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ORIGINAL RESEARCH

Investigation of the Impact Factors and Efficacy of N-Butylphthalide (NBP) on Functional Outcomes Following Mechanical Thrombectomy in Stroke Patients

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Background: Ischemic stroke was a major cause of mortality and disability worldwide. Mechanical thrombectomy (MT) has improved acute ischemic stroke treatment by restoring blood flow in large vessel occlusions. Yet, reperfusion injury remains a challenge, necessitating adjunctive neuroprotective strategies to enhance recovery. N-butylphthalide (NBP), with its anti-inflammatory and antioxidative properties, may improve functional outcomes post-MT.

Methods: This retrospective study analyzed 120 ischemic stroke patients treated with MT at a single institution from December 2020 to December 2022. Patients were divided into a routine care group (n = 56) and an NBP treatment group (n = 64). Baseline characteristics, comorbidities, and biochemical profiles were assessed. Functional outcomes were measured by the modified Rankin Scale (mRS) at 90 days. Statistical analysis included correlation and logistic regression to identify factors influencing recovery.

Results: Among the NBP group, a significantly higher percentage achieved favorable mRS scores (0–2) compared to the routine care group (62.50% vs 37.50%, P = 0.006). Smoking (OR 0.320, P = 0.021), diabetes (OR 0.246, P = 0.022), and elevated hs-CRP levels (OR 0.407, P = 0.004) were identified as negative predictors of functional recovery. Conversely, NBP treatment significantly improved outcomes (OR 3.248, P = 0.008).

Conclusion: The study supports the potential of NBP as an effective adjunctive therapy in improving recovery following MT in ischemic stroke patients. Modifiable factors such as smoking and diabetes, along with elevated hs-CRP, negatively influence outcomes, highlighting the importance of comprehensive management.

Keywords: ischemic stroke, **mechanical thrombectomy**, **N-butylphthalide**, **neuroprotection**, **functional recovery**, **predictors of outcome**

Introduction

Ischemic stroke represents a significant global health burden, ranking as a leading cause of mortality and long-term disability.[1,2] Despite advancements in acute stroke management,[3–5] including the widespread adoption of mechanical thrombectomy (MT), the search for strategies to enhance functional recovery remains imperative. MT has transformed acute ischemic stroke treatment by enabling the removal of occlusive thrombi in larger arteries, thus re-establishing cerebral blood flow and mitigating acute ischemic damage.[6–8] However, the challenge of reperfusion injury and its potential compromise of neurovascular recovery post-thrombectomy necessitates the exploration of adjunctive therapeutic strategies to optimize clinical outcomes.

Neuroprotective agents, such as N-butylphthalide (NBP), have garnered significant interest in the stroke research community due to their potential to ameliorate ischemic injury and augment neurological recovery.[9,10] NBP, originally

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derived from celery seed extracts, was recognized for its pleiotropic pharmacological actions which include anti-inflammatory effects, mitigation of oxidative stress, and improvement of microcirculatory function.[11–13] The agent's capacity to bolster mitochondrial function and enhance cerebral blood flow suggests its potential utility in the acute phases of stroke recovery, particularly by safeguarding penumbral brain tissue from secondary injury during the peri-reperfusion period.[14]

Previous clinical trials and experimental studies have provided preliminary evidence supporting the efficacy of NBP in improving outcomes in ischemic stroke patients,[15] yet there remains a paucity of well-designed trials evaluating its effect as an adjunctive treatment for patients undergoing MT. Moreover, the precise impact factors facilitating or mitigating neuroprotective efficacy post-MT remain insufficiently characterized. Understanding the interplay of neuroprotective agents with patient-specific variables such as comorbidities, individual biochemical profiles, and intraoperative factors was crucial for tailoring personalized therapeutic strategies aimed at the enhancement of functional outcomes.

This study seeks to address these knowledge gaps by systematically investigating the efficacy of NBP in improving functional outcomes among ischemic stroke patients treated with MT, while simultaneously examining potential impact factors that may influence recovery trajectories.

Materials and Methods

Case Selection

This retrospective study included 120 patients with ischemic stroke who visited our hospital between December 2020 and December 2022. They were categorized into the routine care group (56 patients) and the NBP treatment group (64 patients), based on the therapeutic approach employed. Demographic information, including general characteristics and functional outcomes, was collected from the medical record system. Subsequently, patients were further classified into favorable (59 patients) and unfavorable (61 patients) functional outcome groups post-MT to investigate the factors influencing functional recovery in stroke patients following this procedure.

The study was approved by the Institutional Review Board and Ethics Committee of our institution. Informed consent was waived for this retrospective analysis due to the use of de-identified patient data, which posed no risk or impact on patient care. This waiver was granted in compliance with the regulatory and ethical guidelines for retrospective research studies.

Inclusion and Exclusion Criteria

Inclusion criteria for the study were as follows: 1) Participants aged 18 years or older; 2) A diagnosis of acute ischemic stroke with a National Institutes of Health Stroke Scale (NIHSS) score between 4 and 25[16]; 3) Capability to begin the trial medication within 6 hours of symptom onset; and 4) Undergoing endovascular treatment, specifically MT.

Patients who received other endovascular treatments, such as angioplasty without MT, were excluded from the study to ensure homogeneity of the treatment approach and to specifically assess the impact of MT combined with NBP.[17]

The exclusion criteria for the study were as follows: 1) Patients with an Alberta Stroke Program Early Computed Tomography Score (ASPECTS) of 6 or lower, as confirmed by a preoperative computed tomography scan[18]; 2) Patients diagnosed with intracranial hemorrhagic conditions, such as intracranial hemorrhage or subarachnoid hemorrhage; 3) Patients presenting with dysphagia; 4) Patients with a history of coagulation disorders, hemorrhagic diathesis, neutropenia, or thrombocytopenia; 5) Patients with chronic liver disease or liver and kidney dysfunction, defined as levels of alanine transaminase at or exceeding three times the upper normal limit or creatinine levels at or exceeding twice the upper normal limit; 6) Contraindications to the digital subtraction angiography procedure, including a severe allergy to contrast agents with or without iodine; 7) Patients with a history of drug or food allergies, or known allergies to the study drug components; 8) Patients with a history of bradycardia (heart rate below 60 beats per minute) or sick sinus syndrome; 9) Patients with a history of severe cardiopulmonary diseases.

