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Original Article

Enhanced clinical outcome and safety of Danhong injection combined with aspirin and clopidogrel for acute ischemic stroke: a retrospective study

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Abstract: Objective: To evaluate the efficacy and safety of Danhong injection combined with dual antiplatelet therapy (DAPT) in patients with acute ischemic stroke (AIS). Methods: A retrospective analysis was conducted on 110 AIS patients (aged 40-80 years, National Institutes of Health Stroke Scale 3-15) admitted between October 2021 and October 2023. Patients were divided into two groups: the intervention group (n=55) received Danhong injection (40 mL/day for 14 days) plus DAPT (aspirin 100 mg + clopidogrel 75 mg), while the control group (n=55) received DAPT alone. Primary outcomes included neurological function, infarct volume, and inflammatory/hemorheological markers. Safety was also assessed. Results: The intervention group showed greater neurological improvement, with NIHSS scores decreasing from 8.2 to 3.2 compared to 8.5 to 5.1 in the control group (P<0.001). Functional independence rate was higher in the intervention group (81.8% vs. 54.5%, P=0.002). Infarct volume reduction was more pronounced in the intervention group (5.0 cm^3 vs. 6.5 cm^3 at 1 month, P=0.003). Inflammatory markers (C-reactive protein, procalcitonin and neutrophil count) and hemorheological measurements (plasma viscosity, whole-blood viscosity) improved significantly (all P<0.05). No severe adverse events were reported. Conclusion: Danhong injection combined with DAPT significantly enhanced neurological recovery, reduced infarct volume, and modulated systemic inflammation in AIS patients, with a favorable safety profile.

Keywords: Acute ischemic stroke, Danhong injection, dual antiplatelet therapy, neurological recovery, infarct volume

Introduction

Acute ischemic stroke (AIS) is a leading cause of mortality and long-term disability worldwide, resulting in a substantial socioeconomic burden due to its high incidence and associated functional impairments [1]. Despite advancements in acute reperfusion therapies, such as thrombolysis and thrombectomy, a significant proportion of patients either remain ineligible for these interventions or experience incomplete recovery [2]. Dual antiplatelet therapy (DAPT) with aspirin and clopidogrel has become a cornerstone of secondary prevention, especially in minor strokes, by reducing recurrent ischemic events [3]. However, its efficacy is limited by residual risks such as neurological deterioration, incomplete microcirculatory reperfusion, and systemic inflammation, all of which contribute to secondary brain injury [4]. These limitations highlight the need for adjunctive therapies targeting complementary pathways to improve recovery.

Danhong injection, a traditional Chinese medicine derived from Salvia miltiorrhiza and Carthamus tinctorius, has garnered attention for its putative neuroprotective effects. Preclinical studies suggest that its active components, including tanshinones and hydroxysafflor yellow A, have multimodal actions: improving cerebral microcirculation by vasodilation and angiogenesis, suppressing pro-inflammatory cytokines, and mitigating oxidative stress by scavenging reactive oxygen species [5, 6]. Clinically, small-scale trials have shown that Danhong injection, when combined with conventional therapies, improves the TCM syndrome score in AIS

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patients and enhances their quality of life [7]. However, robust evidence supporting its synergistic effect with DAPT is lacking, and its mechanisms of action in modulating systemic inflammation and hemorheology are not well understood.

Inflammation and impaired microcirculation are crucial contributors to stroke pathophysiology. Elevated levels of inflammatory markers, such as C-reactive protein (CRP) and procalcitonin (PCT), correlate with poorer functional outcomes, while abnormal hemorheological functioning exacerbates ischemic penumbral damage [8]. Current antiplatelet regimens do not sufficiently address these pathways, leaving a therapeutic gap. Danhong's possible anti-inflammatory and hemorheology-modulating properties position it as a promising adjunct to DAPT [9], which may help bridge this gap through multi-targeted interventions.

This study aimed to evaluate the efficacy and safety of Danhong injection combined with DAPT in AIS patients, focusing on neurological function, infarct volume dynamics, and inflammatory and hemorheological profiles. We hypothesized that adding Danhong would enhance microcirculatory perfusion, reduce systemic inflammation, and improve functional recovery compared to DAPT alone. By integrating clinical outcomes with mechanistic biomarkers, this study seeks to provide a comprehensive rationale for incorporating traditional Chinese medicine into modern stroke care paradigms.

Materials and methods

Study design

This study was a retrospective analysis designed to evaluate the clinical efficacy and safety of Danhong injection combined with aspirin and clopidogrel in patients with AIS. The study population consisted of AIS patients admitted to Haining Traditional Chinese Medicine Hospital between October 2021 and October 2023. The study adhered to the ethical principles outlined in the Declaration of Helsinki and was approved by the Ethics Committee of Haining Hospital of Traditional Chinese Medicine (Ethics Approval No.: 20240508). All patient data were retrospectively analyzed with strictly no disclosure of personal identifying information. The study complied with the ethical review requirements of our institution.

