Predictors of an Unfavourable Outcome After Mechanical Thrombectomy for Acute Ischaemic Stroke

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Abstract

Background: Mounting evidence has shown that mechanical thrombectomy (MT) improves clinical outcomes for large vessel occlusions (LVOs) in patients with acute ischaemic stroke (AIS) of the anterior circulation. The present study aimed to provide a comprehensive analysis of risk factors associated with clinical outcomes in AIS patients receiving MT.

Methods: A total of 212 consecutive patients who underwent MT for AIS were enrolled in the present study. Clinical characteristics were recorded at admission. Two endpoints were defined according to the 3-month modified Rankin scale (mRS) score after AIS (good outcome, mRS 0–2; and death, mRS 6). Additionally, we compared the clinical outcomes and safety of MT alone and bridging therapy in AIS patients.

Results: Of the 212 patients treated with MT, 114 (53.77%) patients had a good outcome and 31 (14.62%) died. The incidence of a worse outcome after MT was significantly elevated in males and patients with high WBC counts, high admission blood glucose levels, high baseline NIHSS scores and a long interval time from groin puncture to reperfusion in AIS patients treated with MT after adjustment for covariates ($P < 0.05$); these risk factors were further confirmed by our constructed nomograms. In addition, we observed no significant benefit of bridging therapy compared to MT alone in AIS patients.

Conclusions: The factors associated with an unfavourable outcome in AIS patients treated with MT were male sex, admission WBC, admission blood glucose, NIHSS, and the interval time from groin puncture to reperfusion.

Background

Stroke remains a common neurologic emergency and a leading cause of mortality worldwide (1). Among patients with stroke, approximately 85% of the events are ischaemic. Several studies have provided overwhelming evidence that mechanical thrombectomy (MT) is the preferred first-line therapy for large vessel occlusions (LVOs) in patients with acute ischaemic stroke (AIS) of the anterior circulation resulting in better functional outcomes and reduced mortality (2–4). However, a substantial proportion of AIS patients treated with MT have not experienced functional improvement (5). Therefore, to further study MT as the standard of care for AIS patients, it is necessary to identify potential biomarkers associated with clinical outcomes to stratify patients for personalized therapy.

Previous studies have shown that inflammatory mediators, baseline National Institutes of Health Stroke Scale (NIHSS) score, and blood glucose levels predicted death and poor outcome at 90 days after MT for anterior circulation LVO in AIS patients (6, 7). However, a single parameter is inevitably limited in predicting poor outcome in AIS patients treated with MT (8). Mounting evidence indicates that nomograms have gained popularity in the assessment of patient-individualized outcomes (9, 10). However, nomograms for assessing clinical outcomes in AIS patients treated with MT are scarce.

In the present study, we performed a retrospective analysis of all AIS patients treated with MT to screen the significant variables that influence clinical outcomes of AIS patients receiving MT. To accomplish this purpose, we investigated the influence of demographic data, medical history, stroke etiology, laboratory parameters at admission, intervals times for MT, and therapeutic methods on clinical outcomes after 3 months (3-month modified Rankin Scale (mRS)) and identified whether a nomogram based on these parameters can be used to stratify AIS patients for the future treatment. Additionally, we compared the clinical outcomes and safety of MT alone and bridging therapy in AIS patients.

Methods

Study design

The study protocol was approved by the Nanjing Medical University Ethics Committee and complied with the Declaration of Helsinki. We performed a retrospective single-centre review of all consecutive AIS patients treated with MT due to LVO of the anterior circulation, including the middle cerebral artery (M1/M2) and the terminal internal carotid artery (ICA), who were treated at the Nanjing First Hospital, Nanjing Medical University between October 2015 and October 2018.

The selection criteria were as follows: (1) ≥ 18 years of age; (2) LVO in the ICA or M1/M2 segment of the middle cerebral artery confirmed by computed tomography angiography (CTA), magnetic resonance angiography (MRA) or digital subtraction angiography (DSA); (3) time from symptom onset to door (OTD) ≤ 24 hours; (4) baseline NIHSS score ≥ 6 or aphasia if NIHSS 6 on admission; (5) pre-stroke mRS score ≤ 1; (6) MT with first-line thrombectomy technique (stent retriever, contact aspiration or ADAPT) to achieve successful reperfusion, and we switched to the other technique if not successful reperfusion. Eligible patients received intravenous alteplase as bridging therapy according to the guideline criteria (11). A total of 212 eligible patients were enrolled in the present study.

Imaging protocol

All patients underwent non-contrast CT according to the stroke imaging protocol before MT. Patients within 6 hours of symptom onset underwent a CTA protocol or direct DSA to verify LVOs of the anterior circulation. Acute multimodal 3T magnetic resonance imaging (diffusion-weighted imaging [DWI], fluid-attenuated inversion recovery [FLAIR] imaging and perfusion-weighted imaging [PWI]) was administered to 131 patients with unknown symptom onset (38.9% of wake-up stroke) or more than 6 hours of symptom onset (61.1%) to discriminate between terminally infarcted tissue and salvageable tissue according to the PWI/DWI or FLAIR/DWI mismatch in MR imaging. A follow-up CT was conducted routinely within 24 hours of MT.

