Original Contribution

Admission Glucose and Effect of Intra-Arterial Treatment in Patients With Acute Ischemic Stroke

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Background and Purpose—Hyperglycemia on admission is common after ischemic stroke. It is associated with unfavorable outcome after treatment with intravenous thrombolysis and after intra-arterial treatment. Whether hyperglycemia influences the effect of reperfusion treatment is unknown. We assessed whether increased admission serum glucose modifies the effect of intra-arterial treatment in patients with acute ischemic stroke.

Methods—We used data from the MR CLEAN (Multicenter Randomized Clinical trial of Endovascular treatment for acute ischemic stroke in the Netherlands). Hyperglycemia was defined as admission serum glucose >7.8 mmol/L. The primary outcome measure was the adjusted common odds ratio for a shift in the direction of a better outcome on the modified Rankin scale at 90 days, estimated with ordinal logistic regression. Secondary outcome variable was symptomatic intracranial hemorrhage. We assessed treatment effect modification of hyperglycemia and admission serum glucose levels with multiplicative interaction factors and adjusted for prognostic variables.

Results—Four hundred eighty-seven patients were included. Mean admission serum glucose was 7.2 mmol/L (SD, 2.2). Fifty-seven of 226 patients (25%) randomized to intra-arterial treatment were hyperglycemic compared with 61 of 261 patients (23%) in the control group. The interaction of either hyperglycemia or admission serum glucose levels and treatment effect on modified Rankin scale scores was not significant (P=0.67 and P=0.87, respectively). The same applied for occurrence of symptomatic hemorrhage (P=0.39 for hyperglycemia, P=0.39 for admission serum glucose).

Conclusions—We found no evidence for effect modification of intra-arterial treatment by admission serum glucose in patients with acute ischemic stroke.

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Key Words: glucose ■ hyperglycemia ■ hemorrhages ■ stroke ■ thrombectomy

Recent studies have demonstrated that intra-arterial treatment (IAT) by means of thrombectomy with stent retrievers is both effective and safe in patients with acute ischemic stroke caused by a proximal intracranial arterial occlusion in the anterior circulation.[1–5] Hyperglycemia on admission is associated with unfavorable outcome also after IAT. Patients with hyperglycemia are at increased risk of poor functional outcome, symptomatic intracranial hemorrhage, and less successful revascularization after intra-arterial thrombolysis.[6–11] Less evidence is available for patients who have been treated with intra-arterial thrombectomy. Only a few uncontrolled studies suggest that hyperglycemia increases the risk of poor functional outcome after intra-arterial thrombectomy as well, especially after incomplete reperfusion.[12–14]

Admission hyperglycemia is also associated with unfavorable outcome in ischemic stroke patients who have been treated with intravenous tissue plasminogen activator (IV-tPA). Hyperglycemia leads to an increased risk of symptomatic intracerebral hemorrhage, poor functional outcome, and less recanalization after treatment with IV-tPA.[15–17] No clinical trials have reported whether hyperglycemia alters the treatment effect of IV-tPA on functional outcome. One controlled trial study reported no interaction of IV-tPA and 24-hour fall in glucose on early neurological improvement.[18] Another controlled trial study reported that higher admission glucose levels are associated with higher odds for undesirable clinical outcome and symptomatic intracerebral hemorrhage,

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regardless of IV-tPA treatment.[15] Moreover, previous studies reported no significant interaction of diabetes mellitus with IV-tPA on functional outcome at 90 days; however, none of these studies reported admission blood glucose levels.[19–22]

Possible underlying mechanisms of the association between hyperglycemia and poor outcome in stroke patients include impairment of cerebrovascular reactivity in the microvasculature, altered blood–barrier permeability, increased cortical acidosis, and hypercoagulability.[23–27]

Considering the associations with poor outcome and underlying pathophysiological mechanisms, one might expect that IAT has less effect in patients with hyperglycemia compared with patients with normal glucose values. However, no studies have yet reported the influence of hyperglycemia on the treatment effect of IAT.