Treatment Approach

Patients in the routine care group underwent MT. The specific procedure involved preoperative anesthesia and sedation. An 8 French guide catheter (Medtronic plc, Dublin, Ireland) and an intermediate guide catheter (Boston Scientific, Marlborough, MA, USA) were inserted coaxially through the femoral artery into the ipsilateral internal carotid artery, where angiography was performed. A micro-guidewire was used to advance the Rebar 18/27 microcatheter (Medtronic plc, Dublin, Ireland) beyond the thrombus. Once angiography confirmed its position in the true lumen of the vessel, a stent retriever was deployed by withdrawing the microcatheter, allowing the stent to expand for over 5 minutes. Simultaneously, negative pressure aspiration was applied through the intermediate catheter in contact with the thrombus, and the stent along with the intermediate catheter was slowly withdrawn. Post-thrombectomy, angiographic assessments were conducted (Azurion, Philips Healthcare, Eindhoven, Netherlands). If the thrombectomy was unsatisfactory, the procedure could be repeated. In cases where multiple attempts did not achieve adequate recanalization, rescue therapies such as balloon angioplasty or stent implantation were considered. The operation time and the time taken for the guidewire to reach the target position were recorded for each patient.

In addition to MT, patients in the NBP group received NBP treatment. During the first 14 days, patients were administered 100 mL of sodium chloride injection with NBP twice daily. Following this, for the next 76 days, they took soft capsules containing 0.2 g of NBP three times daily. Injections were advised to continue for 10 to 14 days depending on the length of hospitalization, with each injection lasting at least 50 minutes and administered every 6 hours. Patients were instructed to take the capsules daily before meals and to document their medication intake, which was verified by researchers. A steering committee provided guidance on concomitant medications. All secondary prevention strategies, including antithrombotic treatments and risk factor management, adhered to clinical guidelines, and any incidence of intracranial hemorrhage within 24 hours was noted. However, the use of neuroprotective drugs such as human urinary kallidinogenase, edaravone, and any ginkgo-containing injections was prohibited.

Functional Outcomes

A favorable functional outcome was defined based on the modified Rankin Scale (mRS) in relation to the baseline neurological impairment as assessed by the NIHSS:

Patients with an initial NIHSS score between 4 and 7 were considered to have achieved a good functional outcome if their mRS score was 0 at 90 days post-stroke.

Patients with an initial NIHSS score ranging from 8 to 14 were deemed to have a good functional outcome if their mRS score was 0 or 1 at 90 days.

Patients with a baseline NIHSS score between 15 and 25 were regarded as having a good functional outcome if their mRS score was between 0 and 2 at 90 days.

mRS

The mRS was employed to evaluate functional outcomes following a stroke. A score of 0 represents the absence of symptoms, while a score of 6 indicates death. Scores between 1 and 5 correspond to different levels of disability, with higher scores denoting more severe disability and less favorable functional outcomes. The Cronbach's alpha for this scale was calculated to be 0.981, indicating excellent internal consistency.[19]

Biochemical Measurements

Patients' venous blood samples were collected from the antecubital vein after they fasted for at least 10 hours and were taken within the first 24 hours of hospital admission. The samples were centrifuged at 1000 g for 10 minutes to separate serum and plasma. Serum levels of total cholesterol (TC), triglycerides, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, uric acid (UA), and homocysteine (Hcy) were measured using the AU5800 automated biochemical analyzer (Beckman Coulter, CA, USA) with the appropriate kits.

Fasting blood glucose (FBG) levels were determined using the glucose oxidase method, while hemoglobin A1c (HbA1C) levels were measured via high-performance liquid chromatography. Serum creatinine (SCr) and blood urea nitrogen (BUN) levels were assessed using a VITROS 5600 Integrated System (Ortho-Clinical Diagnostics), following the manufacturer's guidelines and corresponding kits.

The quantitative level of lipoprotein-associated phospholipase A2 (Lp-PLA2) in plasma was determined using an enzyme-linked immunosorbent assay (ELISA) kit (Abcam, USA), with a detection range from 0.16 ng/mL to 10 ng/mL. Optical density (OD) values were recorded at 450 nm using an enzyme analyzer. Plasma high-sensitivity C-reactive protein (hs-CRP) was measured using a latex turbidimetric immunoassay kit (Medical System Biotechnology Co., Ltd., Ningbo, China).

Recanalization

Initial vessel occlusion and recanalization were evaluated using the Thrombolysis in Cerebral Infarction (TICI) scale[20], which categorizes results into the following grades: TICI 0, TICI 1, TICI 2a, TICI 2b, and TICI 3. Successful recanalization was typically defined as achieving a TICI grade of 2b or 3. The Kappa coefficient for inter-rater reliability of this scale was 0.82, indicating substantial agreement.[21]

Statistical Analysis

The data were analyzed using SPSS 29.0 statistical software (SPSS Inc., Chicago, IL, USA). For categorical variables, results were presented as [n (%)]. A chi-square test was employed when the sample size was ≥40 and the expected frequency (T) was ≥5, with the test statistic denoted by χ^2. If the sample size was ≥40 but the expected frequency was in the range of $1 \leq T < 5$, the chi-square test was adjusted using a correction formula. For sample sizes <40 or an expected frequency T <1, Fisher's exact test was used for analysis.