Data collection

All consecutive patients were retrospectively documented. This information included demographics, medical history (hypertension, diabetes mellitus, coronary artery disease [CAD], atrial fibrillation, transient ischaemic attack [TIA], ischaemic stroke), stroke etiology, pre-treatment laboratory parameters, wake-up stroke, intravenous thrombolysis, baseline NIHSS score, interval times, occlusion site, thrombolysis in cerebral infarction (mTICI), passes of the retriever, complications and outcomes. Stroke etiology was determined by the Trial of Org 10172 in Acute Stroke (TOAST) criteria (12). The wake-up stroke refers to an unknown exact time of symptom onset. The status of vessel recanalization was determined by the mTICI, and an mTICI of 2b-3 was considered a successful recanalization. Clinical outcomes were explored using 3-month mRS after onset, with a good outcome as an mRS score of 0–2 and the alive outcome as an mRS score of 0–5, as described in our previous study (13).

Statistical analysis

All patients were divided into good and non-good outcomes, or alive and deceased groups. Categorical variables (sex, drinking, smoking, medical history, stroke etiology, MRI, wake-up stroke, intravenous thrombolysis, occlusion site, mTICI, passes of the retriever and complications) were summarized as percentages, which were analyzed using the chi-square test. Continuous variables were summarized as the mean ± S.D. or median (IQR), which were analyzed using the independent t test or the Mann-Whitney *U* test, as appropriate. The correlation between clinical variables and outcomes at 3 months was assessed with a binary logistic regression analysis. Significant variables with a p value < 0.05 from the univariate analyses were included in the multivariate logistic regression analysis. A nomogram was constructed with R software (Institute for Statistics and Mathematics, Vienna, Austria) according to the independent variables, and its predictive capacity was assessed by Harrell's c-index. $P < 0.05$ was considered statistically significant.

Results

Baseline characteristics

Overall, a total of 212 patients met the inclusion criteria. The baseline characteristics of all patients are shown in Table 1. The mean age of patients treated with MT was 71.34 ± 12.02 years, 127 (59.91%) were men, the median OTD was 144 (60–189) min, the baseline NIHSS score was 15 (12–19), 51 (24.06%) patients had wake-up stroke, and 104 (49.06%) underwent intravenous thrombolysis. Successful recanalization was achieved in 191 (90.09%) patients. All patients treated with MT underwent a 3-month follow-up. Of these patients, 114 (53.77%) had a good outcome and 31 (14.62%) died.

Table 1
Baseline characteristics of the study population

Risk factors	Outcome measures (mRS)					
	Good (0–2) (n = 114)	Non-good (3–6) (n = 98)	*P*	Alive (0–5) (n = 181)	Death (6) (n = 31)	*P*
Sex (male)	61 (53.51)	66 (67.35)	0.040	105 (58.01)	22 (70.97)	0.174
Age (years)	69.14 ± 12.39	73.91 ± 11.10	0.004	70.70 ± 12.10	75.10 ± 10.99	0.060
Drinking	24 (21.05)	21 (21.43)	0.947	37 (20.44)	8 (25.81)	0.500
Smoking	26 (22.81)	20 (20.41)	0.673	39 (21.55)	7 (22.58)	0.897
SBP	137.68 ± 23.95	145.34 ± 23.34	0.020	140.05 ± 23.39	147.90 ± 26.22	0.091
DBP	85.71 ± 14.79	87.44 ± 15.67	0.410	86.62 ± 15.11	85.84 ± 15.85	0.791
Medical history						
Hypertension	81 (71.05)	73 (74.49)	0.576	132 (72.93)	22 (70.97)	0.821
Diabetes mellitus	25 (21.93)	24 (24.49)	0.659	42 (23.20)	7 (22.58)	0.939
CAD	36 (31.58)	30 (30.61)	0.880	55 (30.39)	11 (35.48)	0.571
Atrial fibrillation	60 (52.63)	62 (63.27)	0.118	101 (55.80)	21 (67.74)	0.214
TIA	1 (0.88)	2 (2.04)	0.895	3 (1.66)	0 (0)	0.920
Ischaemic stroke	25 (21.93)	17 (17.35)	0.404	38 (20.99)	4 (12.90)	0.296
Stroke etiology						
Atherosclerotic	42 (36.84)	30 (30.61)	0.300	64 (35.36)	8 (25.81)	0.552

SBP, systolic blood pressure; DBP, diastolic blood pressure; CAD, coronary artery disease; TIA, transient ischaemic attack; Hb, hemoglobin; WBC, white blood cell; INR, international normalized ratio; BUN, blood urea nitrogen; TC, total cholesterol; TG, triglycerides; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; HCY, homocysteine; Lp-PLA2, lipoprotein-associated phospholipase A2; ICA, internal carotid artery; IQR, interquartile range; M1,M2, first or second segment of the middle cerebral artery; NIHSS, National Institutes of Health Stroke Scale; mTICI, modified thrombolysis in cerebral infarction score; mRS, modified Rankin scale.

Variables with skewed distributions are expressed as medians (interquartile range). Variables with normal distributions are expressed as the mean ± standard deviation. Categorical variables are expressed as frequencies and percentages.

