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ORIGINAL RESEARCH

Fasting Blood Glucose on Prognosis After Acute Large Vessel Occlusion Reperfusion- A Multi-Center Study Based on Propensity Score Matching

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Purpose: To determine the impact of 24-hour post-reperfusion glycemic control on 90-day functional outcomes in acute large vessel occlusion (ALVO) patients after successful recanalization.

Materials and Methods: This multi-center retrospective study analyzed 2056 ALVO patients (male: 1488; female: 568) from three cerebrovascular centers achieving successful reperfusion via mechanical thrombectomy with/without bridging thrombolysis. Using 1:1 propensity score matching (covariates: gender, age, Diabetes mellitus, hypertension, hyperlipidemia, cardiac disease, smoking status, glucose measurement timing, baseline NIHSS, and preoperative mRS), 194 matched pairs (mean age 63[IQR 55–71] years; male: 278) were stratified by 90-day modified Rankin Scale (mRS) outcomes into favorable (mRS 0–2) and poor prognosis (mRS 3–6) cohorts.

Results: The poor prognosis cohort demonstrated significantly elevated mean fasting blood glucose (MFBG) levels (7.22 mmol/L [6.66–8.50] vs 6.86 mmol/L [6.28–7.58], $P<0.001$). Multivariable logistic regression adjusted for sex, age, vascular risk profile, and baseline NIHSS (adjusted OR=0.819, 95% CI 0.714–0.940, P=0.004) confirmed MFBG elevation as an independent risk factor for unfavorable outcomes.

Conclusion: Sustained hyperglycemia during the initial 24-hour post-recanalization period independently predicts impaired 90-day functional recovery in ALVO patients. These findings highlight the imperative for standardized glucose monitoring protocols during the hyperacute post-thrombectomy phase, while optimal glycemic targets (<7.0 mmol/L vs individualized thresholds) and therapeutic windows for neuroprotection warrant validation through prospective multicenter RCTs.

Keywords: acute large vessel occlusion, blood glucose, propensity matching, mechanical thrombectomy, prognosis

Background

Although mechanical thrombectomy (MT) has achieved higher rates of vascular recanalization in patients with acute large vessel occlusion (ALVO). Reperfusion injury poses a formidable therapeutic challenge in clinical practice, while simultaneously presenting critical knowledge gaps that demand systematic investigation in biomedical research domains. Approximately 20%–50% of ALVO patients may experience stress-induced hyperglycemia, caused by the release of cortisol and adrenaline leading to elevated blood glucose levels, a phenomenon commonly seen even in non-diabetic patients.[1–3] In real-world clinical settings, glycemic management post-thrombectomy remains heterogeneous. While the

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2018 AHA/ASA guidelines suggest targeting blood glucose to 7.8–10.0 mmol/L,[4] implementation is often reactive rather than protocol-driven, with significant variations in monitoring frequency and intervention thresholds across institutions.[5,6] Critically, the optimal timing of glucose assessment (eg, fasting vs random sampling) during the hyperacute post-recanalization window is undefined, and evidence supporting fasting glucose superiority in this context is limited. Interpretation of hyperglycemia's prognostic impact requires careful consideration of confounding factors: (1) Acute hyperglycemia may reflect underlying stroke severity rather than directly causing poor outcomes,[3,7] as patients with higher NIHSS scores exhibit amplified stress responses.[7,8] (2) Differentiating stress-induced hyperglycemia from chronic hyperglycemia in diabetics is clinically challenging, yet diabetics have distinct cerebrovascular pathophysiology that may independently worsen prognosis.[9,10] Patients undergoing MT procedures need to consider factors such as surgery-related stress, and hyperglycemia has been associated with adverse clinical outcomes in ALVO patients.[3–7] High blood glucose levels can further exacerbate the hypoxic status of midbrain cells in the ischemic penumbra, leading to increased acidosis, mitochondrial dysfunction, and even failure.[11] Besides, elevated blood glucose levels are associated with the formation of free radicals and activation of matrix metalloproteinases, which can further worsen brain edema.[1,12,13]

High blood glucose is an independent risk factor for poor prognosis in ALVO patients after vascular recanalization. The good prognosis rate in the low blood Glucose group was 1.62 times higher than that in the high blood glucose group; and for every 1mmol/L decrease in blood glucose, the rate of poor prognosis decreased by 7.2% [OR: 0.928, 95% CI (0.879, 0.979), P=0.007].[14] However, other studies have yielded conflicting results, with no significant difference in the 90-day modified Rankin Scale (90ds-mRS) between patients on intensified glucose lowering (4.44–7.22 mmol/L) and patients at standard glucose levels (4.44–9.93mmol/L).[2,15,16] Further research is needed to determine whether different blood glucose levels affect the 90ds-mRS in patients.