Participant selection

A total of 110 AIS patients treated at the Haining Traditional Chinese Medicine Hospital between October 2021 and October 2023 were enrolled in the study. Inclusion criteria were as follows: (1) diagnosis of AIS confirmed by imaging (CT or MRI) showing infarct lesions; (2) onset time ≤24 hours and receiving standardized treatment; (3) age 40-80 years; (4) NIHSS score of 3-15 (indicating mild to moderate neurological deficits); (5) blood pressure ≤180/100 mmHg or controlled to <180/100 mmHg with medication. Exclusion criteria included: (1) history of hemorrhagic stroke or high risk of intracranial hemorrhage (e.g., cerebral aneurysm, arteriovenous malformation); (2) recent (<3 months) severe bleeding events or peptic ulcer bleeding; (3) significant coagulation abnormalities (e.g., platelet count $<100\times10^9$/L, international normalized ratio >1.5); (4) severe liver or kidney dysfunction (alanine aminotransferase/aspartate aminotransferase >3 times the upper limit of normal, estimated glomerular filtration rate <30 mL/min/1.73 m^2); (5) active malignancy or severe infection; (6) pregnancy or lactation; (7) use of other blood-activating and stasis-resolving traditional Chinese medicine preparations within the past 3 months; (8) history of allergy to aspirin, clopidogrel, or Danhong injection (**Figure 1**).

Grouping design

This study divided patients into two groups based on their treatment regimens. The control group (n=55) received standard DAPT, consisting of aspirin (100 mg orally once daily) and clopidogrel (75 mg orally once daily) for 14 days, along with standard supportive treatments. These included statins for lipid regulation, butylphthalide sodium chloride (twice daily) to improve cerebral metabolism and microcirculation, and edaravone dexborneol (15 mL twice daily) to scavenge free radicals. Patients with underlying conditions such as hypertension or diabetes received appropriate management of blood pressure and glucose.

The intervention group (n=55) received Danhong injection in addition to the control group's treatment regimen. Danhong injection

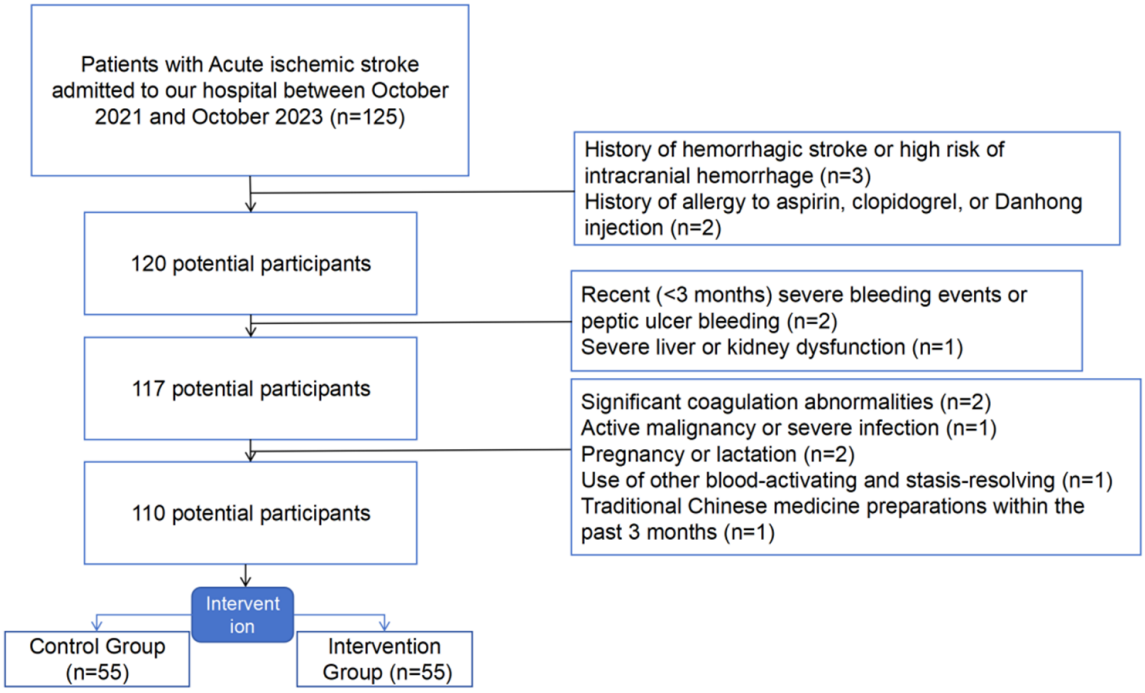

Figure 1. Inclusion and exclusion flowchart.

was administered at a dose of 40 mL once daily, diluted in 250 mL of 0.9% sodium chloride solution for intravenous infusion over 14 days. Following this, patients continued with standard antiplatelet therapy and supportive measures. Both groups received additional symptomatic treatments as per stroke management guidelines. Group allocation was based on actual medication use after admission, and strict screening was applied to ensure adherence to inclusion criteria, minimizing selection bias. Matching analysis was performed to ensure comparability of baseline characteristics between the two groups.