Risk factors	Outcome measures (mRS)					
	Good (0–2) (n = 114)	Non-good (3–6) (n = 98)	*P*	Alive (0–5) (n = 181)	Death (6) (n = 31)	*P*
Cardioembolic	65 (57.02)	65 (66.33)		109 (60.22)	21 (67.74)	
Underdetermined or others	7 (6.14)	3 (3.06)		8 (4.42)	2 (6.45)	
Laboratory parameter						
Hb	124.98 ± 17.04	130.67 ± 22.59	0.043	127.03 ± 18.86	131.00 ± 25.65	0.423
WBC (10^9/L)	8.66 ± 3.29	10.25 ± 3.52	0.001	9.22 ± 3.34	10.44 ± 4.12	0.074
Platelet (10^9/L)	183.92 ± 54.91	179.33 ± 78.40	0.619	183.99 ± 66.80	168.63 ± 65.03	0.243
INR	1.06 ± 0.16	1.05 ± 0.13	0.457	1.05 ± 0.16	1.05 ± 0.11	0.945
BUN	5.94 ± 3.02	6.64 ± 2.23	0.062	6.16 ± 2.69	6.91 ± 2.70	0.154
Creatinine	76.93 ± 26.76	82.32 ± 28.40	0.158	78.31 ± 26.59	85.97 ± 32.59	0.154
Admission glucose (mmol/L)	6.26 ± 1.91	7.83 ± 2.90	< 0.001	6.83 ± 2.42	7.94 ± 3.05	0.026
TC (mmol/L)	4.00 ± 0.84	4.30 ± 1.56	0.093	4.08 ± 0.95	4.46 ± 2.31	0.123
TG (mmol/L)	1.13 ± 0.72	1.31 ± 1.03	0.148	1.19 ± 0.83	1.36 ± 1.15	0.452
LDL-C (mmol/L)	2.42 ± 0.73	2.52 ± 0.87	0.377	2.46 ± 0.82	2.49 ± 0.65	0.859
HDL-C (mmol/L)	1.14 ± 0.28	1.16 ± 0.30	0.692	1.15 ± 0.29	1.13 ± 0.28	0.780

SBP, systolic blood pressure; DBP, diastolic blood pressure; CAD, coronary artery disease; TIA, transient ischaemic attack; Hb, hemoglobin; WBC, white blood cell; INR, international normalized ratio; BUN, blood urea nitrogen; TC, total cholesterol; TG, triglycerides; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; HCY, homocysteine; Lp-PLA2, lipoprotein-associated phospholipase A2; ICA, internal carotid artery; IQR, interquartile range; M1,M2, first or second segment of the middle cerebral artery; NIHSS, National Institutes of Health Stroke Scale; mTICI, modified thrombolysis in cerebral infarction score; mRS, modified Rankin scale.

Variables with skewed distributions are expressed as medians (interquartile range). Variables with normal distributions are expressed as the mean ± standard deviation. Categorical variables are expressed as frequencies and percentages.

Risk factors	Outcome measures (mRS)					
	Good (0–2) (n = 114)	Non-good (3–6) (n = 98)	*P*	Alive (0–5) (n = 181)	Death (6) (n = 31)	*P*
Uric acid (μmol/L)	294.51 ± 116.79	324.12 ± 126.77	0.080	302.11 ± 116.34	344.67 ± 149.35	0.077
HbA1c (%)	6.18 ± 1.34	6.25 ± 1.35	0.723	6.20 ± 1.37	6.34 ± 1.15	0.900
HCY (μmol/L)	22.03 ± 73.19	15.83 ± 8.85	0.428	19.75 ± 7.98	15.44 ± 7.15	0.701
Lp-PLA2 (ng/mL)	261.12 ± 129.42	296.75 ± 135.89	0.067	272.90 ± 131.61	301.32 ± 142.27	0.306
Wake-up stroke	30 (26.32)	21 (21.43)	0.407	47 (25.97)	4 (12.90)	0.116
Bridging therapy	56 (49.12)	48 (48.98)	0.983	86 (47.51)	18 (58.06)	0.278
Baseline NIHSS score	13 (10–17)	18 (14–21)	< 0.001	15 (11–18)	18 (13–24)	0.002
Interval time, min, median (IQR)						
onset to door	118 (60–205)	103 (58–180)	0.308	110 (55–198)	100 (70–180)	0.999
onset to thrombolysis	132 (96–184)	136 (100–174)	0.987	134 (99–180)	140 (107–176)	0.793
onset to reperfusion	338 (280–414)	340 (280–423)	0.610	336 (280–415)	343 (290–420)	0.415
door to groin puncture	119 (87–144)	115 (90–149)	0.692	120 (90–145)	100 (90–145)	0.480
door to reperfusion	210 (169–251)	238 (195–276)	0.004	220 (175–260)	239 (195–280)	0.100

SBP, systolic blood pressure; DBP, diastolic blood pressure; CAD, coronary artery disease; TIA, transient ischaemic attack; Hb, hemoglobin; WBC, white blood cell; INR, international normalized ratio; BUN, blood urea nitrogen; TC, total cholesterol; TG, triglycerides; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; HCY, homocysteine; Lp-PLA2, lipoprotein-associated phospholipase A2; ICA, internal carotid artery; IQR, interquartile range; M1,M2, first or second segment of the middle cerebral artery; NIHSS, National Institutes of Health Stroke Scale; mTICI, modified thrombolysis in cerebral infarction score; mRS, modified Rankin scale.

