SUPPLEMENTAL MATERIAL.

DETERMINANTS OF SYMPTOMATIC INTRACRANIAL HEMORRHAGE AFTER ENDOVASCULAR STROKE TREATMENT: A RETROSPECTIVE COHORT STUDY

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Supplemental Methods

Multiple imputation model

For univariable and multivariable regression analyses, we replaced missing values with multiple imputation using the aregImpute function of the Hmisc package in R version 4.0.5 (www.cran.r-project.org). In the model we included all the variables that were considered as potential determinants (Table I). In addition, we added the outcomes sICH occurrence, sICH-WI, and sICH-OI. There were no missings in sICH occurrence, however, in 14 patients we imputed missing sICH locations. The reason for these missing locations are related to technical issues (missing NCCT scan), and there is no indication that this is associated with the location of the hemorrhage. We performed 5 multiple imputation sets, in which we used 3 knots for continuous variables.

Supplemental Tables

Table I. Baseline clinical, radiological and treatment-related variables that we considered as potential determinants.	
Clinical characteristics	**Radiological characteristics**
Age	ASPECTS on NCCT
Sex	Nucleus lentiformis ischemia
Pre-stroke mRS score	Level of occlusion on CTA
Medical history	Dense artery sign
Ischemic stroke	Poor collateral score <50%
Ischemic stroke in same vascular area	Stenosis of ipsilateral carotid artery
Myocardial infarction	Occlusion of ipsilateral carotid artery
Peripheral artery disease	
Diabetes Mellitus	Extracranial dissection on DSA
Hypertension	
Atrial fibrillation	**Treatment-related characteristics**
Hypercholesterolemia	
Prior drug use	Intravenous alteplase treatment
Antiplatelet	Performed endovascular procedure*
Direct oral anticoagulant	
Coumarine	Total attempts
Heparin	Use of balloon guided catheter
Antihypertensive	Periprocedural use of heparin
Statin	Stent placement in ICA
Current smoking	Pre-EVT mTICI score
NIHSS score at baseline	Post-EVT mTICI score
SBP at baseline	Time from onset to groin puncture
Baseline blood levels	
INR	Duration of procedure
Trombocyte level	
Glucose level	
Creatinine level	
mRS indicates modified Ranking Scale; INR, International Normalized ratio; NIHSS, National Institute of Health Stroke Scale; SBP, systolic blood pressure; ASPECTS, Alberta Stroke Program Early CT score; NCCT, Non-Contrast CT; CTA, CT Angiography; DSA, Digital Substraction Angiography; EVT, Endovascular Treatment; mTICI, modified Thrombolysis in Cerebral Infarction. **Catheterization only, DSA only or Endovascular Treatment.*	

Table II. Univariable regression analysis of determinants of overall sICH occurrence, sICH within infarcted brain tissue and sICH outside infarcted brain tissue