Assignment to the intervention group (Danhong injection + DAPT) or control group (DAPT alone) was determined by clinical decisions made by attending physicians, guided by individualized patient assessments, institutional protocols, and therapeutic preferences. Patients and physicians were not blinded to the treatment regimens.

Data extraction

Data were obtained from the hospital's electronic medical record system, imaging results, and laboratory reports. Clinical information from all eligible patients was collected, including demographic data, underlying diseases, medication use, and imaging indicators. All metrics were assessed at baseline (before treatment) and re-evaluated at three predefined time points: 1 week, 2 weeks, and 1 month post-treatment to observe dynamic changes during the treatment period. Neurological function (National Institutes of Health Stroke Scale (NIHSS) and the modified Rankin Scale (mRS) scores) was assessed at baseline, day 7, day 14, and 1 month. Infarct volume was quantified via MRI at baseline, day 7, day 14, and 1 month. Laboratory indicators (inflammatory markers: CRP, PCT, white blood cell count (WBC), neutrophil count (NEUT); lipid profiles: total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C). Hemorheological measurements of plasma viscosity, and whole-blood viscosity were measured at baseline and 1 month post-treatment. Safety assessments (bleeding events, adverse reactions) were monitored daily during the 14-day treatment period and at 1 month. Imaging data were derived primarily from MRI scans, while laboratory data included blood biochemical indicators, coagulation function,

and inflammatory markers, all of which were provided by the hospital's laboratory department. All data were double-checked to ensure accuracy and completeness.

Primary outcomes: Neurological function improvement: Neurological function improvement was assessed using the NIHSS and the mRS. The NIHSS evaluates the degree of neurological deficits in acute stroke, with scores ranging from 0 (no symptoms) to 42 (most severe). Its reliability and validity have been well-documented in numerous studies, demonstrating high sensitivity and reliability [10]. The mRS assesses functional independence, with scores ranging from 0 (no symptoms) to 5 (complete dependence on others). The mRS has been widely validated and is commonly used as a standard outcome measure in clinical trials [11].

Functional independence recovery rate: Functional independence recovery was evaluated using the mRS, focusing on whether patients achieved a score of ≤2 (indicating mild or no disability) after treatment [12].

Secondary outcomes: Imaging indicators: infarct volume changes: Imaging assessments used MRI or CT scans to quantitatively analyze changes in infarct volume. All patients were scanned using the same imaging equipment and technical parameters to ensure data consistency. Raw imaging data were processed using FSL software, including denoising, normalization, and registration. Infarct regions were manually segmented by experienced radiologists and validated using FSL's automated segmentation function. Infarct volume (in cm^3) was calculated, and changes were determined by comparing volumes at different time points relative to the baseline.

Laboratory indicators: Laboratory indicators included changes in serum inflammatory markers, lipid profiles, and hemorheological data. Inflammatory markers included CRP, PCT, WBC, and NEUT to assess systemic inflammation. Lipid profiles included TC, TG, HDL-C, and LDL-C. Hemorheological measures included plasma viscosity, whole-blood low-shear viscosity, fibrinogen, and whole-blood high-shear viscosity.

Safety analysis: Safety analysis involved monitoring adverse events, including bleeding events (e.g., cerebral hemorrhage, gastrointestinal bleeding), drug-related adverse reactions, and any other treatment-related health issues. These data were used to evaluate the safety of the treatment regimen.

Statistical analysis

All data were analyzed using SPSS 26.0. Continuous variables were expressed as mean ± standard deviation (mean ± SD), and intergroup comparisons were performed using independent samples t-tests. Intragroup comparisons across different time points were conducted using paired t-tests. For non-normally distributed data, median (interquartile range) was used, and non-parametric tests (Mann-Whitney U test or Wilcoxon signed-rank test) were applied. Categorical variables were expressed as frequencies (n) and percentages (%), with intergroup comparisons performed using chi-square or Fisher's exact tests. Repeated measures data were analyzed using repeated measures ANOVA, with Bonferroni correction for multiple comparisons if interaction effects were present. Pearson or Spearman correlation analysis was used to assess relationships between primary efficacy indicators, particularly the correlation between neurological function scores (NIHSS, mRS) and changes in infarct volume. Binary logistic regression analysis was employed to identify factors associated with functional independence (mRS ≤2), including baseline characteristics, treatment regimens, and laboratory indicators, to determine key prognostic factors. To further evaluate the predictive ability of the treatment regimen for functional recovery and neurological improvement, ROC curve analysis was performed. The area under the curve (AUC) was calculated to assess the discriminative ability of the treatment regimen. All tests were two-sided, with $P<0.05$ considered significant. Correlation coefficients (r) or regression coefficients (β) and their 95% confidence intervals (95% CI) were also calculated.

Results

Comparison of baseline characteristics

Table 1 presents the demographic, clinical, and laboratory characteristics of the randomly selected participants at baseline (all $P>0.05$).