Continuous variables were initially assessed for normal distribution using the Shapiro–Wilk test. Normally distributed data were presented as (mean ± standard deviation). Non-normally distributed data were analyzed using the Wilcoxon rank-sum test and were presented as [median (25th percentile, 75th percentile)]. A p-value of <0.05 was considered statistically significant.

Correlation analysis was performed using Pearson's correlation for continuous variables and Spearman correlation for categorical variables. Following the initial correlation analysis to assess variable relationships, a multiple logistic regression analysis was conducted to determine the independent effects of each variable on the study outcome, while controlling for potential confounding factors.

Results

Neuroprotectants

Neuroprotectants Improve Functional Outcomes After MT in Stroke Patients

Baseline Characteristics

In this study, we investigated the baseline characteristics of stroke patients who underwent MT and were treated with or without the neuroprotective agent NBP (Table 1). A total of 120 participants were included, with 56 individuals in the routine treatment group and 64 in the NBP treatment group. The mean age of the participants was 66.31 ± 10.62 years in the routine group and 66.35 ± 9.83 years in the NBP group (P = 0.981). The gender distribution showed 67.86% males in the routine group and 62.5% in the NBP group (P = 0.539). The mean body mass index was similar between groups (24.01 ± 2.35 vs 24.23 ± 2.41, P = 0.615). Additionally, there were no significant differences in medical histories such as previous stroke, hypertension, hypercholesterolemia, diabetes, or heart disease (all P > 0.05). Parameters assessing stroke severity and presentation, including the ASPECTS score, NIHSS score, stroke category, and clot location, also showed no significant differences between groups (all P > 0.05). The mean time from onset to drug administration was 254.37 ± 40.81 minutes in the routine group compared to 261.22 ± 48.34 minutes in the NBP group (P = 0.407). Overall, the baseline characteristics were well-matched between the two treatment groups.

Functional Outcomes

In this study assessing the efficacy of neuroprotective agents on functional outcomes following MT in stroke patients, we compared the mRS scores between the routine treatment group and the NBP group (Table 2). Prior to stroke onset, there

Table 1 Baseline Characteristics of Participants

Parameters	Routine group (n = 56)	NBP group (n = 64)	t/χ^2	*P*
Age (years)	66.31 ± 10.62	66.35 ± 9.83	0.024	0.981
Gender (Male)	38 (67.86%)	40 (62.5%)	0.377	0.539
Body Mass Index (kg/m²)	24.01 ± 2.35	24.23 ± 2.41	0.505	0.615
Drinking history [n (%)]	23 (41.07%)	25 (39.06%)	0.050	0.823
Smoking history[n (%)]	19 (33.93%)	17 (26.56%)	0.772	0.380
Blood pressure (mm Hg)				
Systolic	148.50 ± 11.25	150.39 ± 14.02	0.806	0.422
Diastolic	87.33 ± 7.26	86.34 ± 7.48	0.738	0.462
Medical history[n (%)]				
Stroke	13 (23.21%)	14 (21.88%)	0.031	0.861
Hypertension	32 (57.14%)	36 (56.25%)	0.010	0.922
Hypercholesterolemia	3 (5.36%)	2 (3.12%)	0.023	0.879
Diabetes	12 (21.43%)	12 (18.75%)	0.134	0.714
Heart disease	13 (23.21%)	15 (23.44%)	0.001	0.977
ASPECTS score	9.36 ± 1.02	9.28 ± 1.10	0.391	0.696
NIHSS score	8.33 ± 2.17	8.56 ± 2.36	0.538	0.592
Stroke category[n (%)]			0.340	0.844
Mild	23 (41.07%)	26 (40.62%)		
Moderate	23 (41.07%)	24 (37.50%)		
Severe	10 (17.86%)	14 (21.88%)		
Clot location[n (%)]			0.330	0.850
Internal carotid artery	12 (21.43%)	16 (25.00%)		
Middle cerebral artery	33 (58.93%)	38 (59.38%)		
Anterior cerebral artery	1 (1.79%)	1 (1.56%)		
Vertebral artery	2 (3.57%)	2 (3.12%)		
Posterior cerebral artery	2 (3.57%)	0 (0.00%)		
Basilar artery	6 (10.71%)	7 (10.94%)		
Onset to drug administration (min)	254.37 ± 40.81	261.22 ± 48.34	0.831	0.407
OCSP[n (%)]			0.092	0.993
TACI	16 (28.57%)	17 (26.56%)		
PACI	30 (53.57%)	35 (54.69%)		
POCI	7 (12.50%)	8 (12.50%)		
LACI	3 (5.36%)	4 (6.25%)		

Abbreviations: ASPECTS, Alberta Stroke Program Early Computed Tomography Score; NIHSS, National Institute of Health Stroke Scale; OCSP, Oxfordshire Community Stroke Project; TACI, Total anterior circulation infarct; PACI, Partial anterior circulation infarct; POCI, Posterior circulation infarct; LACI, Lacunar infarct.

Table 2 Comparison of Functional Outcomes Between the Two Patient Groups

Parameters	Routine group (n = 56)	NBP group (n = 64)	χ^2	*P*
mRS score prior to onset[n (%)]			0.033	0.855
0	52 (92.86%)	61 (95.31%)		
1	4 (7.14%)	3 (4.69%)		
mRS score on day 90 [n (%)]	35 (62.50%)	24 (37.50%)	7.469	0.006

Abbreviation: mRS, modified Rankin Scale.

was no significant difference in baseline mRS scores between the groups, with the majority of patients scoring 0 (92.86% in the routine group and 95.31% in the NBP group; P = 0.855). However, significant differences emerged in functional outcomes by day 90 post-treatment. Patients in the NBP group showed a greater improvement, as evidenced by a higher proportion achieving favorable mRS scores of 0 to 2, with 37.50% in the NBP group compared to 62.50% in the routine group, underscoring better functional outcomes in the NBP group (P = 0.006). These results suggest that the neuroprotective agent NBP was associated with improved functional outcomes at 90 days following MT.

