + 1.148 * age + 1.776 * diabetes + 1.818 * hyperlipidemia + 2.114 * lesions at critical sites), and ROC curve analysis revealed that using a risk score with an area under the curve of 0.954 to predict cognitive impairment in patients was an ideal model (**Figure 3**).

Discussion

Thrombolytic therapy with thrombolytic drugs is preferred clinically to restore the blood flow supply to the intracranial ischemic area and to prevent the aggravation of intracranial tissue injury of ischemic stroke patients [18, 19]. It has been reported that platelet adhesion to the injured vessel wall is a key step to form thrombus [20], which may lead to narrowing of the vessel lumen with the gradual increase of local carotid atherosclerotic plaques. As the disease progresses, it will further cause vascular obstruction and plaque rupture due to the increased stress of patient's arterial wall, thereby activating platelets after collagen exposure and causing coagulation in vivo, which eventually leads to thrombosis.

Alteplase is a highly effective thrombolytic drug commonly used in clinical practice. It has become the first choice for thrombolytic therapy of cardiovascular and cerebrovascular

Table 4. Univariate analysis of cognitive function

Variable	Cognitive dysfunction group (n = 41)	Non-disorder group (n = 73)	x^2/t value	*P* value
Age			8.305	0.004
≥ 60 years (n = 63)	30	33		
< 60 years (n = 51)	11	40		
Sex			2.638	0.104
Male (n = 67)	20	47		
Female (n = 47)	21	26		
BMI			0.588	0.443
≥ 25 kg/m^2 (n = 42)	17	25		
< 25 kg/m^2 (n = 72)	24	48		
Time from onset to admission			4.494	0.034
≥ 6 h (n = 49)	23	26		
< 6 h (n = 65)	18	47		
Medical history				
Diabetes (n = 51)	27	24	11.554	0.001
Hyperlipidemia (n = 38)	23	15	14.932	0.001
Lesion at critical sites			11.012	0.001
Critical site (n = 45)	27	18		
Non-critical site (n = 69)	23	55		
NIHSS score before treatment	23.58±3.77	24.97±3.47	1.937	0.055
MRS score before treatment	3.97±1.04	3.97±0.93	0.015	0.987

Note: Body Mass Index (BMI), National Institutes of Health Stroke Scale (NIHSS) score, modified Rankin Scale (mRS) score, frontal lobe, temporal lobe, base, thalamus as critical sites, parietal lobe, occipital lobe, brainstem, cerebellum as non-critical sites.

Table 5. Value assignment

Factor	Assignment value
Age	≥ 60 years = 1, < 60 years = 0
Time from onset to admission	≥ 6 h = 1, < 6 h = 0
Diabetes	Present = 1, Absent = 0
Hyperlipidemia	Present = 1, Absent = 0
Lesions at critical site	Critical = 1, Non-Critical = 0
Cognitive status	Cognitive dysfunction = 1, non-disorder group = 0

embolic diseases due to its rapid and strong thrombolytic effect compared with other thrombolytic drugs [21]. However, it is just a basic therapy, and alteplase alone is relatively insufficient for most patients with severe vascular obstruction because it is difficult to dissolve all embolic substances in a short period of time [22]. Neurointerventional technology is a new revascularization method, which applies a minimally invasive method and delivers the Solitaire stent to the thrombus site under precise localization of fluoroscopic monitoring, which is pulled out of the body when the stent and thrombus are in full contact [23]. Recent studies have shown that [24] the recanalization rate after neurointerventional techniques can reach over 90%, because it quickly opens the diseased vessels and restore blood supply in the cerebral ischemic area, thus relieving brain injury to certain extent. In this study, we found through brain CT reexamination 48 h after treatment that the observation group held a higher recanalization rate than the control group, suggesting that the use of interventional thrombectomy combined with intravenous thrombolysis can improve the recanalization rate in patients with cerebral thrombosis. Moreover, we evaluated the NIHSS score 7 days after treatment and the mRS score 30 days after treatment in the two groups and found that the both NIHSS and mRS scores after treatment were higher in the observation group than those in the control group. This suggests that interventional thrombectomy com-

Table 6. Multivariate logistics regression

Factor	β	Standard Deviation	Wald	*P* value	OR value	95% CI	
						Lower limit	Upper limit
Age	1.148	0.529	4.710	0.030	3.151	1.118	8.884
Time from onset to admission	0.779	0.526	2.190	0.139	2.180	0.777	6.117
Diabetes	1.776	0.552	10.333	0.001	5.906	2.000	17.439
Hyperlipidemia	1.818	0.549	10.962	0.001	6.157	2.099	18.056
Lesions at critical site	2.114	0.539	15.393	< 0.001	8.282	2.881	23.813