Table 1. Comparison of baseline characteristics

Item	Overall (n=110)	Intervention Group (n=55)	Control Group (n=55)	χ^2/t	*P*-value
Demographic Characteristics					
Age (Mean ± SD) (years)	73.5±10.5	74.1±9.8	72.9±11.1	0.58	0.564
Sex - n (%)					
Male	52 (47.3%)	26 (47.3%)	26 (47.3%)	0.00	1.000
Female	58 (52.7%)	29 (52.7%)	29 (52.7%)		
BMI (Mean ± SD) (kg/m^2)	25.2±3.7	25.5±3.5	24.9±3.9	0.47	0.678
Medical History - n (%)					
Atrial fibrillation	6 (5.5%)	2 (3.6%)	4 (7.3%)	0.18	0.658
Hypertension	30 (27.3%)	15 (27.3%)	15 (27.3%)	1.42	0.233
Diabetes mellitus	18 (16.4%)	8 (14.5%)	10 (18.2%)	0.05	0.978
History of TIA/stroke	15 (13.6%)	6 (10.9%)	9 (16.4%)	0.12	0.745
History of smoking	10 (9.1%)	4 (7.3%)	6 (10.9%)	0.13	0.739
History of drinking	7 (6.4%)	3 (5.5%)	4 (7.3%)	0.02	0.902
History of statin use	17 (15.5%)	9 (16.4%)	8 (14.5%)	0.82	0.367
Inflammatory Indicators					
WBC (10^9/L, Mean ± SD)	7.05±2.58	6.82±2.21	7.21±2.93	-0.31	0.534
NEUT (10^9/L, Median [IQR])	4.80 [3.60, 6.50]	4.75 [3.10, 6.40]	4.85 [3.80, 6.75]	0.13	0.568
CRP (mg/L, Median [IQR])	3.18 [1.10, 12.50]	3.00 [0.95, 11.30]	3.35 [1.15, 12.40]	0.01	0.885
PCT (ng/mL, Median [IQR])	0.05 [0.03, 0.07]	0.04 [0.02, 0.06]	0.05 [0.03, 0.08]	0.21	0.637
Lipid Profile					
TC (mmol/L, Mean ± SD)	4.75±1.02	4.80±1.05	4.70±0.99	0.42	0.675
TG (mmol/L, Mean ± SD)	1.55±0.75	1.60±0.80	1.50±0.70	0.33	0.712
HDL-C (mmol/L, Mean ± SD)	1.30±0.35	1.32±0.36	1.28±0.34	0.28	0.734
LDL-C (mmol/L, Mean ± SD)	2.90±0.85	2.95±0.88	2.85±0.82	0.50	0.614
Hemorheological Indicators					
Plasma viscosity (mPa·s, Mean ± SD)	1.25±0.10	1.24±0.09	1.26±0.11	0.40	0.683
Whole blood low-shear viscosity (mPa·s, Mean ± SD)	4.80±0.60	4.75±0.55	4.85±0.65	0.55	0.589
Fibrinogen (g/L, Mean ± SD)	3.20±0.80	3.25±0.82	3.15±0.78	0.53	0.601
Whole blood high-shear viscosity (mPa·s, Mean ± SD)	4.10±0.50	4.05±0.48	4.15±0.52	0.47	0.642

Note: BMI, Body Mass Index; TIA, Transient Ischemic Attack; WBC, White Blood Cell count; NEUT, Neutrophil count; CRP, C-reactive Protein; PCT, Procalcitonin; TC, Total Cholesterol; TG, Triglyceride; HDL-C, High-Density Lipoprotein Cholesterol; LDL-C, Low-Density Lipoprotein Cholesterol.

Comparison of neurological function scores and functional independence recovery rate

As shown in **Table 2**, the intervention group demonstrated significant improvements in NIHSS and mRS scores at all time points compared to baseline (all P<0.001), with the magnitude of improvement significantly greater than that of the control group (P<0.05). The functional independence recovery rate (mRS ≤2) in the intervention group progressively increased, reaching 81.8% at 1 month post-treatment, which was significantly higher than the 54.5% observed in the control group (P=0.002). Additionally, there were significant differences between the two groups before and after treatment.

Binary logistic regression analysis

Binary logistic regression analysis was performed to evaluate the association between functional independence (mRS ≤2) and baseline characteristics, treatment regimens, and laboratory indicators. The probability of achieving functional independence in the intervention group was 5.05 times higher than in the control group (OR=5.05, 95% CI: 2.09-12.20, P<0.001). Elevated levels of inflammatory markers, CRP (OR=0.89, P=0.003) and PCT (OR=0.43, P=0.005), were significantly associated with reduced functional independence. Increased LDL-C (OR=0.56, P=0.022) and plasma viscosity (OR=0.30, P=0.016) were also significantly associated with a lower probability of functional independence. Other variables, including age, sex, BMI, and underlying conditions such as hypertension and diabetes, did not show statistical significance (P>0.05) (**Table 3**).