Taking into account the above factors, we conducted a retrospective study on the fasting blood glucose levels of 2056 post-MT patients with ALVO from three different medical centers, analyzing the relationship between fasting blood glucose levels and 90ds-mRS.

Materials and Methods

Research Objects

Data were obtained from three large medical centers in China. These centers had consistent standards for the assessment and treatment of ALVO. We retrospectively collected data from 2056 patients with acute large vessel occlusion who were seen from January 2019 to June 2023, including 1488 males (72.4%) and 568 females (27.6%). The number of patients included from Tianjin huanhu Hospital was 1376, and from Xianyang Central Hospital and Tianjin Medical University Second Hospital were 253 and 427, respectively.

Inclusion Criteria

① Patients aged 18 or older with acute occlusion of large vessels in the anterior circulation of the brain; ② patients with acute onset, seen within 24 hours of normal appearance, diagnosed with AIS by MRI, and confirmed to have ALVO by MRA or DSA; ④ NIHSS score on admission ≥6; ⑤ pre-stroke mRS ≤1; patients with acute occlusion of large vessels in the anterior circulation, meeting the inclusion criteria of the DAWN and DEFUSE-3 trials, occurring between 6–24 hours; and ⑥ patients who underwent MT or intravenous thrombolysis followed by bridging MT.

Exclusion Criteria

① Incomplete data; ② recurrent stroke; ③ non-occlusion of large vessels in the anterior circulation; ④ patients with post-stroke seizures or those with confirmed patency of occluded vessels partially or completely before MT surgery; ⑤ patients with active bleeding or a tendency to bleed in the perioperative period, coagulation disorders, etc.; ⑥ patients in the time window for intravenous thrombolysis, meeting the indications for intravenous thrombolysis and achieving patency with thrombolytic drugs; ⑦ conditions caused by non-vascular diseases such as tumors, trauma, hematologic diseases, etc.; ⑧ systolic blood pressure ≥185mmHg or diastolic blood pressure ≥110mmHg on admission; blood glucose ≤2.7mmol/L or ≥22.2mmol/L; ⑨ patients with heart, liver, or kidney dysfunction, unstable vital signs in the perioperative period.

Research Method

Research Methods According to the latest guidelines from the American Heart Association/American Stroke Association (AHA/ASA) in 2019,[17] screening for intracranial large vessel occlusion was conducted in patients diagnosed with acute stage cerebral infarction. Patients who experienced onset within 4.5 hours and met the criteria for intravenous thrombolysis received treatment with recombinant tissue plasminogen activator (rt-PA) at a dose of 0.9mg/kg. Patients with concurrent acute large vessel occlusion underwent mechanical thrombectomy in conjunction with intravenous thrombolysis. Patients with a high thrombus burden underwent direct stent retriever thrombectomy or a combination of stent retriever thrombectomy and aspiration therapy [Solitaire™ FR (Medtronic) and/or Penumbra ACE™ 68]. For patients with stenosis or dissection, angioplasty was performed in conjunction with mechanical thrombectomy, and for patients with large arterial occlusion related to atherosclerosis, antiplatelet aggregation drugs and statins were used intraoperatively. The modified Thrombolysis in Cerebral Infarction classification (mTICI) was used to evaluate the effectiveness of vascular recanalization, with perfusion reaching mTICI 2b or 3 considered a successful recanalization. Vascular recanalization (confirmed by mTICI ≥2b) served as the time-zero reference. Capillary blood glucose levels were measured using a calibrated point-of-care device (ACCU-CHEK Inform II®, Roche Diabetes Care) at three standardized intervals: immediately post-recanalization (0–30 min), at 6±0.5 hours, and at 12±1 hours. The mean fasting blood glucose (MFBG) was calculated from these triplicate measurements.

A stepwise glycemic intervention protocol was initiated when MFBG exceeded 7.8 mmol/L or any single measurement surpassed 11.1 mmol/L. This involved an intravenous bolus of regular insulin (0.1 U/kg) followed by continuous infusion (0.05–0.1 U/kg/h), with strict maintenance of glucose levels within the 7.0–7.8 mmol/L target range. Hypoglycemic events (glucose ≤3.9 mmol/L) triggered immediate corrective measures: intravenous administration of 20 mL 50% dextrose solution with subsequent glucose verification at 10, 20, and 30-minute intervals until euglycemia was re-established.[17,18]

This study was reviewed and approved by the Institutional Ethics Committees of all three participating centers. The research strictly adhered to the principles outlined in the Declaration of Helsinki and the Ethical Review Measures for Biomedical Research Involving Humans (issued by the National Health Commission of China).