We aimed to assess whether increased admission serum glucose modifies the effect of IAT in patients with acute ischemic stroke and a proximal intracranial arterial occlusion in the anterior circulation in the MR CLEAN (Multicenter Randomized Clinical trial of Endovascular treatment for acute ischemic stroke in the Netherlands) cohort.

Methods

Study Design

The study protocol of the MR CLEAN trial was described previously.[1,28] In summary, MR CLEAN was a phase 3, multicenter clinical trial with randomized treatment-group assignments, open-label treatment, and blinded end point evaluation. The study was conducted in 16 centers throughout the Netherlands. Patients were aged ≥18 years with acute ischemic stroke caused by an intracranial arterial occlusion of the anterior circulation. Initiation of IAT had to be possible within 6 hours after stroke onset. IAT consisted of intra-arterial thrombolysis, mechanical thrombectomy, or both. Patients were randomized to IAT plus usual care or usual care alone.[28]

The study protocol[28] was approved by the central medical ethics committee and the research board of each participating center. All patients or their legal representatives gave written informed consent before randomization.

Clinical Definitions

All patients with available admission serum glucose levels were included. The serum glucose values were measured before IAT. As usual care also consisted of administration of IV-tPA when possible, patients with serum glucose levels of >22.2 mmol/L were excluded from the MR CLEAN trial. Hyperglycemia was defined as blood glucose levels on admission of >7.8 mmol/L.[29,30]

Outcome Measures

The primary outcome measure was the modified Rankin scale (mRS) score at 90 days. Secondary outcome measures were good functional outcome, defined as mRS score 0 to 2 at 90 days; National Institute Health Stroke Scale (NIHSS) score at 24 hours; NIHSS score at 5 to 7 days or discharge if earlier; intracranial occlusion on follow-up computed tomographic (CT) angiography at 24 hours; symptomatic intracranial hemorrhage, defined as parenchymal hemorrhage at any site in the brain shown on the CT scan being compatible with neurological deterioration during admission; recanalization, defined as modified Thrombolysis in Cerebral Infarction score 2b or 3 on digital subtraction angiography imaging at the end of the procedure in the intervention group; and mortality. Observers were blinded for the baseline data of the patient and for the outcome.

Statistical Analysis

All analyses were based on the intention-to-treat principle. Baseline characteristics were compared between patients with hyperglycemia on admission and normal serum glucose values. Categorical variables were tested by χ^2 and continuous variables by Students *t* test. Non-normally distributed variables were compared by Mann–Whitney test. $P<0.05$ was considered to indicate statistical significance. The primary effect parameter was the adjusted common odds ratio for a shift in the direction of an improved outcome on the mRS at 90 days, estimated by means of multivariable ordinal logistic regression. The binary outcome measures were analyzed using multivariable logistic regression, expressed as adjusted odds ratio. Adjustments were made for age, sex, NIHSS score on admission, atrial fibrillation, ASPECTS (Alberta Stroke Program Early CT Score), and history of hypertension. Treatment effect modification by admission serum glucose values or hyperglycemia with IAT was assessed by means of a multiplicative interaction variable.

The prediction scores of the HIAT2 (Houston Intra-Arterial Therapy 2) were used to predict poor outcome after IAT.[31] The score ranges from 0 to 10: age (≤59 years=0, 60–79 years=2, ≥80 years=4), glucose (≤8.3 mmol/L=0, >8.3 mmol/L=3), NIHSS (≤10=0, 11–20=1, ≥21=2), and ASPECTS (8–10=0, ≤7=3). A cutoff point of 5 was used to predict poor functional outcome, with the use of logistic regression. The analysis was performed using STATA 12.1 statistical package (StataCorp, College Station, Texas).

Role of the Funding Source

The study sponsors were not involved in the study design, study conduct, protocol review, manuscript preparation, or review.