Comparison of infarct volume changes

At baseline and day 7, there were no significant differences in infarct volume between the inter-

Table 2. Comparison of neurological function score and functional independence recovery rate between two groups

Item	Time Point	Intervention Group (n=55)	Control Group (n=55)	χ^2/t/Z	P1	P2	P3
NIHSS Score	Before Treatment	8.2±3.1	8.5±3.4	t=0.51	0.612	-	-
	Day 7	6.1±2.7	7.4±3.0	t=2.39	0.019	<0.001	<0.001
	Day 14	4.6±2.5	6.3±2.8	t=3.47	0.001	<0.001	<0.001
	1 Month	3.2±2.0	5.1±2.5	t=4.86	<0.001	<0.001	<0.001
	P	<0.001	<0.001				
mRS Score	Before Treatment	3 (2, 4)	3 (2, 4)	Z=0.18	0.857	-	-
	Day 7	2 (1, 3)	3 (2, 4)	Z=3.12	0.002	<0.001	<0.001
	Day 14	2 (1, 3)	3 (2, 4)	Z=3.85	<0.001	<0.001	<0.001
	1 Month	1 (1, 2)	2 (1, 3)	Z=4.21	<0.001	<0.001	<0.001
	P	<0.001	<0.001				
Functional Independence Recovery Rate (mRS ≤2, n%)	Day 7	26 (47.3%)	18 (32.7%)	χ^2=2.56	0.109	-	-
	Day 14	38 (69.1%)	24 (43.6%)	χ^2=7.52	0.006	-	-
	1 Month	45 (81.8%)	30 (54.5%)	χ^2=9.74	0.002	-	-
	P	<0.001	<0.001				

Note: P1 (Intervention Group vs. Control Group); P2 (Intervention Group vs. Before Treatment); P3 (Control Group vs. Before Treatment). NIHSS, National Institutes of Health Stroke Scale; mRS, modified Rankin Scale.

Table 3. Binary logistic regression analysis of factors affecting functional independence (mRS ≤2)

Variable	β	Standard Error (SE)	Odds Ratio (OR)	95% CI	P
Demographic characteristics					
Age (per year)	-0.04	0.02	0.96	0.92-1.01	0.112
Sex (Male vs. Female)	0.25	0.31	1.28	0.70-2.35	0.418
BMI (per kg/m^2)	0.08	0.05	1.08	0.98-1.20	0.134
Medical History					
Hypertension (Yes vs. No)	0.18	0.35	1.20	0.60-2.40	0.604
Diabetes (Yes vs. No)	-0.42	0.38	0.66	0.31-1.39	0.272
Atrial Fibrillation (Yes vs. No)	-0.71	0.52	0.49	0.18-1.35	0.171
Treatment Group					
Intervention Group vs. Control Group	1.62	0.45	5.05	2.09-12.20	<0.001
Inflammatory Indicators					
CRP (per mg/L)	-0.12	0.04	0.89	0.82-0.96	0.003
PCT (per 0.1 ng/mL)	-0.85	0.30	0.43	0.24-0.77	0.005
Lipid Profile					
LDL-C (per mmol/L)	-0.58	0.25	0.56	0.34-0.92	0.022
Hemorheological Indicators					
Plasma Viscosity (per 0.1 mPa·s)	-1.20	0.50	0.30	0.11-0.80	0.016

Note: The model passed the Hosmer-Lemeshow test (χ^2=7.23, P=0.512), indicating a good model fit. The analysis was based on functional independence (mRS ≤2) at 1-month post-treatment as the outcome variable, incorporating all baseline characteristics and significantly changed laboratory indicators after treatment. BMI, Body Mass Index; CRP, C-reactive Protein; PCT, Procalcitonin; LDL-C, Low-Density Lipoprotein Cholesterol.

vention group and the control group (P=0.728 and P=0.222, respectively). Compared to baseline, the intervention group showed a significant reduction in infarct volume (P=0.048), while the control group did not reach statistical significance (P=0.092). By day 14, the infarct volume in the intervention group further decreased to 6.0±2.1 cm^3, which was significantly lower than that of the control group (7.5±2.3 cm^3, P=0.034). Compared to baseline, both groups showed significant improvements (P=0.006 for the intervention group and P=0.038 for the control group). At 1 month post-treatment, the infarct volume in the inter-

Table 4. Comparison of infarct volume changes

Time Point	Intervention Group (n=55)	Control Group (n=55)	t	P1	P2	P3
Before Treatment	8.4±2.2	8.6±2.3	-0.35	0.728	-	-
Day 7 (cm^3)	7.1±2.3	7.9±2.4	1.23	0.222	0.048	0.092
Day 14 (cm^3)	6.0±2.1	7.5±2.3	2.15	0.034	0.006	0.038
1 Month After Treatment (cm^3)	5.0±2.0	6.5±2.2	3.01	0.003	0.001	0.012
P	<0.001	<0.001				

Note: P1 (Intervention vs. Control Group); P2 (Intervention Group vs. Before Treatment); P3 (Control Group vs. Before Treatment).