Determinants	**overall sICH occurrence (n=203)**	**sICH within infarcted brain tissue (n=166)**	**sICH outside infarcted brain tissue (n=139)**
Clinical characteristics	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**
Age (per 10 years)	1.16 (1.04-1.29)*	1.16 (1.03-1.30)*	1.19 (1.05-1.35)*
Sex (male)	0.79 (0.59-1.05)	0.84 (0.62-1.14)	0.77 (0.55-1.07)
Pre-stroke mRS score > 2	1.39 (0.92-2.09)	1.43 (0.93-2.21)	1.52 (0.96-2.40)*
Medical history			
Ischemic stroke	0.91 (0.61-1.35)	0.88 (0.58-1.35)	0.85 (0.53-1.36)
Ischemic stroke in same vascular area	1.19 (0.70-2.03)	1.12 (0.62-2.03)	1.13 (0.56-2.30)
Myocardial infarction	1.92 (1.34-2.74)*	2.00 (1.38-2.91)*	1.69 (1.10-2.59)*
Peripheral artery disease	1.00 (0.61-1.66)	1.07 (0.63-1.81)	0.89 (0.48-1.65)
Diabetes Mellitus	1.46 (1.03-2.07)*	1.61 (1.12-2.32)*	1.48 (0.99-2.23)*
Hypertension	1.53 (1.14-2.06)*	1.64 (1.19-2.26)*	1.58 (1.11-2.25)*
Atrial fibrillation	0.94 (0.67-1.32)	0.94 (0.65-1.35)	0.84 (0.56-1.26)
Hypercholesterolemia	1.14 (0.84-1.54)	1.22 (0.88-1.68)	1.06 (0.74-1.52)
Prior drug use			
Antiplatelets	1.79 (1.33-2.39)*	1.96 (1.44-2.66)*	1.80 (1.28-2.53)*
Direct oral anticoagulant	0.25 (0.05-1.31)*	0.28 (0.05-1.51)*	0.26 (0.04-1.85)*
Coumarine	0.93 (0.60-1.44)	0.82 (0.50-1.35)	0.71 (0.40-1.26)
Heparin	1.14 (0.52-2.49)	0.88 (0.36-2.20)	1.36 (0.58-3.16)
Antihypertensive	1.61 (1.20-2.17)*	1.69 (1.22-2.33)*	1.57 (1.10-2.23)*
Statin	1.33 (0.99-1.77)*	1.40 (1.02-1.91)*	1.33 (0.94-1.87)
Current smoking	1.03 (0.71-1.50)	1.02 (0.67-1.55)	1.11 (0.70-1.75)
NIHSS at baseline (per point)	1.03 (1.01-1.05)*	1.03 (1.01-1.06)*	1.02 (1.00-1.05)*
SBP at baseline (per 10 mmHg)	1.12 (1.06-1.18)*	1.12 (1.06-1.19)*	1.14 (1.07-1.21)*
Baseline blood levels			
INR (per value)	0.89 (0.61-1.29)	0.91 (0.61-1.34)	0.77 (0.47-1.28)
Trombocyte count (per 10 * 10^9/L)	1.01 (0.99-1.02)	1.01 (0.99-1.02)	1.01 (0.99-1.03)
Creatinine level (per 10 µmol/L)	0.99 (0.95-1.04)	1.00 (0.96-1.04)	1.00 (0.96-1.05)
Radiological characteristics			
Level of occlusion on CTA			
ICA or ICA-T	1.53 (1.11-2.11)	1.44 (1.02-2.02)	2.06 (1.39-3.04)
M1	Ref.*	Ref.	Ref.*
M2	1.26 (0.83-1.90)	1.08 (0.68-1.70)	1.46 (0.89-2.41)
Other (M3/anterior/none)	1.16 (0.27-4.90)	1.27 (0.30-5.41)	0.88 (0.12-6.59)
ASPECTS on NCCT (per point increase)	0.97 (0.90-1.05)	0.97 (0.89-1.05)	0.98 (0.90-1.08)
Nucleus lentiformis ischemia	0.87 (0.63-1.19)	0.85 (0.61-1.21)	0.91 (0.63-1.32)
Dense artery sign	1.17 (0.85-1.61)	1.25 (0.90-1.74)	1.10 (0.76-1.58)
Poor collateral score (<50%)	1.63 (1.22-2.16)*	1.62 (1.19-2.20)*	1.65 (1.18-2.32)*
Stenosis of ipsilateral carotid artery	1.24 (0.77-2.01)	1.08 (0.62-1.88)	1.10 (0.60-2.00)
Occlusion of ipsilateral carotid artery	1.32 (0.85-2.06)	1.36 (0.85-2.19)	1.72 (1.07-2.75)*
Extracranial dissection	2.02 (0.95-4.27)*	1.93 (0.85-4.38)	1.88 (0.75-4.69)
Treatment-related characteristics			
Intravenous alteplase treatment	1.07 (0.76-1.50)	1.06 (0.73-1.53)	1.23 (0.81-1.88)
Performed endovascular procedure			
Catheterization only (no access)	Ref.	Ref.	Ref.*
DSA only (spontaneous reperfusion)	0.85 (0.33-2.16)	0.83 (0.30-2.29)	0.51 (0.19-1.39)
Endovascular treatment	1.29 (0.66-2.54)	1.18 (0.58-2.40)	1.14 (0.55-2.34)
Total attempts (per extra attempt)	1.01 (0.93-1.09)	1.01 (0.93-1.10)	1.02 (0.93-1.12)