Factors Influencing Analysis of Functional Outcomes in Stroke Patients After MT

Baseline Characteristics

In our exploration of baseline characteristics influencing functional outcomes in stroke patients following MT, we identified several key factors associated with poor versus good outcomes (Table 3). The analysis included 120 patients, divided into those with poor (n = 61) and good (n = 59) outcomes. There were no significant differences in age, gender, body mass index, baseline systolic and diastolic blood pressures, or prior history of stroke and heart disease between the two groups (all P > 0.05). However, significant associations were observed for certain factors. A history of smoking was more prevalent in the poor outcome group (40.98% vs 18.64%, P = 0.008), as well as histories of hypertension (70.49% vs 42.37%, P = 0.002) and diabetes (29.51% vs 10.17%, P = 0.008). Moreover, the use of the neuroprotective agent NBP

Table 3 Baseline Characteristics by Functional Outcome Groups

Parameters	Poor group (n = 61)	Good group (n = 59)	t/χ^2	*P*
Age (years)	66.23 ± 10.58	66.44 ± 10.13	0.108	0.915
Gender (Male/Female)	40 (65.57%)	38 (64.41%)	0.018	0.893
Body Mass Index (kg/m²)	23.98 ± 2.44	24.12 ± 2.37	0.325	0.746
Drinking history [n (%)]	26 (42.62%)	22 (37.29%)	0.356	0.551
Smoking history [n (%)]	25 (40.98%)	11 (18.64%)	7.127	0.008
Blood pressure (mm Hg)			0.107	0.915
Systolic	149.36 ± 10.13	149.57 ± 11.26		
Diastolic	86.27 ± 7.53	87.30 ± 7.24		
Medical history[n (%)]			0.014	0.904
Stroke	14 (22.95%)	13 (22.03%)		
Hypertension	43 (70.49%)	25 (42.37%)	9.657	0.002
Hypercholesterolemia	2 (3.28%)	3 (5.08%)	0.001	0.970
Diabetes	18 (29.51%)	6 (10.17%)	7.010	0.008
Heart disease	14 (22.95%)	14 (23.73%)	0.010	0.920
NIHSS score	9.97 ± 3.12	9.38 ± 2.15	1.198	0.233
Stroke category[n (%)]			3.330	0.189
Mild	20 (32.79%)	29 (49.15%)		
Moderate	27 (44.26%)	20 (33.9%)		
Severe	14 (22.95%)	10 (16.95%)		
Clot location[n (%)]			0.578	0.526
Internal carotid artery	13 (21.31%)	15 (25.42%)		
Middle cerebral artery	37 (60.66%)	34 (57.63%)		
Anterior cerebral artery	2 (3.28%)	0 (0.00%)		
Vertebral artery	2 (3.28%)	2 (3.39%)		
Posterior cerebral artery	2 (3.28%)	0 (0.00%)		
Basilar artery	5 (8.20%)	8 (13.56%)		
Onset to drug administration (min)	256.38 ± 40.23	260.79 ± 45.03	0.566	0.572
Application of NBP[n (%)]	22 (36.07%)	42 (71.19%)	14.864	< 0.001
OCSP[n (%)]			0.222	0.974
TACI	17 (27.87%)	16 (27.12%)		
PACI	32 (52.46%)	33 (55.93%)		
POCI	8 (13.11%)	7 (11.86%)		
LACI	4 (6.56%)	3 (5.08%)		

Abbreviations: NIHSS, National Institute of Health Stroke Scale; NBP, N-butylphthalide; OCSP, Oxfordshire Community Stroke Project; TACI, Total anterior circulation infarct; PACI, Partial anterior circulation infarct; POCI, Posterior circulation infarct; LACI, Lacunar infarct.

was significantly higher in the good outcome group (71.19% vs 36.07%, P < 0.001). There were no significant differences in NIHSS scores or clot locations between groups, nor were there differences based on the Oxfordshire Community Stroke Project classifications (all P > 0.05). These findings suggest that smoking, hypertension, and diabetes may negatively influence stroke recovery, while the application of NBP was associated with better functional outcomes.

Blood Glucose and Lipid Profiles

The mean Glycated HbA1C levels were 9.26 ± 1.37% in the poor outcome group and 9.02 ± 0.98% in the good outcome group (P = 0.270) (Figure 1A). FBG levels were slightly higher in the poor outcome group at 6.05 ± 1.32 mmol/L