Variables with skewed distributions are expressed as medians (interquartile range). Variables with normal distributions are expressed as the mean ± standard deviation. Categorical variables are expressed as frequencies and percentages.

Risk factors	Outcome measures (mRS)					
	Good (0–2) (n = 114)	Non-good (3–6) (n = 98)	*P*	Alive (0–5) (n = 181)	Death (6) (n = 31)	*P*
groin puncture to reperfusion	81 (65–113)	110 (80–143)	< 0.001	90 (70–125)	115 (90–142)	0.005
Occlusion site						
ICA	15 (13.16)	11 (11.22)	0.793	24 (13.26)	2 (6.45)	0.404
M1/M2	60 (52.63)	56 (57.14)		96 (53.04)	20 (64.52)	
ICA + M	39 (34.21)	31 (31.63)		61 (33.70)	9 (29.03)	
mTICI						
0-2a	13 (11.40)	8 (8.16)	0.431	18 (9.94)	3 (9.68)	0.963
2b-3	101 (88.60)	90 (91.84)		163 (90.06)	28 (90.32)	
Passes of the retriever						
<3	67 (58.77)	58 (59.18)	0.952	106 (58.56)	19 (61.29)	0.776
≥3	47 (41.23)	40 (40.82)		75 (41.44)	12 (38.71)	

SBP, systolic blood pressure; DBP, diastolic blood pressure; CAD, coronary artery disease; TIA, transient ischaemic attack; Hb, hemoglobin; WBC, white blood cell; INR, international normalized ratio; BUN, blood urea nitrogen; TC, total cholesterol; TG, triglycerides; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; HCY, homocysteine; Lp-PLA2, lipoprotein-associated phospholipase A2; ICA, internal carotid artery; IQR, interquartile range; M1,M2, first or second segment of the middle cerebral artery; NIHSS, National Institutes of Health Stroke Scale; mTICI, modified thrombolysis in cerebral infarction score; mRS, modified Rankin scale.

Variables with skewed distributions are expressed as medians (interquartile range). Variables with normal distributions are expressed as the mean ± standard deviation. Categorical variables are expressed as frequencies and percentages.

Correlation of baseline characteristics with clinical outcomes

Table 1 shows that the non-good outcome groups had significantly higher SBP, WBC, admission blood glucose, higher Hb levels and baseline NIHSS scores; longer door to reperfusion and groin puncture to reperfusion interval times; and a higher proportion of males, atrial fibrillation and older age ($P < 0.05$).

Patients who died suffered higher admission blood glucose, baseline NIHSS, and a longer groin puncture to reperfusion interval time ($P < 0.05$).

Risk factors for clinical outcomes

For non-good outcomes, multivariate logistic regression analyses showed that male sex (odds ratio [OR] = 2.75, 95% confidence interval [CI] = 1.30–5.84), higher WBC counts (OR = 1.11, 95% CI = 1.01–1.23), higher admission glucose levels (OR = 1.32, 95% CI = 1.13–1.55), higher baseline NIHSS score (OR = 1.16, 95% CI = 1.08–1.24), and longer groin puncture to reperfusion interval time (OR = 1.01, 95% CI = 1.00-1.02) were independent indicators. For patients who died, a higher baseline NIHSS score was an independent predictor.

Clinical outcomes and safety of MT and bridging therapy

Whether intravenous thrombolysis before MT (bridging therapy) is essential for AIS patients with LVO remains controversial. Our results showed that the influences of MT alone and bridging therapy on clinical outcomes were not significantly different ($P > 0.05$, Table 1, Fig. 1). To further explore their clinical outcomes and safety, we performed a correlation analysis between the therapeutic methods and baseline characteristics (Table 3). The results suggested that patients with MT alone suffered more often from wake-up stroke, higher BUN levels, and longer consultation time compared to those with bridging therapy ($P < 0.05$). However, no significant difference was found in baseline NIHSS score, mTICI, hemorrhagic transformation, pulmonary infection, and 3-month outcomes between the patients who received MT alone and the patients who received bridging therapy ($P > 0.05$).

Table 3
Details of procedural, clinical, and safety outcomes

Risk factors	MT alone (n = 108)	Bridging therapy (n = 104)	*P*
Sex (male/female)	58/50	69/35	0.060
Age (years)	71.98 ± 11.96	70.68 ± 12.11	0.433
Drinking	20 (18.52)	25 (24.04)	0.326
Smoking	23 (21.30)	23 (22.12)	0.885
SBP	142.37 ± 23.61	140.00 ± 24.29	0.472
DBP	86.27 ± 15.21	86.75 ± 15.23	0.819
Medical history			
Hypertension	77 (71.30)	77 (74.04)	0.654
Diabetes mellitus	27 (25.00)	22 (21.15)	0.507
CAD	34 (31.48)	32 (30.77)	0.911
Atrial fibrillation	61 (56.48)	61 (58.65)	0.749
TIA	1 (0.93)	2 (1.92)	0.539
Ischaemic stroke	25 (23.15)	17 (16.35)	0.214
Stroke etiology			
Atherosclerotic	39 (36.11)	33 (31.73)	0.623
Cardioembolic	63 (58.33)	67 (64.42)	
Underdetermined or others	6 (5.56)	4 (3.85)	
Laboratory parameter			
Hb	126.98 ± 21.10	128.24 ± 18.73	0.647
WBC (10^9/L)	9.16 ± 3.28	9.63 ± 3.68	0.325