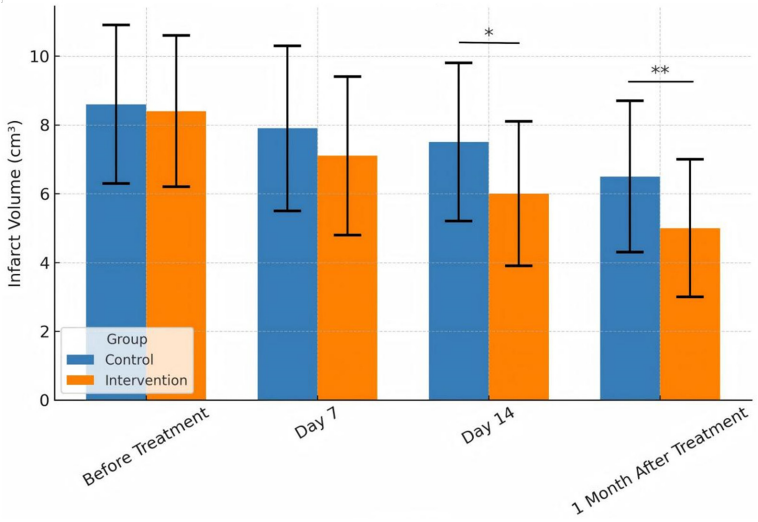

Figure 2. Comparison of dynamic changes in infarct volume in acute ischemic stroke patients between the intervention and control groups. The blue bar chart represents the intervention group (Danhong injection combined with DAPT), and the orange bar chart represents the control group (only treated with DAPT). The error line represents the standard deviation (SD). Four-time points are marked on the X-axis: before treatment, 7 days after treatment, 14 days after treatment, and 1 month after treatment. The Y-axis unit is cubic centimeters (cm^3), representing the infarct volume. The asterisk indicates significant differences between groups (*P<0.05, **P<0.01).

vention group continued to decrease and was significantly lower than that in the control group (P=0.003). Intragroup comparisons revealed that the reduction in infarct volume was more pronounced in the intervention group (P=0.001 compared to baseline) than in the control group (P=0.012), suggesting a more significant trend of infarct volume reduction in the intervention group during long-term follow-up. Additionally, significant differences were observed between the two groups before and after treatment (**Table 4**; **Figure 2**).

Correlation analysis

To further explore the relationship between neurological function scores (NIHSS, mRS) and changes in infarct volume, Spearman rank correlation analysis was performed (**Table 4**). In the intervention group, NIHSS scores showed significant positive correlations with infarct volume changes at day 7 (r=0.55, P=0.002), day 14 (r=0.63, P<0.001), and 1 month (r=0.70, P<0.001). In the control group, the correlations between NIHSS scores and infarct volume changes were weaker but still significant at all time points (day 7: r=0.46, P=0.015; day 14: r=0.52, P=0.009; 1 month: r=0.58, P=0.002).

For mRS scores, the intervention group demonstrated significant correlations with infarct volume changes at day 7 (r=0.50, P=0.006), day 14 (r=0.58, P=0.003), and 1 month (r=0.62, P<0.001). In the control group, the correlations were slightly weaker but remained significant (day 7: r=0.42, P=0.021; day 14: r=0.47, P=0.014; 1 month: r=0.55, P=0.003). Overall, the correlations between NIHSS/mRS scores and infarct volume changes were stronger in the intervention group compared to the control group, suggesting a more pronounced relationship between neurological recovery and infarct volume reduction in patients receiving Danhong injection combined with DAPT (**Table 5**).

Comparison of laboratory indicators

In the intervention group, significant reductions from baseline were observed in CRP (P=0.015), PCT (P=0.031), and NEUT (P=0.050) after treat-

Table 5. Group-wise correlation analysis between neurological function scores and infarct volume changes

Variable	Intervention Group: NIHSS		Control Group: NIHSS		Intervention Group: mRS		Control Group: mRS	
	r	P	r	P	r	P	r	P
Infarct Volume Change (Day 7)	0.55	0.002	0.46	0.015	0.5	0.006	0.42	0.021
Infarct Volume Change (Day 14)	0.63	<0.001	0.52	0.009	0.58	0.003	0.47	0.014
Infarct Volume Change (1 Month)	0.7	<0.001	0.58	0.002	0.62	<0.001	0.55	0.003

ment. Intergroup comparisons revealed that the improvements in CRP (P=0.018), PCT (P=0.024), and NEUT (P=0.042) were significantly greater in the intervention group compared to the control group (P<0.05). WBC levels also decreased significantly in the intervention group (P=0.039), but the intergroup difference did not reach significance (P=0.072).

In terms of lipid profiles, the intervention group showed significant reductions in TC (P=0.037), TG (P=0.048), and LDL-C (P=0.041), along with a significant increase in HDL-C (P=0.022). However, the intergroup difference for LDL-C was only close to significant (P=0.073). Hemorheological measurements also improved in the intervention group, with significant reductions in whole blood low-shear viscosity (P=0.024) and whole blood high-shear viscosity (P=0.031). The intergroup difference in whole blood low-shear viscosity was significant (P=0.029). Plasma viscosity (P=0.034) and fibrinogen (P=0.047) showed improvements in the intervention group, but the intergroup differences were not significant (P=0.085 and P=0.071, respectively). Additionally, there were significant differences between the two groups before and after treatment (**Table 6**).