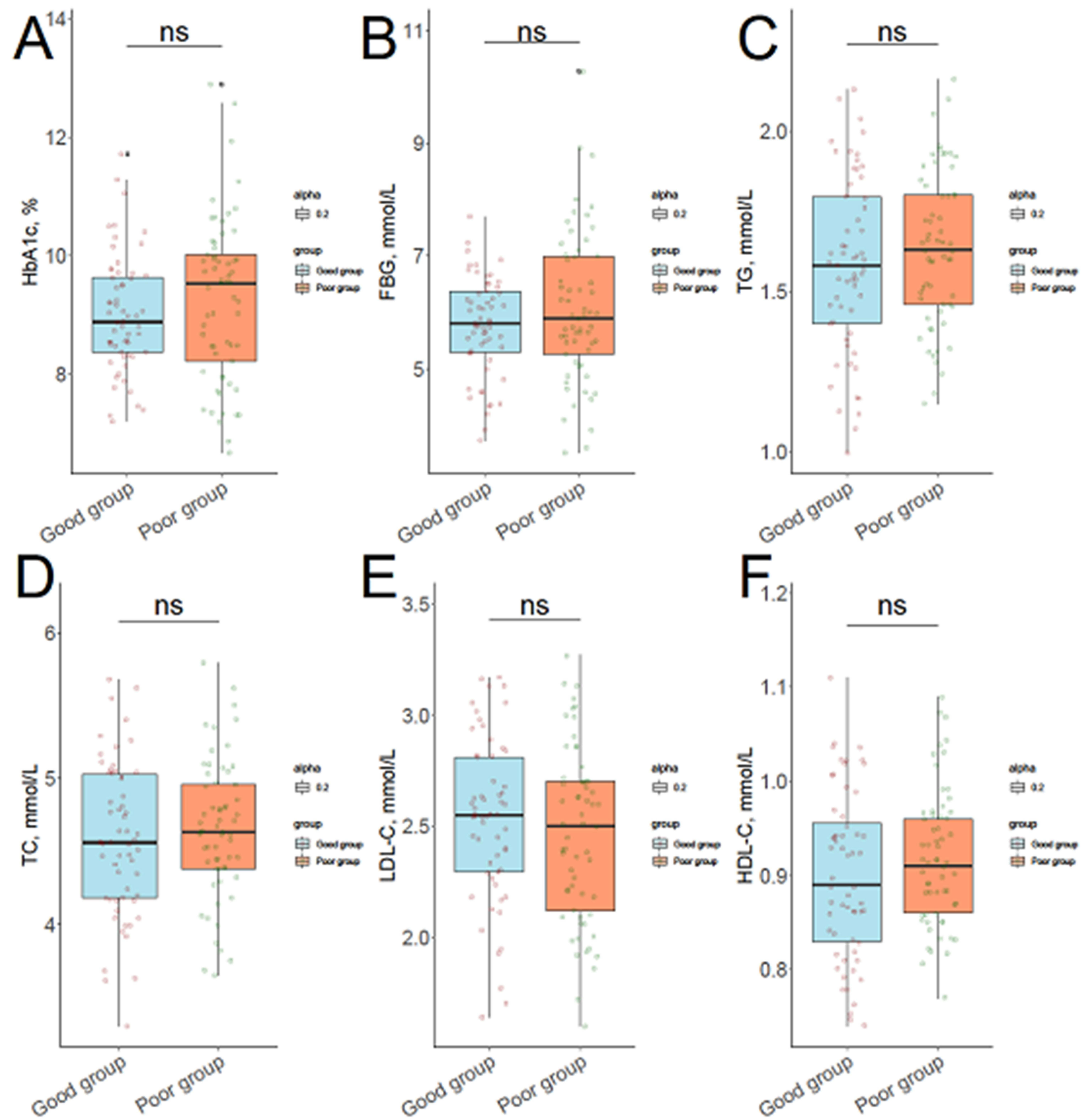

Figure 1 Comparison of Blood Glucose and Lipid Profiles Between Two Patient Groups. (**A**) HbA1c (**B**) FBG (**C**) TG (**D**) TC (**E**) LDL-C (**F**) HDL-C ns: no significant difference.

Note: HbA1c, Glycated Hemoglobin A1c; FBG, Fasting Blood Glucose; TG, triglyceride; TC, serum total cholesterol; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol.

compared to 5.76 ± 0.87 mmol/L in the good outcome group, although this difference was not statistically significant (P = 0.156) (Figure 1B). Similarly, no significant differences were found for triglycerides (TG), TC, low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C), with P values of 0.277, 0.478, 0.280, and 0.205, respectively (Figure 1C-F). These findings suggest that blood glucose and lipid profiles do not significantly differ between patients with varying functional recovery post-thrombectomy.

Additional Biochemical Parameters

The poor outcome group exhibited significantly higher levels of hs-CRP (3.58 ± 0.81 mg/L) compared to the good outcome group (2.97 ± 0.73 mg/L), indicating a potential association between elevated inflammatory markers and poorer recovery (P < 0.001) (Figure 2E). Other biochemical parameters, including UA, SCr, Hcy, BUN, and lipoprotein-associated phospholipase A2 (Lp-PLA2), did not show statistically significant differences between the groups, with corresponding P values of 0.695, 0.271, 0.809, 0.433, and 0.089, respectively (Figure 2A-D, F). These results suggest that while hs-CRP may be correlated with functional outcomes, other examined biochemical markers do not significantly differentiate between the recovery groups.

Intraoperative Factors

The mean procedure times were similar between the groups, with 93.37 ± 29.31 minutes for the poor outcome group and 94.21 ± 30.04 minutes for the good outcome group (P = 0.877) (Table 4). Aspiration guide catheter (AGC) times were also comparable, averaging 57.19 ± 14.58 minutes for the poor outcome group and 57.34 ± 15.60 minutes for the good outcome group (P = 0.957). The use of anticoagulant therapy during the operation was slightly higher in the good outcome group (57.63%) compared to the poor outcome group (45.90%), but this difference was not statistically significant (P = 0.199). Additionally, the occurrence of intracranial hemorrhage within 24 hours post-operation was low, with 3.28% in the poor outcome group and none in the good outcome group (P = 0.491). Overall, intraoperative factors did not demonstrate significant associations with functional outcomes in this cohort.

Vascular Recanalization Outcomes

Patients in the poor outcome group had a mean ASPECTS score of 8.76 ± 1.10, while the good outcome group had a slightly higher score of 9.08 ± 1.09, but this difference was not statistically significant (P = 0.109) (Table 5). The distribution of TICI grades 0–2a and 2b–3 between the groups was similar, with 21.31% of the poor outcome group achieving TICI grades 0–2a compared to 16.95% in the good outcome group, and 78.69% versus 83.05% achieving TICI grades 2b–3, respectively (P = 0.544). These findings suggest that the degree of vascular recanalization and initial infarct severity, as measured by ASPECTS and TICI scores, were not significantly associated with the functional outcomes observed in this study cohort.