SBP, systolic blood pressure; DBP, diastolic blood pressure; CAD, coronary artery disease; TIA, transient ischaemic attack; Hb, hemoglobin; WBC, white blood cell; INR, international normalized ratio; BUN, blood urea nitrogen; TC, total cholesterol; TG, triglyceride; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; HCY, homocysteine; Lp-PLA2, lipoprotein-associated phospholipase A2; ICA, internal carotid artery; IQR, interquartile range; M1,M2, first or second segment of the middle cerebral artery; NIHSS, National Institutes of Health Stroke Scale; mTICI, modified thrombolysis in cerebral infarction score; mRS, modified Rankin Scale.

Variables with a skewed distribution are expressed as medians (interquartile range). Variables with a normal distribution are expressed as the mean ± standard deviation. Categorical variables are expressed as frequencies and percentages.

Risk factors	MT alone (n = 108)	Bridging therapy (n = 104)	*P*
Platelet (10^9/L)	183.85 ± 68.73	179.67 ± 64.59	0.650
INR	1.06 ± 0.18	1.04 ± 0.11	0.394
BUN	6.69 ± 3.27	5.82 ± 1.84	0.019
Creatinine	82.15 ± 32.05	76.58 ± 21.79	0.144
Admission glucose (mmol/L)	7.10 ± 2.63	6.86 ± 2.44	0.492
TC (mmol/L)	4.28 ± 1.53	4.00 ± 0.81	0.101
TG (mmol/L)	1.30 ± 0.94	1.13 ± 0.81	0.170
LDL-C (mmol/L)	2.54 ± 0.86	2.39 ± 0.72	0.151
HDL-C (mmol/L)	1.11 ± 0.28	1.18 ± 0.29	0.065
Uric acid (μmol/L)	314.65 ± 144.47	301.35 ± 93.01	0.432
HbA1c (%)	6.38 ± 1.55	6.04 ± 1.09	0.074
HCY (μmol/L)	15.47 ± 8.23	22.93 ± 76.24	0.339
Lp-PLA2 (ng/mL)	272.93 ± 141.45	281.20 ± 124.48	0.671
Wake-up stroke	48 (44.44)	3 (2.88)	< 0.001
Baseline NIHSS score	16 (12–19)	14 (11–19)	0.170
Intervals times, min, median (IQR)			
onset to door	160 (71–252)	89 (50–120)	< 0.001
onset to thrombolysis	-	133 (100–180)	
onset to reperfusion	383 (300–483)	320 (270–373)	< 0.001
door to groin puncture	110 (82–135)	126 (97–160)	0.002
door to reperfusion	210 (166–265)	230 (180–263)	0.129
groin puncture to reperfusion	98 (70–130)	90 (74–125)	0.654

SBP, systolic blood pressure; DBP, diastolic blood pressure; CAD, coronary artery disease; TIA, transient ischaemic attack; Hb, hemoglobin; WBC, white blood cell; INR, international normalized ratio; BUN, blood urea nitrogen; TC, total cholesterol; TG, triglyceride; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; HCY, homocysteine; Lp-PLA2, lipoprotein-associated phospholipase A2; ICA, internal carotid artery; IQR, interquartile range; M1,M2, first or second segment of the middle cerebral artery; NIHSS, National Institutes of Health Stroke Scale; mTICI, modified thrombolysis in cerebral infarction score; mRS, modified Rankin Scale.

Variables with a skewed distribution are expressed as medians (interquartile range). Variables with a normal distribution are expressed as the mean ± standard deviation. Categorical variables are expressed as frequencies and percentages.

Risk factors	MT alone (n = 108)	Bridging therapy (n = 104)	*P*
Occlusion site			
ICA	13 (12.04)	13 (12.50)	0.789
M1/M2	57 (52.78)	59 (56.73)	
ICA + M	38 (35.19)	32 (30.77)	
mTICI			
0-2a	11 (10.19)	10 (9.62)	0.890
2b-3	97 (89.81)	94 (90.38)	
Passes of the retriever			
<3	60 (55.56)	65 (62.50)	0.304
≥3	48 (44.44)	39 (37.50)	
Hemorrhagic transformation	20 (18.52)	24 (23.08)	0.413
Pulmonary infection	70 (64.81)	69 (66.35)	0.815
mRS at 3 months			
0–1	38 (35.19)	49 (47.12)	0.078
0–2	58 (53.70)	56 (53.85)	0.983
Mortality at 3 months	13 (12.04)	18 (17.31)	0.278

SBP, systolic blood pressure; DBP, diastolic blood pressure; CAD, coronary artery disease; TIA, transient ischaemic attack; Hb, hemoglobin; WBC, white blood cell; INR, international normalized ratio; BUN, blood urea nitrogen; TC, total cholesterol; TG, triglyceride; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; HCY, homocysteine; Lp-PLA2, lipoprotein-associated phospholipase A2; ICA, internal carotid artery; IQR, interquartile range; M1,M2, first or second segment of the middle cerebral artery; NIHSS, National Institutes of Health Stroke Scale; mTICI, modified thrombolysis in cerebral infarction score; mRS, modified Rankin Scale.