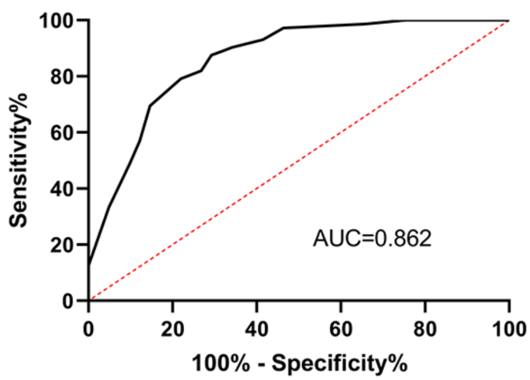

Figure 3. ROC curve for risk score to predict cognitive recovery in patients. Note: Receiver Operating characteristic (ROC), area under the curve (AUC).

bined with intravenous thrombolysis is more effective in the recovery of neurological function for cerebral thrombosis patients. In the previous study by Zhao et al. [25], thrombolysis combined with interventional therapy was found to be effective in promoting the prognosis of patients with acute basilar artery occlusion. Moreover, in the study by Li et al. [26], it was found that neurointervention combined with intravenous thrombolysis could not only effectively improve the diseased vessels of patients and restore the damaged neurological function, but also reduce the occurrence of complications. We believe this is mainly due to the fact that alteplase, as a natural plasminogen activator mainly formed in vascular endothelial cells, activates human plasminogen and promotes fibrin degradation, which causes thrombolysis by acting directly on thrombi, thereby improving local microcirculatory disturbances and increasing blood supply to hypoperfusion areas. Interventional therapy can accurately locate the occluded vessel segment, effectively and rapidly open the occluded vessel, improve the hypoxic-ischemic state of brain tissue, and promote the recovery of blood flow, so as to further improve postoperative recanalization rate of patients.

Cognitive dysfunction is one of the common complications of stroke that seriously affects the prognosis of patients [13]. It has been found that the prevalence of dementia is 3.5 to 5.8 times higher in patients with a history of ischemic stroke than those without [27, 28]. And 3-6 months of stroke is the peak period for the occurrence of cognitive dysfunction in patients. Therefore, early recognition of the risk of cognitive impairment in stroke is conducive to subsequent cognitive rehabilitation. In this study, we also analyzed the factors affecting cognitive function, and it was found that age, diabetes, hyperlipidemia and lesions at critical sites were independent risk factors affecting cognitive function in patients. Age as a risk factor affecting patients' cognitive function has been reported in several reports [29, 30], and there may be deterioration of cognitive function due to the increase of age. Diabetes and hyperlipidemia are common underlying diseases among the elderly, and it has been found that hyperglycemia can thicken the vascular basement membrane, increase the incidence of hypoxic-ischemic brain damage, and affect other metabolic disorders as well as neurobiochemical changes, ultimately leading to brain cognitive impairment [31, 32]. Dyslipidemia, an independent risk factor for ischemic stroke, can accelerate systemic atherosclerosis and affect cognitive function [33]. Basal ganglia infarction was found to affect cognition after stroke in recent studies [34], and patients with such syndrome have a higher risk of cognitive dysfunction than patients without. In this study, the risk of cognitive dysfunction in patients with lesions at critical sites was found to be evidently higher than that in patients with lesions at non-critical sites. When basal ganglia infarcts affect learning task speed, impaired performance is similar to that of frontal lobe damage, thereby increasing the risk of cognitive dysfunction. At the end of the study, we calculated the risk score by a risk model, and the plotted ROC curve showed that the area under the curve of risk score was 0.862 for predicting cognitive dysfunction in patients.

However, this study has some limitations. First, we failed to perform a long-term follow-up in this study, and only the mRS score within 30 days was retrieved from the electronic medical records. Second, this study was a retrospective study, so samples collected were limited and the analysis of the results may also be biased. Finally, while we constructed predictive models for cognitive function, we did not validate them with external samples. Therefore, we hope to carry out more experiments in future studies to refine our research conclusions.

In summary, interventional thrombectomy combined with intravenous thrombolysis is effective in the treatment of cerebral infarction, with the effect of reducing neurological deficits and improving recanalization rate. In addition, age, diabetes, hyperlipidemia and lesions at critical sites are independent risk factors for the development of cognitive impairment in AIS patients.

Disclosure of conflict of interest

None.

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