Correlation Analysis

The correlation analysis between various factors and functional outcomes in stroke patients undergoing MT revealed several significant associations (Table 6). Smoking history was negatively correlated with functional outcomes (rho = −0.244, P = 0.007), indicating that smokers experienced poorer recovery. Hypertension and diabetes also demonstrated negative correlations with outcomes (rho = −0.284, P = 0.002 and rho = −0.242, P = 0.008, respectively), suggesting that these comorbidities were linked to diminished recovery post-thrombectomy. Conversely, the application of the neuroprotective agent NBP showed a positive correlation with improved functional outcomes (rho = 0.352, P < 0.001), highlighting its potential efficacy in enhancing recovery. Additionally, hs-CRP was negatively correlated with outcomes (rho = −0.359, P < 0.001), suggesting that higher levels of inflammation were associated with poorer recovery. Overall, this analysis underscores the impact of specific health factors and treatments on the functional prognosis of stroke patients post-thrombectomy.

Univariate Logistic Regression Analysis

The univariate logistic regression analysis identified several factors significantly associated with functional outcomes in post-thrombectomy stroke patients (Table 7). A history of smoking was inversely related to favorable outcomes, with a coefficient of −1.109 (Wald = 2.617, P = 0.009), and an odds ratio (OR) of 0.330 (95% CI, 0.139–0.742), indicating

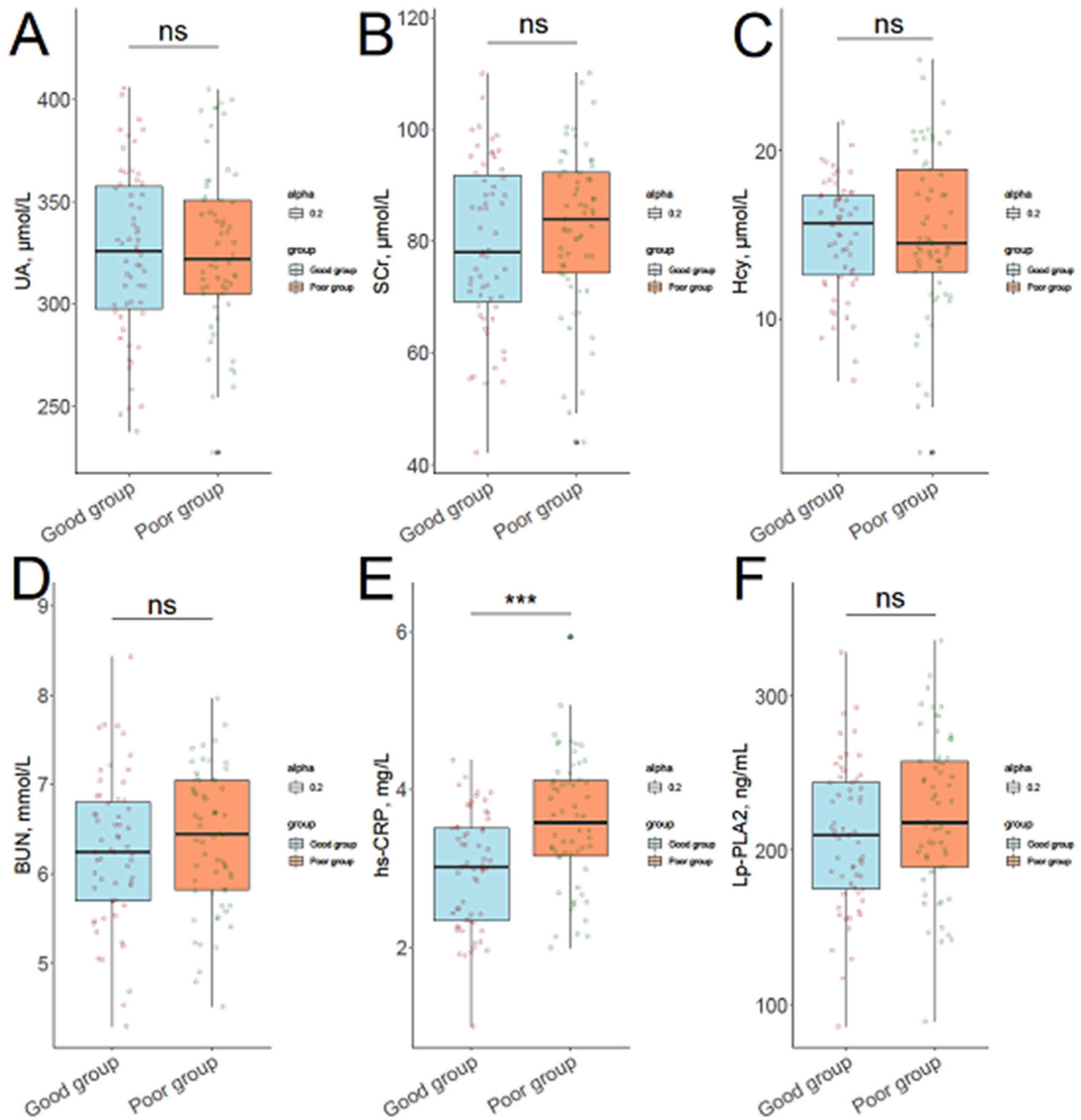

Figure 2 Comparison of Additional Biochemical Parameters Between Two Patient Groups. (**A**) UA (**B**) SCr (**C**) Hcy (**D**) BUN (**E**) hs-CRP (**F**) Lp-PLA2 *** P < 0.001, ns: no significant difference.