Variables with a skewed distribution are expressed as medians (interquartile range). Variables with a normal distribution are expressed as the mean ± standard deviation. Categorical variables are expressed as frequencies and percentages.

A novel nomogram to predict outcomes

To accurately assess clinical outcomes in AIS patients treated with MT, we constructed a nomogram to stratify AIS patients for future treatment. Significant factors in the univariable analyses were entered into the predictive model by stepwise logistic regression analyses. The nomograms suggested that female sex, lower WBC counts, lower admission glucose levels, baseline NIHSS score, and a shorter groin puncture to reperfusion interval time were independent indicators for good outcome; higher baseline

NIHSS score was an independent predictor for patient death (Fig. 2). Our established nomograms showed similar findings with the multivariate logistic models (Table 2).

Table 2
Multivariate logistic regression analysis for all patients

Risk factors	Outcome measures (mRS)			
	Good outcome (0–2)		Alive (0–5)	
	OR (95% CI)	*P*	OR (95% CI)	*P*
Sex (male)	2.75 (1.30–5.84)	0.008	-	-
Age (years)	1.02 (0.99–1.06)	0.213	-	-
SBP	1.01 (0.99–1.02)	0.513	-	-
Atrial fibrillation	-	-	-	-
Hb	1.00 (0.98–1.02)	0.964	-	-
WBC (10^9/L)	1.11 (1.01–1.23)	0.040	-	-
Admission glucose (mmol/L)	1.32 (1.13–1.55)	0.001	1.14 (0.99–1.30)	0.068
Baseline NIHSS score	1.16 (1.08–1.24)	< 0.001	1.10 (1.03–1.17)	0.005
Door to reperfusion time	1.00 (1.00–1.00)	0.465	-	-
Groin puncture to reperfusion	1.01 (1.00-1.02)	0.002	1.01 (1.00-1.02)	0.038

SBP, systolic blood pressure; Hb, hemoglobin; WBC, white blood cell; NIHSS, National Institutes of Health Stroke Scale; mRS, modified Rankin scale. OR, odds ratio; CI, confidence interval.

Discussion

In the present study, we explored (1) the influence of risk factors on related outcomes in AIS patients treated with MT caused by anterior circulation LVOs; and (2) the efficacy and safety of MT alone and bridging therapy. First, with the use of multivariate logistic regression, we observed that two factors (baseline NIHSS score and groin puncture to reperfusion interval time) determined outcomes in patients treated with MT; lower admission glucose levels determined a good outcome, showing in the decision ranking that these factors were primary factors for outcomes in patients treated with MT. Second, bridging therapy had no significant benefit over MT alone in terms of procedural outcomes, recanalization rate, and clinical and safety outcomes. Finally, our constructed nomograms could accurately predict outcomes in AIS patients treated with MT.

A previous meta-analysis study showed that patients with low NIHSS scores (< 6) experienced better functional outcomes following treatment with MT (14). Our study also demonstrated that patients treated with MT experienced superior clinical outcomes in low and high NIHSS scores. Madsen and colleagues

revealed that males suffered a poor 90-day outcome after MT for AIS (15), which was similar to our findings. Previous studies reported that advanced age was associated with a worse outcome (16, 17). Our results showed that age was not an independent factor for clinical outcomes, which was similar to the results published by Andrews (18). Elkind and colleagues have reported that systemic inflammation is correlated with poorer outcomes in patients with stroke (19). The WBC (neutrophil and lymphocyte counts) was associated with long-term outcome and hemorrhagic complications in patients treated with MT (20). Broocks also reported that elevated admission blood glucose was associated with increased brain edema in patients with endovascular therapy (21). Our findings showed that high WBC and admission glucose levels were unfavourable outcomes in AIS patients treated with MT, suggesting that these laboratory values could help to identity patients at higher risk of impending unfavourable outcomes. Additionally, in our study, the groin puncture to reperfusion interval time was a predictor of a favourable outcome. Therefore, we should shorten the groin puncture to reperfusion interval time to improve functional outcomes in patients treated with MT.

The nomogram is a visual and widely approval approach to predict tumour prognosis according to clinical features (22). In recent years, emerging reports have shown a better predictive ability of nomogram for predicting clinical outcomes in patients with AIS (9, 10). However, nomograms are rarely applied for functional outcomes in AIS after MT. The present study aimed to establish a nomogram to predict 3-month outcomes in patients treated with MT. According to our nomograms, admission glucose, baseline NIHSS score and groin puncture to reperfusion interval time were included in the final model for a good outcome through a stepwise algorithm, and the findings for death were similar to those of the good outcome multivariate analyses. Therefore, our constructed models further demonstrated that these factors should be considered when predicting the outcomes of AIS after MT.