Safety analysis

Pre-treatment imaging excluded intracranial hemorrhage in both groups. Follow-up cranial CT scans at 1 week post-treatment showed no evidence of intracranial hemorrhage. Routine blood tests and coagulation function tests revealed no significant abnormalities. No adverse events were observed in either group during the treatment period.

ROC analysis

To further evaluate the predictive ability of the treatment regimen for functional recovery and neurological improvement, ROC curve analysis was performed. The model for predicting functional independence (mRS ≤2) achieved an AUC of 0.695 (95% CI: 0.62-0.77) at the optimal cutoff, with a sensitivity of 68.2% and specificity of 61.5%. For neurological improvement (defined as a reduction in NIHSS score ≥2 points), the model showed an AUC of 0.716 (95% CI: 0.65-0.78), with a sensitivity of 72.4% and specificity of 63.8%. Both AUC values were statistically superior to the random classifier (AUC=0.5, P<0.001 for all comparisons) (**Figure 3**).

Discussion

This intervention demonstrated that combining Danhong injection with DAPT (aspirin and clopidogrel) significantly improved neurological recovery, reduced infarct volume, and modulated inflammatory and hemorheological data in patients with AIS, while maintaining a favorable safety profile.

The addition of Danhong injection to standard DAPT resulted in superior outcomes across multiple functions. First, the intervention group showed more significant reductions in NIHSS scores and mRS scores, corresponding to a higher functional independence rate. Second, infarct volume reduction was more pronounced in the intervention group. Third, significant improvements in inflammatory markers (CRP, PCT, NEUT) and hemorheological parameters (plasma viscosity, whole-blood viscosity) were observed in the intervention group. Importantly, no severe adverse events were reported, further underscoring the regimen's safety.

These outcomes are consistent with previous studies highlighting the neuroprotective effects of Danhong injection. For instance, Chi et al. [13] reported similar reductions in NIHSS scores among patients receiving Danhong ther-

Table 6. Comparison of laboratory indicator changes between the two groups

Data	Intervention Group (n=55)			Control Group (n=55)			t/Z	P1	P2	P3
	Before Treatment	After Treatment	P	Before Treatment	After Treatment	P				
CRP (mg/L)	3.00 [0.95, 11.30]	2.10 [0.70, 8.50]	0.001	3.35 [1.15, 12.40]	3.00 [1.00, 11.00]	0.001	Z=-2.43	0.015	0.018	0.062
PCT (ng/mL)	0.04 [0.02, 0.06]	0.03 [0.01, 0.05]	0.011	0.05 [0.03, 0.08]	0.04 [0.02, 0.07]	0.021	Z=-2.16	0.031	0.024	0.081
WBC ($\times 10^9$/L)	6.82±2.21	5.90±2.05	0.001	7.21±2.93	6.70±2.50	0.001	t=1.82	0.072	0.039	0.092
NEUT ($\times 10^9$/L)	4.75 [3.10, 6.40]	4.10 [2.90, 5.80]	<0.001	4.85 [3.80, 6.75]	4.50 [3.50, 6.20]	<0.001	Z=-1.96	0.050	0.042	0.089
TC (mmol/L)	4.80±1.05	4.35±0.98	<0.001	4.70±0.99	4.55±1.02	0.001	t=-1.08	0.282	0.037	0.065
TG (mmol/L)	1.60±0.80	1.40±0.65	0.001	1.50±0.70	1.45±0.68	0.021	t=-0.38	0.706	0.048	0.077
HDL-C (mmol/L)	1.32±0.36	1.42±0.35	<0.001	1.28±0.34	1.33±0.33	0.001	t=1.45	0.149	0.022	0.128
LDL-C (mmol/L)	2.95 ± 0.88	2.60±0.82	0.001	2.85±0.82	2.75±0.85	<0.001	t=-0.96	0.339	0.041	0.073
Plasma Viscosity (mPa·s)	1.24±0.09	1.18±0.08	<0.001	1.26±0.11	1.22±0.10	<0.001	t=-1.88	0.063	0.034	0.085
Whole Blood Low-Shear Viscosity (mPa·s)	4.75±0.55	4.40±0.50	<0.001	4.85±0.65	4.65±0.60	<0.001	t=-2.28	0.024	0.029	0.069
Fibrinogen (g/L)	3.25±0.82	2.95±0.75	<0.001	3.15±0.78	3.05±0.79	<0.001	t=-0.65	0.515	0.047	0.071
Whole Blood High-Shear Viscosity (mPa·s)	4.05±0.48	3.80±0.45	<0.001	4.15±0.52	4.00±0.50	<0.001	t=-1.96	0.052	0.031	0.074

Note: CRP, C-reactive Protein; PCT, Procalcitonin; WBC, White Blood Cell count; NEUT, Neutrophil count; TC, Total Cholesterol; TG, Triglyceride; HDL-C, High-Density Lipoprotein Cholesterol; LDL-C, Low-Density Lipoprotein Cholesterol.