Extraction of Blood Glucose Data

Blood glucose values were collected using portable glucose meters, obtaining three fasting blood glucose values for each patient within 24 hours post-surgery (at 30-minute intervals), and calculating the mean fasting blood glucose level (MFBG).

Outcome Assessment Measure

The 90-day modified Rankin Scale (90ds-mRS)[19] is used to evaluate the degree of functional impairment in stroke patients. A good prognosis was defined as 90ds-mRS (0–2), and a poor prognosis was defined as 90ds-mRS (3–6). The mRS scale ranges from 0–6, with 0 indicating no residual symptoms, and 6 indicating death. 0 point: No residual symptoms; 1 point: Residual symptoms present, but no functional impairment, able to live normally; 2 points: Mild residual disability, but still able to live independently; 3 points: Moderate disability, able to walk independently but requires assistance with some daily activities; 4 points: Moderate to severe disability, unable to walk independently, requiring assistance with most daily activities; 5 points: Severe disability, bedridden, incontinence, completely dependent on others for daily activities; 6 points: Death.

Statistical Analysis

All statistical analyses were conducted using SPSS version 27.0. Categorical variables were expressed as counts (percentages) (n%), while continuous variables were expressed as [median (interquartile range), m(IQR)]. According to the latest fasting blood glucose classification criteria,[18] a propensity score matching (PSM) was conducted with a 1:1

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ratio using 7mmol/L (≤7mmol/L or >7mmol/L) as the cutoff point. The nearest neighbor matching method was employed to match gender, age, smoking, diabetes, hypertension, cardiovascular disease, dyslipidemia, baseline NIHSS, preoperative mRS, and the timing of three blood glucose measurements as covariates, with a caliper set at 0.02. Minimize residual confounding in our observational design. Avoid model dependency (unlike IPTW, which relies on weighting accuracy). Ensure direct comparability between hyperglycemic/normoglycemic groups. While PSM reduced the sample size, it achieved excellent covariate balance (SMD<0.1), strengthening causal inference (Figure S1). Sensitivity analysis reveals that although the effect size (OR) exhibits magnitude fluctuations (0.478–0.897) as the caliper width varies from 0.01 to 0.05, the inverse association between elevated MFBG and adverse outcomes remains statistically significant (all $P < 0.05$). Notably, lenient matching (caliper = 0.05) led to abnormal effect size amplification (OR = 0.478) and widened confidence intervals, suggesting residual confounding bias. In contrast, stringent matching (caliper = 0.01) improved precision but incurred sample size attrition. The selected caliper of 0.02 in this study ensures matching quality while maximizing statistical power, with OR = 0.819 (95% CI: 0.714–0.940) representing the most reliable effect estimate (Table S1).

After matching, *t*-tests were used for comparing means between the two groups, and McNemar's test was used for comparing rates between the two groups. Cox regression analysis was used to assess the correlation between fasting blood glucose levels and other relevant indicators as independent variables with 90ds-mRS as the dependent variable. $P < 0.05$ is considered statistically significant.

Results

A total of 2056 patients with acute large vessel occlusion were enrolled in this study, with an average age of 63 (55,71) years. There were 1488 males (72.4%) with a mean age of 61 (53,69) years and 568 females (27.6%) with a mean age of 67 (60,74) years. MFBG was taken as the dependent variable, 90ds-mRS was used as the outcome variable, and gender, age, smoking, diabetes, hypertension, cardiovascular disease, dyslipidemia, baseline NIHSS, preoperative mRS, and the timing of three blood glucose measurements following successful vascular recanalization were used as covariates for PSM by nearest matching method. Finally, 388 patients were enrolled, with an average age of 63 (55,71) years, including 278 males and 110 females. (Figure 1 and Table 1).