A recent meta-analysis conducted by the HERMES collaborators suggested a significant benefit of bridging therapy over intravenous thrombolysis, with a positive odds ratio of 1.72 (23). However, the findings regarding the efficacy and safety of bridging therapy and MT alone remain uncertain. Mistry and colleagues published a meta-analysis that bridge therapy had a better functional outcome and a higher rate of successful recanalization compared with MT alone (24). However, the MR CLEAN, ESCAPE and REVASCAT trials suggested no significant difference in the effect between bridging therapy and MT alone (4, 25, 26). Subgroup analyses showed that patients with MT alone had higher mortality at 3 months compared with patients who received bridging therapy in the ESCAPE trial. The mortality of MT alone was slightly increased but without statistical heterogeneity in the REVASCAT trial. In the subgroup analyses of these trials, each group had a small size: 30 (13%) patients with MT alone in MR CLEAN, 45 (27%) in ESCAPE, and 33 (32%) in REVASCAT. In this study, although the group that received MT alone had higher blood urea nitrogen (BUN) levels, a higher proportion of wake-up stroke and longer OTD time compared with patients who received bridging therapy, no significant difference was found in the procedural outcomes, recanalization rate, and clinical and safety outcomes between MT alone and bridging therapy. More importantly, the sample size of each group was more than 100 in the present study. Therefore, our study suggested that bridging therapy had no significant benefit over MT alone in terms of clinical and safety outcomes.

A major advantage of the current study is that this study explored the prognostic significance of both MT alone and bridging therapy for LVO in AIS patients of the anterior circulation. The limitations of this study should be acknowledged when interpreting these results. First, this was a retrospective and single-centre study, and the sample size of this study was small. There might be a selection bias in the retrospective study regarding different time of symptom onset of MT alone and bridging therapy. Validation with a prospective and multi-centre randomized study with a large sample is required. Additionally, our nomograms were further confirmed in an external cohort.

Conclusions

In summary, our results suggested that male sex, high WBC counts, high admission glucose levels, high baseline NIHSS scores and long interval time of groin puncture to reperfusion were strongly associated with worse functional outcome at 3 months. Additionally, we observed no significant benefit of bridging therapy compared to MT alone in AIS patients.

List Of Abbreviations

MT, mechanical thrombectomy; AIS, acute ischaemic stroke; BUN, blood urea nitrogen; LVO, large vessel occlusion; DWI, diffusion-weighted imaging; FLAIR, fluid-attenuated inversion recovery; NIHSS, National Institutes of Health Stroke Scale.

Declarations

Ethics approval and consent to participate

The study protocol was approved by the Nanjing Medical University Ethics Committee and complied with the Declaration of Helsinki. Written informed consent was obtained from all individuals or their family members.

Consent for publication

Not applicable.

Availability of data and materials

All data supporting our results are available from the corresponding authors upon reasonable.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Data curation, Feng Zhou, Guoxing Zhang and Jian-Kang Hou; Formal analysis, Yu-Kai Liu; Investigation, Xiang-Liang Chen and Yu-Qiao Zhang; Methodology, Teng Jiang, Wei Wang, Hui-Ling Sun, Rui Shen; Writing – original draft, Qi-Wen Deng; Writing – review & editing, Jun-Shan Zhou and Hong-Chao Shi.