Results

Admission serum glucose values were available for 487 of the 500 patients included in the MR CLEAN trial. In total, 226 patients were randomized to IAT (46%) and 261 patients (54%) to the control group. Mechanical treatment was performed in 189 of the 226 patients (84%). No intervention was given in 36 patients (16%).

Mean admission serum glucose was 7.2 mmol/L (SD, 2.2; Figure 1). Fifty-seven of 226 patients (25%) assigned to IAT were hyperglycemic compared with 61 of 261 patients (23%) in the control group. Hyperglycemic patients were older and more often had a medical history of diabetes mellitus, hypertension, and hypercholesterolemia than patients with normal serum glucose values (Table 1). Hyperglycemic patients in the intervention group had higher NIHSS scores after 24 hours and at 5 to 7 days compared with patients with normal serum glucose values. In addition, hyperglycemic patients in the intervention group less often experienced a good functional outcome, more often had symptomatic intracerebral hemorrhages, and had died more often than patients with normal serum glucose values (Table 2).

Overall, there was a shift toward an improved outcome in favor of the intervention in the distribution of mRS scores (adjusted common odds ratio, 1.6; 95% confidence interval, 1.1–2.2). Hyperglycemia on admission did not modify this shift toward improved outcome (Figure 2). The interaction of admission serum glucose levels and IAT effect for all outcome measures was not significant for the mRS score ($P=0.87$) nor for the other outcome measures (Table 3). In addition, the interaction of hyperglycemia on admission with effect of IAT was not significant ($P=0.67$) for mRS nor for the other outcome measures (Table 3, Table I in the online-only Data Supplement). Moreover, there was no significant effect modification of increasing admission glucose levels and IAT on the mRS scores when the admission glucose levels were divided

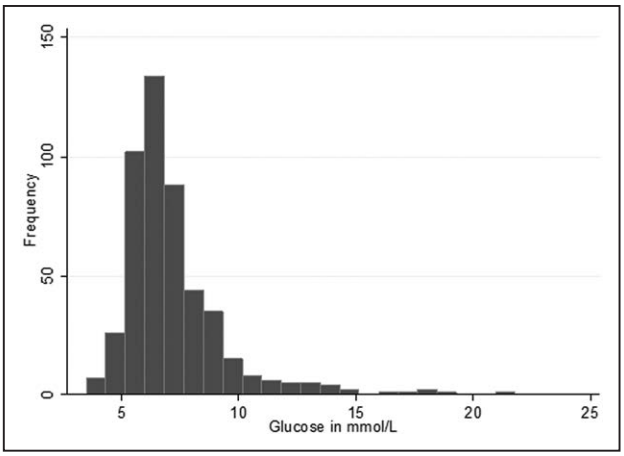

Figure 1. Distribution of admission serum glucose levels in 487 patients from the MR CLEAN (Multicenter Randomized Clinical trial of Endovascular treatment for acute ischemic stroke in the Netherlands) cohort.

into quintiles (*P*=0.21, *P*=0.31, *P*=0.49, *P*=0.99, respectively). Hundred ninety-seven patients (46%) assigned to IAT received IV-tPA compared with 236 patients (55%) assigned to the control group.

Of the 226 patients who received IAT, 111 patients (49%) reached recanalization. Twenty-eight patients (25%) who had recanalization were hyperglycemic compared with 29 patients (25%) who had no recanalization. The interaction of admission serum glucose levels and recanalization was not significant for the mRS score (*P*=0.55); the interaction of hyperglycemia and recanalization was also not significant (*P*=0.55; Table 4, Tables II and III in the online-only Data Supplement). Of the patients who received IAT, 136 patients (75%) had no intracranial occlusion on follow-up CT angiography at 24 hours compared with 67 patients (26%) in the control group. In the intervention group, the interaction of admission serum glucose levels and no intracranial occlusion on follow-up CT angiography at 24 hours for the mRS score was not significant (*P*=0.60) nor was the interaction of hyperglycemia and intracranial occlusion (*P*=0.67). The same applied for the control group (*P*=0.99 for admission serum glucose and *P*=0.06 for hyperglycemia).