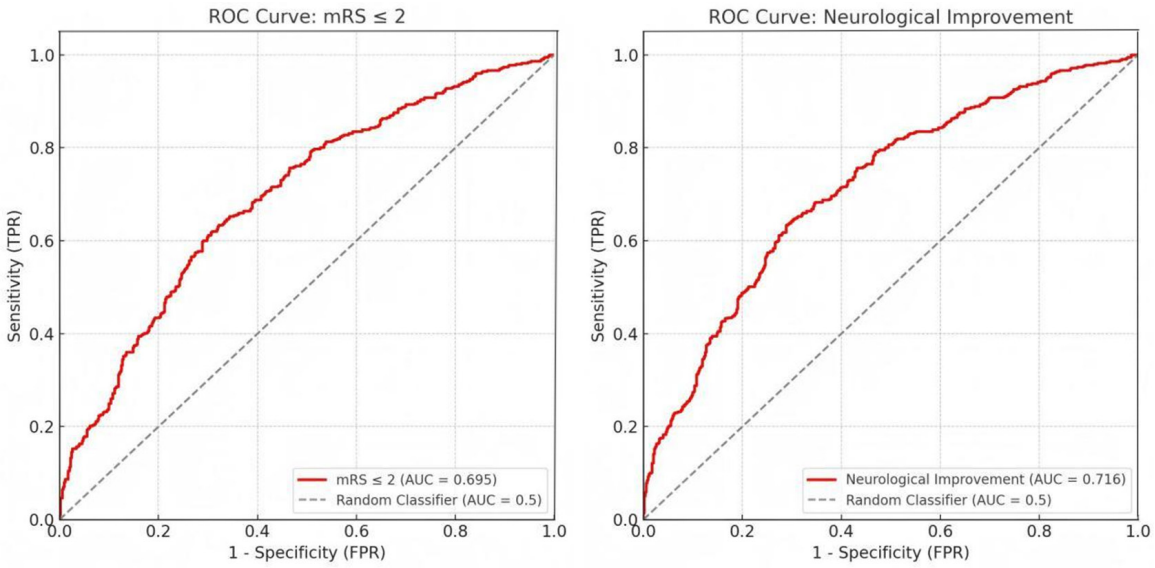

Figure 3. ROC curves for predicting functional independence and neurological improvement. The x-axis represents 1 - specificity (false positive rate), and the y-axis represents sensitivity (true positive rate).

apy, attributing these effects to enhanced microcirculation. Our findings expand this understanding by demonstrating a stronger correlation between infarct volume reduction and neurological improvement in the intervention group compared to the control group, suggesting mechanisms beyond clot prevention. This discrepancy may arise from Danhong's multimodal actions, which are not typically addressed by conventional antiplatelet agents. For example, preclinical studies have shown that Danhong's active components, such as tanshinones from Salvia miltiorrhiza and hydroxysafflor yellow A from Carthamus tinctorius, inhibit platelet aggregation while promoting nitric oxide-mediated vasodilation, thereby improving cerebral perfusion [14]. Additionally, its anti-inflammatory effects, evidenced by reduced CRP and PCT levels, likely mitigate secondary neuronal damage by suppressing NF-κB and TNF-α pathways [15, 16]. Antioxidant properties, including ROS scavenging and upregulation of endogenous antioxidants like SOD and GSH, further contribute to neuroprotection, as demonstrated in animal models [17]. The lipid-modulating effects observed here, particularly the reduction in LDL-C and increase in HDL-C, may also stabilize atherosclerotic plaques, thus reducing the risk of recurrent stroke [18, 19].

Despite these promising results, several limitations must be acknowledged. The single-center, retrospective design introduced potential selection bias, and the modest sample size limited subgroup analyses and generalizability. The absence of blinding, although mitigated by objective outcome measures (e.g., infarct volume quantification), may have influenced subjective assessments. Furthermore, the short follow-up period limited conclusions about long-term efficacy, and the lack of mechanistic biomarkers restricts deeper insights into Danhong's molecular actions. These limitations underscore the need for cautious interpretation of the findings.

The clinical implications of this study are significant. Danhong injection, with its multimodal mechanisms and favorable safety profile, could be integrated into acute stroke management protocols, particularly for patients with heightened inflammatory responses or impaired microcirculation. However, broader clinical adoption necessitates validation through multicenter, randomized controlled trials with extended follow-up periods (6-12 months) to assess the durability of the benefits. Future research should also explore interactions between Danhong and newer antiplatelet agents or thrombolytics, as well as dose-response relationships and optimal treatment durations. Advanced imaging techniques, such as perfusion-weighted MRI, could further elucidate microcirculatory improvements, while predic-

tive models require validation in diverse populations to refine patient selection criteria.

In conclusion, this study provided compelling evidence that Danhong injection enhances the efficacy of DAPT in acute ischemic stroke, improving neurological recovery, reducing infarct volume, and modulating systemic inflammation. Its likely mechanisms involve synergistic effects on microcirculation, inflammation, and oxidative stress. While limitations exist, these findings highlight the potential of integrating traditional and modern therapies to optimize stroke care, warranting further investigation to confirm and expand upon these results.

Disclosure of conflict of interest

None.

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