Note: UA, Uric Acid; SCr, Serum Creatinine; Hcy, Homocysteine; BUN, Blood Urea Nitrogen; hs-CRP, high-sensitivity CRP; Lp-PLA2, lipoprotein-associated phospholipase A2.

a higher likelihood of poor outcomes among smokers. Hypertension was similarly associated with adverse functional recovery, evidenced by a coefficient of −1.178 (Wald = 3.061, P = 0.002) and an OR of 0.308 (95% CI, 0.142–0.647). Diabetes also showed a negative association with outcomes (coefficient −1.308, Wald = 2.543, P = 0.011), with an OR of 0.270 (95% CI, 0.091–0.707). In contrast, the application of NBP significantly improved functional outcomes (coefficient 1.477, Wald = 3.767, P < 0.001), with an OR of 4.380 (95% CI, 2.063–9.641), suggesting that NBP administration dramatically enhances recovery. Additionally, elevated hs-CRP levels were negatively correlated with favorable outcomes (coefficient −1.025, Wald = 3.792, P < 0.001), with an OR of 0.359 (95% CI, 0.205–0.594). These findings

Table 4 Comparison of Intraoperative Factors Between Two Patient Groups

Parameters	Poor group (n = 61)	Good group (n = 59)	*t*/χ^2	*P*
Procedure time (min)	93.37 ± 29.31	94.21 ± 30.04	0.155	0.877
AGC time (min)	57.19 ± 14.58	57.34 ± 15.60	0.054	0.957
Anticoagulant therapy during operation[n (%)]	28 (45.90%)	34 (57.63%)	1.651	0.199
Within 24 hours of ICH	2 (3.28%)	0 (0.00%)	0.475	0.491

Abbreviations: AGC, aspiration guide catheter; ICH, intracranial hemorrhage.

Table 5 Comparison of Vascular Recanalization Outcomes Between Two Patient Groups

Parameters	Poor group (n = 61)	Good group (n = 59)	*t*/χ^2	*P*
ASPECTS score	8.76 ± 1.10	9.08 ± 1.09	1.616	0.109
Recanalization			0.368	0.544
TICI 0–2a	13 (21.31%)	10 (16.95%)		
TICI 2b–3	48 (78.69%)	49 (83.05%)		

Abbreviations: ASPECTS, Alberta Stroke Program Early Computed Tomography Score; TICI, Thrombolysis in Cerebral Infarction.

Table 6 Correlation Analysis of Each Factor and Functional Outcomes of Patients

Parameters	rho	*P*
Smoking history[n (%)]	−0.244	0.007
Hypertension	−0.284	0.002
Diabetes	−0.242	0.008
Application of NBP[n (%)]	0.352	< 0.001
hs-CRP, mg/L	−0.359	< 0.001

Table 7 Univariate Logistic Regression Analysis of Factors Associated With Patient Functional Outcomes

Parameters	Coefficient	Std Error	Wald	P	OR	95% CI
Smoking history [n (%)]	−1.109	0.424	2.617	0.009	0.330	0.139–0.742
Hypertension	−1.178	0.385	3.061	0.002	0.308	0.142–0.647
Diabetes	−1.308	0.514	2.543	0.011	0.270	0.091–0.707
Application of NBP[n (%)]	1.477	0.392	3.767	< 0.001	4.380	2.063–9.641
hs-CRP, mg/L	−1.025	0.270	3.792	< 0.001	0.359	0.205–0.594

highlight the impact of comorbidities and therapeutic interventions on the functional recovery of stroke patients following MT.

Multivariate Logistic Regression Analysis

The multivariate logistic regression analysis highlights several independent risk factors associated with functional outcomes in stroke patients following MT. A smoking history was significantly associated with poorer outcomes, reflected in a coefficient of −1.139 (Wald Stat = −2.303, P = 0.021), with an odds ratio (OR) of 0.320 (95% CI, 0.122–0.844) (Table 8). Although hypertension showed a negative tendency towards functional outcomes (coefficient −0.741, Wald Stat = −1.651, P = 0.099), it did not reach statistical significance, with an OR of 0.477 (95% CI,

Table 8 Multivariate Logistic Regression Analysis of Factors Associated With Patient Functional Outcomes

Parameters	Coefficient	Std Error	Wald Stat	P	OR	OR CI Lower	OR CI Upper
Smoking history[n (%)]	−1.139	0.494	−2.303	0.021	0.320	0.122	0.844
Hypertension	−0.741	0.448	−1.651	0.099	0.477	0.198	1.148
Diabetes	−1.403	0.613	−2.288	0.022	0.246	0.074	0.818
Application of NBP[n (%)]	1.178	0.444	2.651	0.008	3.248	1.360	7.759
hs-CRP, mg/L	−0.899	0.316	−2.842	0.004	0.407	0.219	0.757

0.198–1.148). Diabetes remained a significant negative predictor of outcomes with a coefficient of −1.403 (Wald Stat = −2.288, P = 0.022) and an OR of 0.246 (95% CI, 0.074–0.818). The use of the neuroprotective agent NBP was significantly associated with improved outcomes, as evidenced by a coefficient of 1.178 (Wald Stat = 2.651, P = 0.008) and an OR of 3.248 (95% CI, 1.360–7.759). Additionally, elevated hs-CRP levels continued to demonstrate a negative impact on functional recovery (coefficient −0.899, Wald Stat = −2.842, P = 0.004), with an OR of 0.407 (95% CI, 0.219–0.757). These findings suggest that smoking and diabetes were detrimental to patient recovery, while the application of NBP may significantly enhance functional outcomes.

Discussion

In this study, we aimed to explore the impact factors and efficacy of neuroprotective agents, particularly NBP, on functional outcomes following mechanical MT in stroke patients.