Furthermore, the prediction scores of the HIAT2 were used.[31] Of all the patients with HIAT2 score ≥5 (n=152), 20 patients (13%) had good functional outcome compared with 103 of the 335 patients (31%) with HIAT2 score <5 (*P*<0.01). Patients with HIAT2 score ≥5 were less likely to have good functional outcome than patients with HIAT2 score <5 (odds ratio, 0.4; confidence interval, 0.2–0.6).

Discussion

We found no evidence for effect modification of IAT by increased admission serum glucose in patients with acute ischemic stroke caused by an intracranial occlusion in an artery of the anterior circulation. Although poor functional outcome, symptomatic intracerebral hemorrhage, and mortality occurred more often in hyperglycemic patients, there was no significant interaction between increased serum glucose and IAT on these outcome measures.

Table 1. Clinical Baseline Characteristics

Characteristics	Hyperglycemia on Admission (n=118)	No Hyperglycemia (n=369)	*P*
Age in y, mean (SD)	70 (11.5)	63 (14.1)	<0.01
Male, n (%)	68 (57.6)	213 (57.7)	0.99
Glucose at admission in mmol/L, mean (SD)	10.1 (2.6)	6.2 (0.8)	<0.01
History of diabetes mellitus, n (%)	41 (34.8)	26 (7.1)	<0.01
History of hypertension, n (%)	63 (53.4)	158 (42.8)	0.05
History of hypercholesterolemia, n (%)	40 (33.9)	87 (23.6)	0.03
History of atrial fibrillation, n (%)	35 (29.7)	95 (25.8)	0.40
History of ischemic stroke, n (%)	15 (12.7)	36 (9.8)	0.36
History of myocardial infarction, n (%)	20 (17.0)	52 (14.1)	0.45
History of peripheral arterial disease	6 (5.1)	18 (4.9)	0.93
Current smoking, n (%)	27 (22.9)	116 (31.4)	0.08
Current statin use, n (%)	41 (34.8)	100 (27.1)	0.11
Current antihypertensive medication use, n (%)	69 (58.5)	169 (45.8)	0.02
NIHSS at admission, median (IQR)	18 (15–21)	18 (14–22)	0.98
Prestroke mRS scores, n (%)			
0	89 (75.4)	308 (83.5)	0.05
1	13 (11.0)	32 (8.7)	0.44
2	8 (6.8)	17 (4.6)	0.35
>2	8 (6.8)	12 (3.3)	0.09
Treatment with IV-tPA, n (%)	100 (84.8)	333 (90.2)	0.10
Time of stroke onset to IAT in minutes, median (IQR)	255 (223–329)	260 (210–300)	0.42
ASPECTS, median (IQR)	9 (8–10)	9 (8–10)	0.63

ASPECTS indicates Alberta Stroke Program Early CT score; IAT, intra-arterial treatment; IQR, interquartile range; IV-tPA, intravenous tissue plasminogen alteplase; mRS, modified Rankin scale; NIHSS, National Institute Health Stroke Scale; and SD, standard deviation.

To our knowledge, no clinical studies have yet investigated possible modification of IAT effect by hyperglycemia. Only a few studies indicate that increased serum glucose leads to a higher risk of poor functional outcome after intra-arterial thrombectomy.[12–14] In addition, other studies report associations between hyperglycemia and poor functional outcome, symptomatic intracerebral hemorrhage, and less recanalization after intra-arterial thrombolysis.[6–11] Only one animal study found that interaction between hyperglycemia and IV-tPA increases hemorrhagic transformation, edema, and neurological deficits.[32]

Table 2. The Frequency of the Primary and Secondary Outcome Measures in the Control Group Compared With the Intra-Arterial Treatment Group, Within Each Group Hyperglycemia on Admission Is Compared With No Hyperglycemia