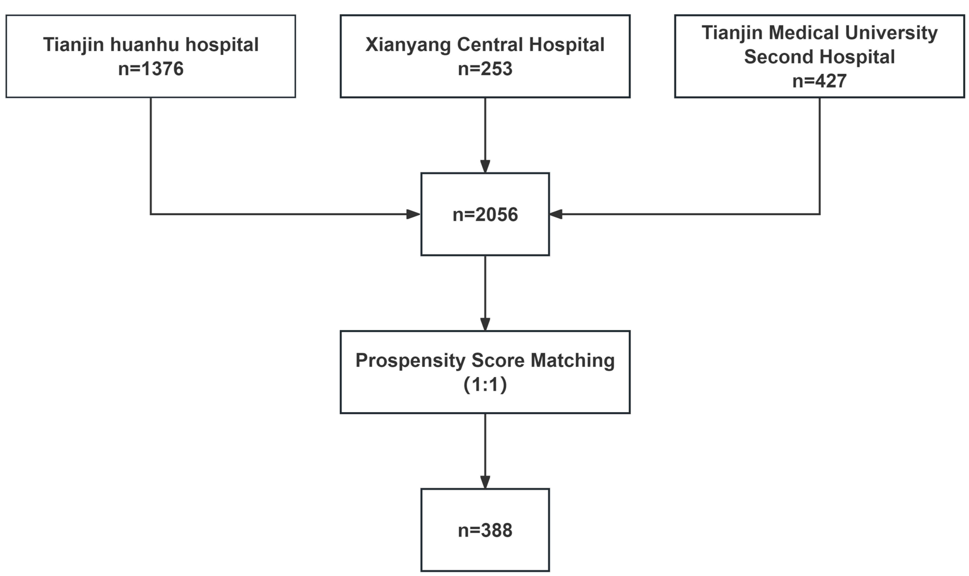

Figure 1 The flow chart for patient selection and propensity score matching.

Table 1 The Baseline Data of Patients Before and After PSM Were Compared

Variables		Before PSM		P	After PSM		P
		Normoglycemic n=385	Hyperglycemia n=1671		Normoglycemic n=194	Hyperglycemia n=194	
Gender	Male(n%)	278(18.7)	1210(81.3)	0.936	138(49.6)	140(50.4)	0.822
	Female(n%)	107 (18.8)	461(81.2)		56(50.9)	54(49.1)	
Age [m(IQR)]		63(53, 71)	63(55, 71)	0.574	63(53, 72)	62(55, 70)	0.865
Tobacco Use History	No(n%)	215(19.5)	890(80.5)	0.360	109(49.8)	110(50.2)	0.918
	Yes(n%)	170(17.9)	781(82.1)		85(50.3)	84(49.7)	
Diabetes mellitus	No(n%)	339(22.3)	1180(77.7)	<0.001*	152(49.5)	155(50.5)	0.708
	Yes(n%)	46(8.6)	491(91.4)		42(51.9)	39(48.1)	
Hypertension	No(n%)	115(18.7)	501(81.3)	0.966	56(47.9)	61(52.1)	0.580
	Yes(n%)	270(18.8)	1170(81.2)		138(50.9)	133(49.1)	
Cardiovascular Disease	No(n%)	285(19.4)	1185(80.6)	0.223	143(49.0)	149(51.0)	0.480
	Yes(n%)	100(17.1)	486(82.9)		51(53.1)	45(46.9)	
Dyslipidemia	No(n%)	263(18.6)	1150(81.4)	0.846	138(49.3)	142(50.7)	0.650
	Yes(n%)	122(19.0)	521(81.0)		56(51.9)	52(48.1)	
Baseline NIHSS Score		18(17, 20)	18(17, 20)	0.134	18(17, 20)	18(17, 20)	0.545
Preoperative mRS	0-2(n%)	24(15.8)	128(84.2)	0.335	15(55.6)	12(44.4)	0.549
	3-6(n%)	361(19.0)	1543(81.0)		179(49.6)	182(50.4)	
TSR-1stBGM (h)		2 (1, 3)	9 (6, 12)	<0.001*	3(2, 5)	3(3, 4.25)	0.613
TSR-2ndBGM (h)		6 (5, 7)	13 (10, 16)	<0.001*	7(6, 9)	7(7, 8.25)	0.614
TSR-3rdBGM (h)		11 (10, 12)	18 (15, 21)	<0.001*	12(11, 14)	12(12, 13.25)	0.613

Note: *P<0.05.
Abbreviations: PSM, propensity score matching; m(IQR), median (interquartile range); 90ds-mRS, Modified Rankin Scale at 90 days of onset; TSR-1stBGM, Time Since Recanalization for First Blood Glucose Measurement; TSR-2ndBGM, Time Since Recanalization for Second Blood Glucose Measurement; TSR-3rdBGM, Time Since Recanalization for Third Blood Glucose Measurement.

Baseline Characteristics and Validation of Propensity Score Matching Performance

Participants were stratified into a normoglycemic group (postoperative 24-hour MFBG≤7mmol/L, n=385) and a sustained hyperglycemic group (MFBG>7 mmol/L, n=1671) based on glycemic status. Given significant baseline confounders, propensity score matching (PSM) using the nearest-neighbor approach (caliper width=0.02) was implemented, yielding 194 rigorously balanced matched pairs (overall retention rate: 85.7%).

Pre-matching analyses revealed marked disparities between unmatched cohorts: the hyperglycemic group exhibited a substantially higher prevalence of pre-existing diabetes (91.4% vs 8.6%; χ^2=231.4, P<0.001) and significantly delayed timing of glucose monitoring post-recanalization. Specifically, the time since recanalization for first blood glucose measurement (TSR-1stBGM: 9h [IQR 6–12] vs 2h [1–3], P<0.001), second measurement (TSR-2ndBGM: 13h [10–16] vs 6h [5–7], P<0.001), and third measurement (TSR-3rdBGM: 18h [15–21] vs 11h [10–12], P<0.001) were prolonged in the hyperglycemic group (all P<0.001), indicative of substantial measurement-time confounding in the unmatched cohort.