Use of balloon guided catheter	0.85 (0.63-1.15)	0.85 (0.61-1.18)	0.96 (0.68-1.36)
Periprocedural use of heparin	1.22 (0.88-1.69)	1.21 (0.86-1.72)	1.20 (0.83-1.74)
Stent placement in ICA	1.23 (0.72-2.12)	1.33 (0.76-2.32)	0.90 (0.45-1.82)
Pre-EVT mTICI score			
0	1.25 (0.62-2.51)	1.25 (0.59-2.64)	2.14 (0.79-5.80)
1	1.36 (0.56-3.28)	1.45 (0.57-3.67)	2.35 (0.72-7.67)
2A	0.90 (0.35-2.33)	0.91 (0.33-2.51)	0.69 (0.15-3.09)
2B	1.02 (0.41-2.52)	1.07 (0.40-2.87)	1.62 (0.48-5.45)
3	Ref.	Ref.	Ref.*
Post-EVT mTICI score			
0	1.60 (1.05-2.46)	1.43 (0.90-2.27)	1.77 (1.06-2.94)
1	2.70 (1.38-5.28)	2.75 (1.26-5.97)	2.87 (1.32-6.27)
2A	1.60 (1.06-2.42)	1.51 (0.97-2.36)	1.90 (1.18-3.06)
2B	1.04 (0.69-1.57)	1.11 (0.72-1.69)	1.10 (0.68-1.79)
3	Ref.*	Ref.*	Ref.*
Time from onset to groin puncture (per hr)	1.10 (0.98-1.23)	1.10 (0.98-1.25)	1.00 (0.87-1.14)

Univariable regression coefficients are presented as adjusted Odds Ratio (aOR) with 95% confidence interval (CI). Ref. indicates reference value; sICH indicates symptomatic Intracranial Hemorrhage; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; SBP, systolic blood pressure; INR, International Normalized Ratio; CTA, CT angiography; ICA(-T), internal carotid artery (terminus);M(segment), middle cerebral artery; ASPECTS, Alberta Stroke Program Early CT score; NCCT, Non-Contrast CT; DSA, Digital Subtraction Angiography; EVT, Endovascular Treatment; mTICI, modified Thrombolysis in Cerebral Infarction.

**Odds Ratios with a p-value < 0.10*

Supplemental Figure

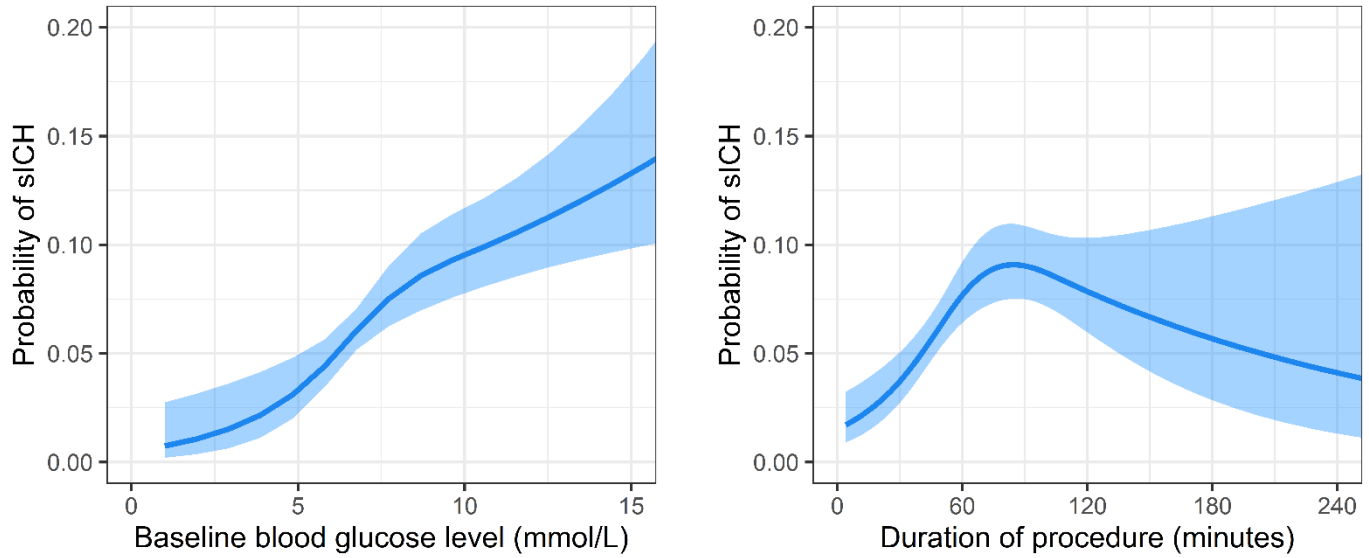

Figure I. Non-linear univariable relationship of baseline blood glucose level (left figure) and duration of procedure (right figure) with overall sICH occurrence (Blue lines). Lightblue areas indicate 95% confidence interval. Both variables showed similar non-linear univariable relationships to sICH occurrence within infarcted brain tissue and sICH occurrence outside infarcted brain tissue.

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