Outcome	Control Group (n=261)		Intra-Arterial Treatment (n=226)	
	Hyperglycemia on Admission (n=61)	No Hyperglycemia (n=200)	Hyperglycemia on Admission (n=57)	No Hyperglycemia (n=169)
mRS score at 90 d, median (IQR)	2 (0–2)	2 (1–3)	2 (0–3)	3 (2–4)
NIHSS score after 24 h, median (IQR)	18 (14–23)	16 (12–21)	15 (7–21)	13 (6–19)
NIHSS score at 5–7 d, median (IQR)	17 (8–19)	14 (7–18)	12 (2–18)	7 (2–16)
Good functional outcome, n (%)	6 (9.8)	44 (22.0)	13 (22.8)	60 (35.5)
Absence of intracranial occlusion, n (%)	7 (17.5)	60 (37.0)	30 (71.4)	106 (76.3)
Safety measures				
Symptomatic intracranial hemorrhage, n (%)	6 (9.8)	11 (5.5)	10 (17.5)	7 (4.1)
Mortality, n (%)	20 (32.8)	38 (19)	19 (33.3)	29 (17.2)

IQR indicates interquartile range; IV-tPA intravenous tissue plasminogen alteplase; mRS, modified Rankin scale; and NIHSS, National Institute Health Stroke Scale.

When taking these previous studies into consideration, it is surprising that we found no effect modification of IAT by hyperglycemia. Several reasons might explain our findings. First, hyperglycemia may have inhibitory effects on intravenous thrombolysis by reduction of the fibrinolytic activity of tPA by inhibiting plasma fibrinolysis and increasing