Post-PSM optimization demonstrated successful covariate balance across demographics (male sex: 50.4% vs 49.6%; P=0.822), vascular risk profiles (diabetes prevalence: 51.9% vs 48.1%; P=0.708), neurological severity (baseline NIHSS: 18 [17–20] vs 18 [17–20], P=0.545), and pre-interventional disability levels (mRS distribution, P=0.549), with all standardized mean differences (SMD) <0.1. Crucially, the temporal biases in perioperative glucose monitoring were fully mitigated after PSM adjustment (median intergroup differences in TSR-BGMs: <1h; all P>0.6). These results validate that the PSM framework effectively addressed residual confounding from delayed glucose monitoring timepoints, establishing a robust methodological foundation for isolating the net effect of MFBG on 90-day mRS in subsequent analyses (Table 1).

Association Between Glycemic Parameters and 90-Day Functional Outcomes

In the propensity score-matched cohort (n=388), the 90-day modified Rankin Scale (mRS) was dichotomized into favorable (90ds mRS 0–2, n=249) and unfavorable (90ds mRS 3–6, n=139) outcome groups for analysis.

Prognostic Discrimination of Mean Fasting Blood Glucose (MFBG)

The unfavorable outcome group exhibited significantly higher postoperative MFBG levels compared to the favorable outcome group (7.22 mmol/L [IQR 6.66–8.50] vs 6.86 mmol/L [6.28–7.58]; *Mann–Whitney U*=12.14, P<0.001).

Validation of Confounding Factor Interactions

Despite balanced baseline covariates (eg, sex, baseline NIHSS score; P>0.05 for all), residual imbalances persisted in diabetes prevalence (50.6% vs 49.4% in unfavorable vs favorable groups; χ^2 =9.21, P=0.002) and age distribution (median age 66 years [IQR 58–73] vs 60 years [53–69.5], P=0.002). These findings align with established prognostic associations in stroke research, where advanced age and pre-existing diabetes are recognized modifiers of post-interventional recovery trajectories (Table 2).

Interpretation of Cox Proportional Hazards Regression Analysis

After adjusting for sex, age, vascular risk factors, and baseline neurological deficits (NIHSS), elevated MFBG was significantly associated with a reduced likelihood of favorable outcomes (mRS 0–2) (adjusted OR=0.819; 95% CI 0.714–0.940; P=0.004). This finding corroborates prior univariate analyses, confirming that postoperative glycemic levels remain an independent predictor of functional prognosis even after covariate adjustment. Specifically, each 1 mmol/L increase in MFBG corresponded to an 18.1% decrease in the probability of achieving favorable functional outcomes.

Notably, despite significant differences in diabetes prevalence between groups in the propensity score-matched (PSM) cohort (χ^2 =9.21, P=0.002), diabetes mellitus exhibited no independent effect in the multivariable model (adjusted

Table 2 Comparison of Clinical Data Between the 90ds-mRS (0–2) Group and the 90ds-mRS (3–6) Group After PSM

Variables		90ds-mRS (0–2) n= 249	90ds-mRS (3–6) n= 139	*P*
Gender	Male(n%)	178(64.0)	100(36.0)	0.924
	Female(n%)	71(64.5)	39(35.5)	
Age [m(IQR)]		60(53, 69.5)	66(58, 73)	0.002*
Tobacco Use History	No(n%)	144(65.8)	75(34.2)	0.460
	Yes(n%)	105(62.1)	64(37.9)	
Diabetes mellitus	No(n%)	209(68.1)	98(31.9)	0.002*
	Yes(n%)	40(49.4)	41(50.6)	
Hypertension	No(n%)	79(67.5)	38(32.5)	0.366
	Yes(n%)	170(62.7)	101(37.3)	
Cardiovascular Disease	No(n%)	189(64.7)	103(35.3)	0.693
	Yes(n%)	60(62.5)	36(37.5)	
Dyslipidemia	No(n%)	182(65.0)	98(35.0)	0.585
	Yes(n%)	67(62.0)	41(38.0)	
Baseline NIHSS Score		18(17, 20)	18(17, 20)	0.474
Preoperative mRS	0-2(n%)	21(77.8)	6(22.2)	0.126
	3-6(n%)	228(63.2)	133(36.8)	
MFBG (mmol/L) [m(IQR)]		6.86(6.28, 7.58)	7.22(6.66, 8.50)	<0.001*

Note: *P<0.05.
Abbreviations: m(IQR), median(interquartile range; 90ds-mRS, Modified Rankin Scale at 90 days of onset; MFBG, Mean fasting blood glucose.