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Figures

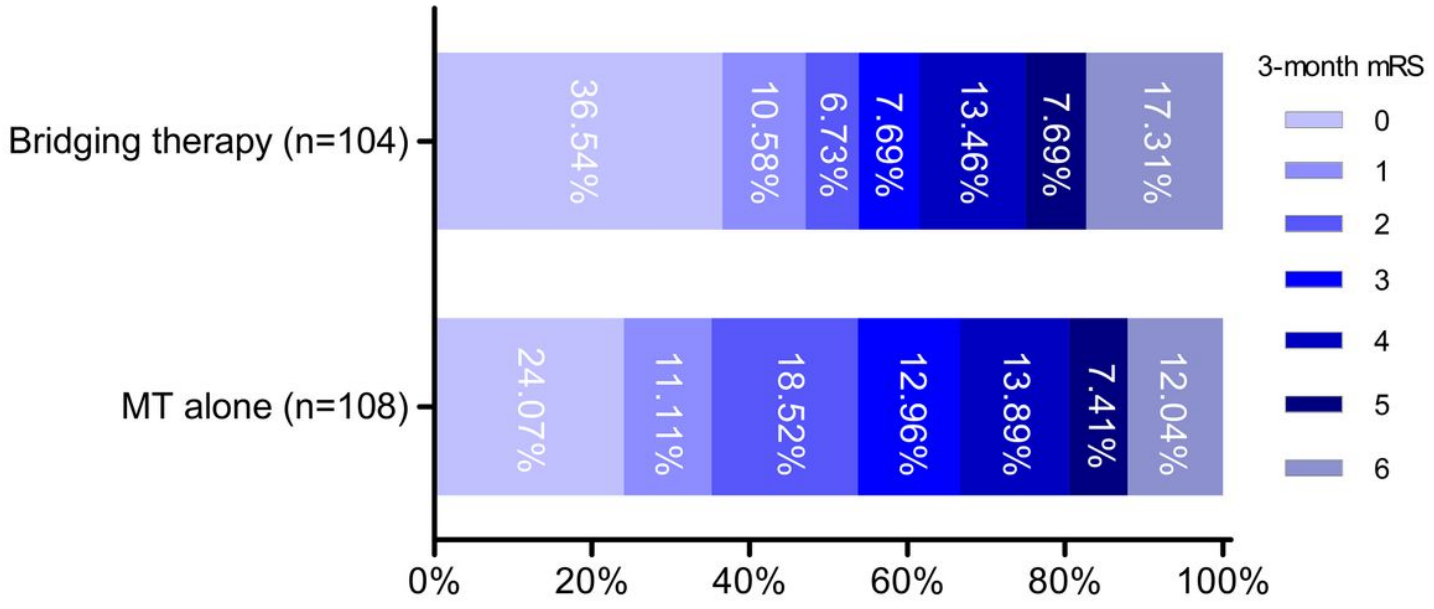

Figure 1

Distribution of mRS in patients with acute ischaemic stroke stratified according to therapeutic methods. No significant difference in 3-month mRS was observed between bridging therapy and MT alone in AIS patients (P>0.05). mRS, modified Rankin Scale; MT, mechanical thrombectomy; AIS, acute ischaemic stroke.

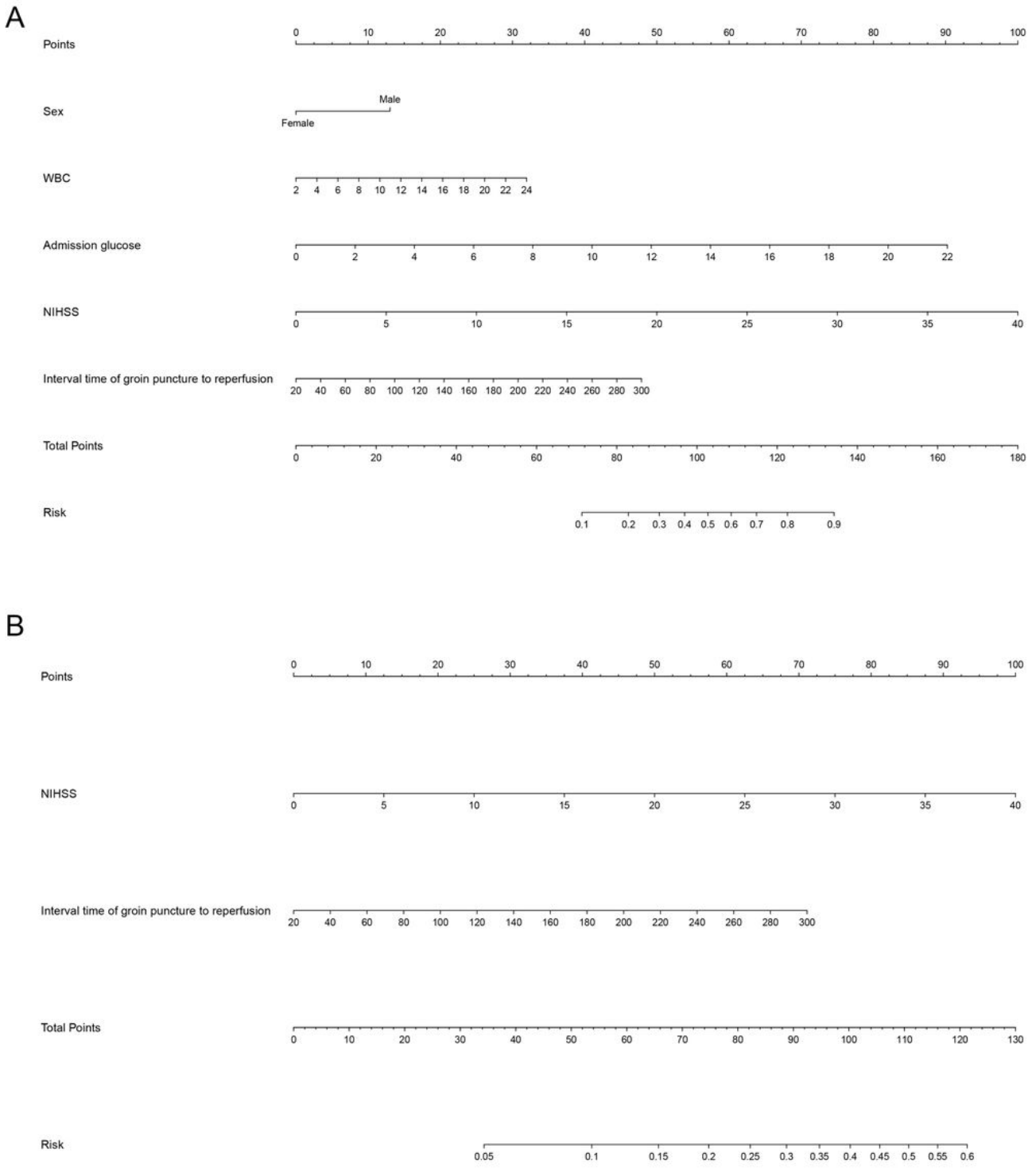

Figure 2

Nomograms of AIS patients to predict worse outcomes after MT. Locate the factors on the respective axis; draw a straight line up to the Points axis to determine how many points towards worse outcome the patient receives for each factor; add the points and locate this number on the Total points axis; draw a straight line down to find the patient's assessed risk of worse outcome. The c-indexes for the good and death outcomes are 0.835 (A) and 0.723 (B), respectively. AIS, acute ischaemic stroke; MT, mechanical thrombectomy; NIHSS, National Institutes of Health Stroke Scale; WBC, white blood cell.