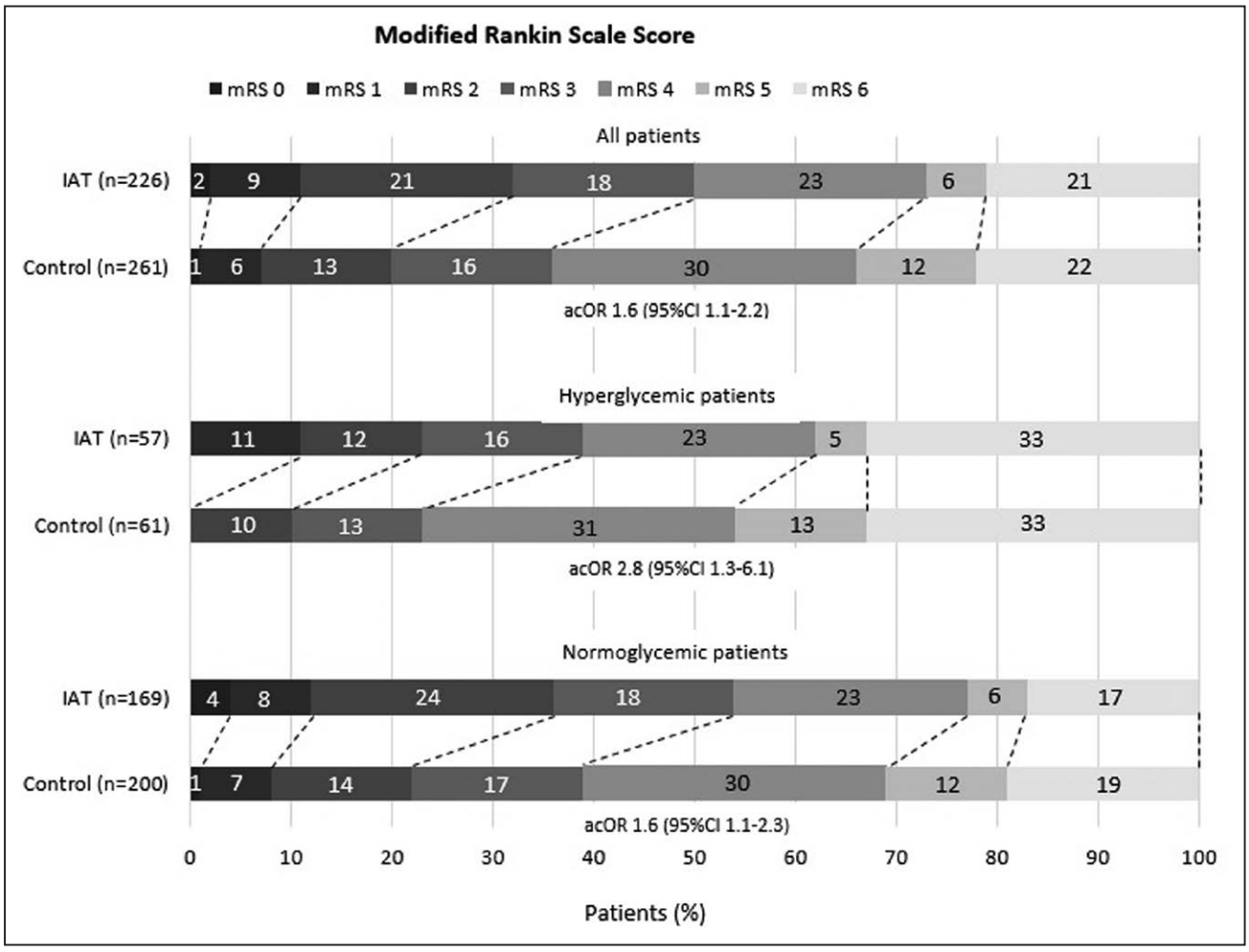

Figure 2. Effect of treatment on the distribution of the modified Rankin scale (mRS) scores at 90 days in hyperglycemia on admission vs no hyperglycemia. Numbers in the horizontal bars are percentages. Corresponding adjusted common odds ratios* (acOR) are reported below the bars. *Adjusted for age, sex, atrial fibrillation, history of hypertension, National Institute Health Stroke Scale at admission, and Alberta Stroke Program Early CT score (ASPECTS). CI indicates confidence interval; and IAT, intra-arterial treatment.

Table 3. Interaction of Admission Serum Glucose Levels or Hyperglycemia With IAT Effect on Several Outcome Measures

Outcome	Admission Glucose		Hyperglycemia	
	Unadjusted Interaction, *P*	Adjusted Interaction*, *P*	Unadjusted Interaction, *P*	Adjusted Interaction*, *P*
mRS score at 90 d	0.88	0.87	0.90	0.67
NIHSS score after 24 h	0.18	0.10	0.68	0.89
NIHSS score at 5–7 d	0.18	0.16	0.81	0.83
Good functional outcome (mRS 0–2)	0.60	0.57	0.57	0.47
Absence of intracranial occlusion†	0.16	0.14	0.20	0.29
Safety measures				
Symptomatic intracranial hemorrhage	0.22	0.39	0.19	0.39
Mortality	0.71	0.53	0.76	0.66

mRS indicates modified Rankin scale; and NIHSS, National Institute Health Stroke Scale.

*Adjusted for age, sex, atrial fibrillation, use of antihypertensive medication, NIHSS at admission, and Alberta Stroke Program Early CT score.

†Absence of intracranial occlusion on follow-up CT angiography at 24 h.

the production of plasminogen activator inhibitor-1.[33] These negative effects of hyperglycemia could be less in patients who receive intra-arterial thrombectomy and could partially explain why we found no modification of the treatment effect of IAT by hyperglycemia.

Second, one could hypothesize that hyperglycemia is a transient stress response after stroke and, therefore, mainly reflects the severity of the stroke itself rather than a pre-existent state of abnormal glucose metabolism in this study population.[34,35] Patients with more severe strokes might benefit more from IAT, and this could compensate for possible negative effects of hyperglycemia on IAT.

Strengths of our study are that admission glucose was a prespecified baseline characteristic of the MR CLEAN trial and that the hypothesis of possible modification of treatment effect by hyperglycemia was also prespecified. However, our study had a few limitations. First, patients with an admission serum glucose higher than 22.2 mmol/L were excluded from the MR CLEAN trial. Therefore, the possible effect modification of serum glucose levels higher than 22.2 mmol/L could not be analyzed. Second, most patients in our study were normoglycemic, with an interquartile range of 5.8 to 7.8 mmol/L. This could have affected the precision of our estimates.