The data revealed that NBP administration was significantly associated with improved functional outcomes at 90 days post-stroke, as evidenced by higher percentages of patients achieving favorable mRS scores in the NBP group compared to the routine care group. This outcome aligns with existing literature suggesting the neuroprotective properties of NBP,[22,23] which may work through various mechanisms, including anti-inflammatory effects, anti-oxidative properties, and enhancement of cerebral blood flow. Furthermore, recent findings have corroborated our results, demonstrating that NBP significantly improves functional recovery when used as an adjunct to MT in acute ischemic stroke patients.[17]

Smoking, hypertension, and diabetes were identified as negative predictors of functional outcomes post-thrombectomy. The detrimental impact of smoking was likely multifactorial, potentially involving endothelial dysfunction, increased platelet aggregation, and oxidative stress, all of which can exacerbate ischemic injury and hinder recovery.[24] The adverse effects of hypertension and diabetes on stroke recovery were well-documented,[25–27] with both conditions contributing to microvascular damage, increased blood-brain barrier permeability, and the promotion of pro-inflammatory states. These comorbidities may exacerbate brain injury during the acute phase of ischemic stroke and impede neuronal repair mechanisms, resulting in less favorable outcomes.[28,29]

Interestingly, while hypertension did not achieve statistical significance as an independent predictor in multivariate analysis, it showed a negative tendency toward recovery. This observation suggests that while hypertension was a critical factor in stroke risk, its impact on recovery may be modulated by other variables, such as age, baseline stroke severity, and treatment strategies. The intricate interplay of these factors warrants further exploration to tailor individualized therapeutic approaches.

Elevated levels of hs-CRP were inversely correlated with functional outcomes, highlighting the potential role of systemic inflammation in stroke recovery. Higher hs-CRP levels likely reflect a heightened inflammatory response, which could aggravate post-ischemic brain injury through mechanisms such as the release of pro-inflammatory cytokines, activation of microglia, and the perpetuation of neurotoxicity.[30,31] Managing inflammation may thus represent a viable therapeutic target to enhance post-thrombectomy recovery.

Contrary to expectations, other biochemical markers, including UA, SCr, and lipid profiles, did not show significant associations with functional outcomes. These findings suggest that while metabolic parameters were essential in stroke pathogenesis, their direct influence on recovery may be less pronounced or overshadowed by other dominant factors such as inflammation and neuroprotection. Additionally, the lack of significance in lipid profiles may be attributable to the

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homogeneous lipid management across treatment groups or the possibility that lipid levels play a less direct role in functional recovery compared to inflammatory markers.

The absence of significant differences in procedure times, anticoagulation use, and initial vessel occlusion/recanalization grades between outcome groups suggests that intraoperative factors and immediate procedural success may not be the primary determinants of long-term recovery in this cohort. Instead, post-procedural care and early neuroprotective interventions might play more pivotal roles.

It was noteworthy that baseline characteristics, including age, gender, and body mass index, showed no significant association with outcomes. This may reflect the homogeneity of the study population regarding these factors or indicate that other clinical, biochemical, and therapeutic factors exert more substantial influences on recovery.

The positive impact of NBP on functional outcomes could be attributed to its multifaceted neuroprotective actions. NBP has been shown to improve mitochondrial function, reduce oxidative stress, and promote neurogenesis.[32] It also has a modulating effect on cerebral blood flow, which might confer protective effects by sustaining penumbral tissue post-reperfusion.[33] Moreover, NBP's anti-inflammatory properties may complement its antioxidative actions, attenuating both acute and delayed neuronal injury processes.[34] However, it is important to acknowledge that serious adverse events associated with NBP, such as prolonged hospital stays, permanent organ damage, and in rare cases, death, have been reported in some patients. These adverse effects warrant cautious application and further investigation to optimize dosing and minimize risks.

The finding that NBP administration was associated with better outcomes underscores the potential benefits of integrating neuroprotective strategies alongside acute revascularization therapies. The superiority of NBP might be due to its specific targeting of pathophysiological processes active during the peri-reperfusion phase, a critical window where neuronal salvage can profoundly impact long-term recovery.

While this study provides significant insights into the factors influencing stroke recovery and the potential efficacy of neuroprotective agents like NBP, several limitations must be acknowledged. The observational design of the study limits the ability to establish causality between the interventions and outcomes. Additionally, the study's sample size may not provide sufficient power to detect all clinically relevant associations, particularly among less prevalent variables. The cohort was drawn from a single institution, potentially limiting the generalizability of the findings to broader, more diverse populations. Moreover, the reliance on de-identified data, while ensuring patient privacy, may omit nuanced patient-specific factors that could influence recovery. The study also did not account for variations in post-thrombectomy care and rehabilitation, which could significantly impact functional outcomes. Future research should aim to address these limitations through multicenter randomized controlled trials with larger sample sizes and a more comprehensive collection of patient data.

Conclusion

In conclusion, this study highlights the potential efficacy of NBP as a neuroprotective agent in enhancing functional recovery post-MT. The identification of smoking, diabetes, and elevated hs-CRP as negative predictors of outcomes emphasizes the need for comprehensive management of modifiable risk factors and systemic inflammation. Additionally, the integration of NBP with standard MT treatment protocols may offer a promising therapeutic avenue for improving patient outcomes. Further controlled trials are warranted to confirm these findings and explore the integration of neuroprotective strategies with standard care for acute ischemic stroke. Such efforts could herald significant advancements in the quest to improve the functional prognosis for stroke patients undergoing MT.

Data Sharing Statement

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

Ethics Statement

This study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Third Hospital of Shanxi Medical University (SX-TY-35).

Consent for Publication

Written informed consent was obtained from all participants.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

All authors declare that they have no conflicts of interest in this work.

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