Table 3 Cox Regression Analysis

Variables	Cox Regression Analysis	
	OR (95% CI)	P
Gender	0.966(0.631, 1.480)	0.875
Age [m(IQR)]	0.992(0.978, 1.007)	0.299
Tobacco Use History	1.050(0.707, 1.559)	0.809
Diabetes mellitus	0.680(0.404, 1.144)	0.146
Hypertension	1.016(0.634, 1.626)	0.949
Cardiovascular Disease	0.904(0.570, 1.434)	0.668
Dyslipidemia	0.802(0.529, 1.216)	0.299
Baseline NIHSS Score	0.986(0.911, 1.066)	0.716
Preoperative mRS	0.818(0.270, 2.473)	0.722
MFBG (mmol/L) [m(IQR)]	0.819(0.714, 0.940)	0.004*

Note: $^*P<0.05$.

Abbreviations: OR, odd ratio; CI, Confidence interval; mRS, Modified Rankin Scale; MFBG, Mean fasting blood glucose.

OR=0.680; 95% CI 0.404–1.144; *P*=0.146). This suggests that acute-phase glycemic fluctuations may exert a more direct impact on stroke prognosis than chronic diabetic status.

While univariate analysis revealed substantial age disparity between outcome groups (median age 60 vs 66 years in favorable vs unfavorable groups; *P*=0.002), the multivariable model demonstrated no independent age effect (adjusted OR=0.992; 95% CI 0.978–1.007; *P*=0.299). This implies that age-related prognostic influence may be mediated through interactions with other covariates, such as metabolic dysregulation captured by MFBG.

Traditional vascular risk factors (hypertension, tobacco use, dyslipidemia) and baseline NIHSS score showed no statistically significant associations (*P*> 0.05 for all). These results suggest diminished predictive utility of baseline NIHSS assessment for long-term prognosis in patients achieving successful endovascular thrombectomy (EVT) recanalization (Table 3 and Figure 2).

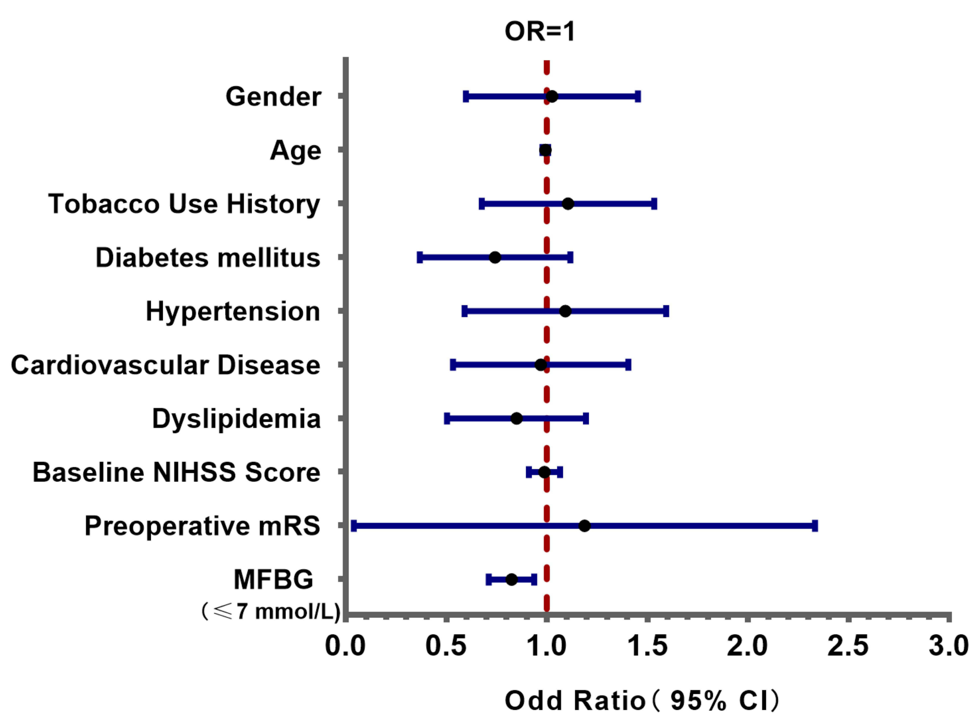

Figure 2 90ds-mRS Forest Map of Risk Factors.