In conclusion, we demonstrated that increased glucose on admission does not modify the effect of IAT in patients with acute ischemic stroke due to intracranial proximal arterial occlusion of the anterior circulation. This study provides no arguments for withholding IAT from patients with glucose levels up to 22.2 mmol/L. Further studies are needed to

Table 4. Interaction of Admission Serum Glucose Levels or Hyperglycemia on Recanalization and the Outcome Measures

Outcome	Admission Glucose		Hyperglycemia	
	Unadjusted Interaction, *P*	Adjusted Interaction*, *P*	Unadjusted Interaction, *P*	Adjusted Interaction*, *P*
mRS score at 90 d	0.33	0.55	0.55	0.55
NIHSS score after 24 h	0.46	0.43	0.89	0.62
NIHSS score at 5–7 d	0.70	0.97	0.68	0.90
Good functional outcome (mRS 0–2)	0.63	0.92	0.96	0.99
Absence of intracranial occlusion†	0.94	0.99	0.66	0.68
Safety measures				
Symptomatic intracranial hemorrhage	0.67	0.73	0.22	0.30
Mortality	0.26	0.14	0.31	0.60

mRS indicates modified Rankin scale; and NIHSS, National Institute Health Stroke Scale.

*Adjusted for age, sex, atrial fibrillation, use of anti-hypertensive medication, NIHSS at admission, and Alberta Stroke Program Early CT score.

†Absence of intracranial occlusion on follow-up CT-angiography at 24 h.

confirm our findings and to study the effects of higher glucose levels on the treatment effect of IAT in patients with acute ischemic stroke.

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Supplementary Table I Effect of IAT on outcome by hyperglycemic status on admission and p (interaction) of IAT with hyperglycemia.

	Unadjusted effect estimate			Adjusted effect estimate†		
Outcome	Hyper-glycemia on admission (n=118) cOR (95%CI)	No hyper-glycemia (n=369) cOR (95%CI)	Unadjusted interaction, p	Hyper-glycemia on admission (n=118) acOR (95%CI)	No hyper-glycemia (n=369) acOR (95%CI)	Adjusted interaction †, p
mRS score at 90 days	1.6 (0.8-3.0)	1.6 (1.1-2.4)	0.90	2.8 (1.3-6.1)	1.6 (1.1-2.3)	0.67
NIHSS score after 24 hours	0.6 (0.3-1.3)	0.5 (0.4-0.8)	0.68	0.5 (0.3-1.1)	0.5 (0.4-0.8)	0.89
NIHSS score at 5-7 days	0.5 (0.3-1.1)	0.5 (0.3-0.7)	0.81	0.5 (0.2-1.1)	0.5 (0.3-0.7)	0.83
	OR (95%CI)	OR (95%CI)		aOR (95%CI)	aOR (95%CI)	
Good functional outcome (mRS 0-2)	2.7 (1.0-7.7)	2.0 (1.2-3.1)	0.57	5.1 (1.4-18.2)	2.1 (1.2-3.4)	0.47

Absence of intracranial occlusion*	11.8 (4.1-33.9)	5.5 (3.3-9.0)	0.20	26.5 (5.9-119.2)	5.8 (3.4-9.7)	0.29
Safety measures						
Sympto-matic intracranial hemor-rhage	2.0 (0.7-5.8)	0.7 (0.3-2.0)	0.19	1.7 (0.5-5.5)	1.0 (0.3-2.6)	0.39
Mortality	1.0 (0.5-2.2)	0.9 (0.5-1.5)	0.76	0.7 (0.3-1.9)	1.0 (0.6-1.9)	0.66

* Absence of intracranial occlusion on follow-up CT-angiography at 24 hours

† Adjusted for age, sex, atrial fibrillation, use of anti-hypertensive medication, NIHSS at admission, Alberta Stroke Program Early CT score

Supplementary Table II Interaction of admission serum glucose levels on recanalization and the outcome measures

Outcome	Effect estimate, cOR (95%CI)	Unadjusted interaction term, p	Effect estimate, acOR (95%CI)	Adjusted interaction †, p
mRS score at 90 days	0.9 (0.7-1.1)	0.33	0.9 (0.7-1.2)	0.55
NIHSS score after 24 hours	1.1 (0.9-1.4)	0.46	1.1 (0.9-1.4)	0.43
NIHSS score at 5-7 days	1.1 (0.8-1.4)	0.70	1.0 (0.8-1.3)	0.97
	OR (95%CI)		aOR (95%CI)	
Good functional outcome (mRS 0-2)	0.9 (0.7-1.3)	0.63	1.0 (0.7-1.4)	0.92
Absence of intracranial occlusion*	1.0 (0.6-1.9)	0.94	1.0 (0.5-1.8)	0.99
Safety measures				

Symptomatic intracranial hemorrhage	0.9 (0.6-1.4)	0.67	0.9 (0.6-1.4)	0.73
Mortality	1.2 (0.9-1.6)	0.26	1.3 (0.9-1.9)	0.14

mRS indicates modified Rankin Scale, NIHSS National Institute Health Stroke Scale

* Absence of intracranial occlusion on follow-up CT-angiography at 24 hours

† Adjusted for age, sex, atrial fibrillation, use of anti-hypertensive medication, NIHSS at admission, Alberta Stroke Program Early CT score

Supplementary Table III Effect estimates in hyperglycemia on admission vs no hyperglycemia and interaction of hyperglycemia on admission with recanalization and outcome measures

	Unadjusted effect estimate			Adjusted effect estimate†		
Outcome	Hyper-glycemia on admission (n=57) cOR (95%CI)	No hyper-glycemia (n=169) cOR (95%CI)	Unadjusted interaction, p	Hyper-glycemia on admission (n=57) acOR (95%CI)	No hyper-glycemia (n=169) acOR (95%CI)	Adjusted interaction †, p
mRS score at 90 days	2.8 (1.1-7.5)	2.1 (1.2-3.5)	0.55	6.1 (1.9-19.7)	2.5 (1.4-4.5)	0.55
NIHSS score after 24 hours	0.4 (0.1-1.0)	0.3 (0.2-0.6)	0.89	0.2 (0.1-0.5)	0.3 (0.2-0.5)	0.62
NIHSS score at 5-7 days	0.5 (0.2-1.4)	0.3 (0.2-0.6)	0.68	0.1 (0.04-0.6)	0.2 (0.1-0.4)	0.90
	OR (95%CI)	OR (95%CI)		aOR (95%CI)	aOR (95%CI)	
Good functional	3.0 (0.8-11.1)	2.9 (1.5-5.5)	0.96	11.3 (1.4-91.5)	3.7 (1.8-7.7)	0.99

outcome (mRS 0-2)						
Absence of intracranial occlusion*	25.7 (2.9-(229.6)	14.7 (4.8-45.1)	0.66	N/A	17.3 (5.3-56.2)	0.68
Safety measures						
Sympto-matic intracranial hemor-rhage	0.4 (0.1-1.6)	1.4 (0.3-6.6)	0.22	0.2 (0.03-1.6)	1.5 (0.3-7.6)	0.30
Mortality	0.2 (0.1-0.8)	0.5 (0.2-1.1)	0.31	0.1 (0.01-1.0)	0.4 (0.2-1.1)	0.60

mRS indicates modified Rankin Scale, NIHSS National Institute Health Stroke Scale

* Absence of intracranial occlusion on follow-up CT-angiography at 24 hours

† Adjusted for age, sex, atrial fibrillation, use of anti-hypertensive medication, NIHSS at admission, Alberta Stroke Program Early CT score