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Discussion

Nearly 80% of patients with Acute Large Vessel Occlusion (ALVO) experience varying degrees of disability or mortality. Despite continuous advancements in endovascular treatment devices and recanalization techniques leading to improved rates of vessel recanalization, the favorable prognosis rate for ALVO patient post-recanalization remains relatively low (approximately 46%), with over 50% of successfully recanalized patients having suboptimal outcomes.[8]

Around 40% of patients experience adverse effects on the prognosis of Acute Ischemic Stroke (AIS) due to diabetes or acute stress-induced hyperglycemia.[2,20] However, there is currently controversy regarding the baseline blood glucose levels and the prognosis of patients post-ALVO recanalization. Goyal et al[6] reported that high blood glucose upon admission is an independent predictor of adverse functional outcomes in 231 AIS patients with large vessel occlusions, whereas Osei et al[21] summarized the results of the MR CLEAN study involving 487 patients, suggesting that: there was no statistical difference in the baseline blood glucose levels of patients receiving endovascular treatment and their favorable prognosis at 90 days post-onset (90d-mRS 0–2) (P=0.87).

Notably, the high-quality SHINE trial[2] demonstrated comparable findings: the intensive glucose control group (mean BG 6.56 mmol/L) showed no significant difference in 90-day modified Rankin Scale (mRS) outcomes compared to standard therapy (mean BG 9.94 mmol/L), with favorable functional outcomes (mRS 0–2) observed in 20.5% vs 21.6% of patients, respectively. This suggests that glycemic reduction per se did not translate into clinical benefits. Furthermore, hypoglycemic events (particularly <2.22 mmol/L) may induce detrimental neurological injuries, potentially offsetting the hypothetical advantages of intensive glucose management. Importantly, only 13% of the SHINE cohort underwent mechanical thrombectomy (MT), precluding subgroup analysis to draw definitive conclusions regarding patients achieving successful large-vessel recanalization.[2]

The study cohort demonstrated consistent male predominance both before (1488 males [72.4%] vs 568 females [27.6%]) and after matching (278 males [71.6%] vs 110 females [28.4%]), reflecting broader epidemiological trends in China's stroke burden. As the country accounts for a disproportionate share of global ischemic stroke cases-2.772 million incident cases in 2021 (1.89 times the global incidence rate)-male predominance (~62% of cases)[22] and regional disparities (higher incidence in northern vs southern China) are well-documented. Notably, all three participating centers were located in northern China, a factor that may further contextualize the observed sex distribution.

Our findings regarding the 7 mmol/L glycemic threshold should be interpreted considering our analytical approach: Notably, propensity score matching (PSM) was employed to address substantial baseline imbalance (1671 hyperglycemic vs 385 normoglycemic patients) through 1:1 pairing, thereby establishing a counterfactual framework analogous to randomized controlled trials. When limited overlap existed in propensity score distributions (median: 0.84 hyperglycemic vs 0.12 normoglycemic groups), PSM demonstrated superior robustness over inverse probability weighting by preventing extreme weight bias. Crucially, post-matching standardized mean differences <0.1 for all covariates ensured unbiased estimation of the net effect of the 7 mmol/L glycemic threshold on clinical outcomes. This methodology strengthens causal inference regarding postoperative glycemic control.

This contextual limitation underscores the significance of our observational study, which specifically investigates post-MT populations with confirmed vascular reperfusion. Our data indicate that glycemic variability during the acute phase may exert a measurable influence on 90-day mRS trajectories in this targeted cohort. However, given the inherent limitations of observational designs, the optimal post-recanalization glycemic parameters warrant validation through prospective randomized controlled trials to establish causality and refine precision medicine approaches for stroke survivors.

Therefore, does blood glucose post-recanalization affect the 90d-mRS of ALVO patients? Research by Yao et al[23] on the SMART study (n=2862) demonstrated: The finding that there was a significant association between elevated blood Glucose after stroke and poor function in patients with diabetes who were not previously diagnosed confirms the importance of controlling blood Glucose levels during the acute phase of AIS. A meta-analysis conducted by Lu et al[10] on patients undergoing mechanical thrombectomy showed that: the rate of favorable prognosis in patients with a history of diabetes was significantly lower compared to patients without a history of diabetes (OR: 0.48, 95% CI: 0.33–0.71). Kim et al[24] collected data from 309 thrombectomy patients, indicating that for every 1 mmol/L increase in blood glucose levels, the rate of poor prognosis increased by 10.6%. These findings align with our previous retrospective results: high blood glucose is an independent risk factor for poor prognosis post-vessel recanalization in ALVO patients; the rate of favorable prognosis in the low blood glucose group is 1.62 times higher than the high blood glucose group; for every 1 mmol/L increase in blood glucose, the rate of poor prognosis increases by 7.2% [OR: 0.928, 95% CI (0.879, 0.979), P=0.007].[14] Possible cause: high blood glucose may delay the resolution of focal brain edema in the ischemic brain region, reducing reperfusion blood flow in the ischemic brain tissue. High blood glucose can exacerbate intracellular acidosis in the ischemic penumbra cells and worsen brain damage.[3,9] Desilles et al[9] found that high blood glucose triggers a cascade of thrombo-inflammatory reactions, amplifying downstream microvascular thrombo-inflammation induced by arterial occlusion in the brain. High blood glucose increases oxidative stress and protein hydrolysis at the blood–brain barrier, further leading to brain ischemia-reperfusion injury, brain edema, and even hemorrhage.[25,26] It suggests that in clinical practice, high attention should be paid to ALVO patients with elevated blood Glucose levels, with proper blood Glucose control, dietary management, and personalized treatment options being crucial for improving prognosis rates.

This study was supported by regional science funding, which may reflect certain local clinical practices; future prospective, multi-center trials across diverse populations are needed to confirm our findings.

Limitations of This Study

1. This retrospective study was constrained by the lack of inclusion of comprehensive laboratory parameters (eg, inflammatory biomarkers or glycated hemoglobin), limiting mechanistic exploration of metabolic influences.
2. The observed high prevalence of diabetes (51.9%) in our cohort suggests a critical direction for future research: stratified validation of glycemic effects between diabetic and non-diabetic subgroups is warranted to verify mechanism-related findings and subsequently refine targeted preventive care strategies.
3. The absence of prospectively collected glycemic trajectory data precludes definitive determination of optimal post-recanalization glucose target ranges.
4. Further mechanistic investigations are warranted to elucidate the pathophysiological interplay between acute-phase glycemic variability and cerebral reperfusion injury in large-vessel occlusion.
5. While the current study primarily evaluated short-term outcomes, we fully recognize the scientific merit of longitudinal assessment. Future research will implement extended follow-up protocols to investigate the long-term implications of glycemic control in acute large vessel occlusion recanalization.

Conclusions

Persistent hyperglycemia maintained for 24 hours post-recanalization is an independent predictor of compromised 90-day functional recovery. While this emphasizes the necessity of strict glucose monitoring during the hyperacute phase post-thrombectomy, the optimal therapeutic window for neuroprotective interventions and specific glycemic control targets still require clarification through multicenter randomized controlled trials.

Data Confidentiality Statement

All data were handled in strict compliance with the Declaration of Helsinki and relevant regulations (including China's Personal Information Protection Law and Ethical Review Measures for Biomedical Research Involving Humans). The following safeguards were implemented:

De-identification: Direct identifiers (eg, names, ID numbers) and indirect identifiers (eg, rare diagnoses, exact dates) were removed before analysis. Original medical records were replaced with anonymized codes.

Access Control: Data were stored on encrypted servers within secure hospital networks. Physical access required biometric authentication, while digital access was restricted to principal investigators via role-based permissions.

Data Processing: Only aggregated statistical outputs were used for analysis—no individual-level data or original medical images were shared.

Retention Policy: Original records remain archived per institutional guidelines, while research datasets will be permanently deleted five years after project completion.

Abbreviations

ALVO, Acute large vessel occlusion; MFBG, mean fasting blood glucose; MT, mechanical thrombectomy; preoperative-mRS, preoperative modified Rankin Scale; AHA/ASA, American Heart Association/American Stroke Association; 90ds-mRS, 90-day modified Rankin Scale; SMD, standardized mean differences; rt-PA, recombinant tissue plasminogen activator; mTICI, modified Thrombolysis in Cerebral Infarction Score; m(IQR), median (interquartile range); PSM, propensity score matching; AIS, Acute Ischemic Stroke; TSR-1stBGM, Time Since Recanalization for First Blood Glucose Measurement; TSR-2ndBGM, Time Since Recanalization for Second Blood Glucose Measurement; TSR-3rdBGM, Time Since Recanalization for Third Blood Glucose Measurement.

Data Sharing Statement

The analysis code supporting the results of this study are available on request from the corresponding author, upon reasonable request.

Ethics Approval and Consent to Participate

This study was reviewed and approved by the Institutional Ethics Committees of Tianjin Huanhu Hospital, Ethics Committee of Xianyang Central Hospital, Ethics Committee of Tianjin Medical University Second Hospital.

The research strictly adhered to the principles outlined in the Declaration of Helsinki and the Ethical Review Measures for Biomedical Research Involving Humans (issued by the National Health Commission of China.)

This study was approved by each center's ethics committee for retrospective data analysis. All patient information was anonymized, and as this was an observational study without any intervention, it posed no additional risk to participants. Therefore, written informed consent was waived by the respective ethics committees, though verbal consent was obtained in all cases.

Author Contributions

Bin Luo, Yi Xiang and Yueming Pan have contributed equally to this work and share first authorship. 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

This paper has been uploaded to Research Square as a preprint: https://www.researchsquare.com/article/rs-4445050/v1. The authors declare that they have no competing interests.

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