

SUPPLEMENTAL MATERIAL

Supplemental Tables

Table I. Characteristics of patients with and without thin slice non-contrast CT images

Characteristic	Included n=286	Excluded n=175	P-value*
Age, mean±SD	67±14	65±15	0.090
Male sex, n (%)	162 (57)	102 (58)	0.803
Admission NIHSS, median (Q1-Q3)	13 (7-17)	13 (9-19)	0.061
Time from symptom onset to scan, minutes, median (Q1-Q3)	113 (68-160)	85 (62-135)	0.011
Intravenous tPA, n (%)	201 (70)	131 (75)	0.339
Endovascular treatment, n (%)	33 (12)	27 (15)	0.288
Medical history			
Hypertension, n (%)	145 (51)	89 (51)	1.000
Diabetes mellitus, n (%)	36 (13)	25 (15)	0.651
Hyperlipidemia, n (%)	80 (28)	45 (27)	0.800
Smoking			0.792
- Smoking currently, n (%)	79 (30)	45 (30)	
- Former smoking, n (%)	83 (32)	52 (35)	
- Never smoked, n (%)	100 (38)	53 (35)	
Atrial fibrillation, n (%)	47 (17)	24 (14)	0.491
History of stroke/TIA, n (%)	56 (20)	25 (14)	0.180
History of MI, n (%)	41 (15)	15 (9)	0.093
Imaging findings			
Hyperdense vessel sign, n (%)	126 (44)	106 (62)	<0.001
NCCT ASPECTS, median (Q1-Q3)	10 (8-10)	10 (8-10)	0.717
CBV ASPECTS, median (Q1-Q3)	7 (5-9)	7 (5-9)	0.054
MTT ASPECTS, median (Q1-Q3)	3 (2-6)	4 (3-6)	0.021
Terminal ICA/proximal M1 occlusion, n (%)	69 (24)	48 (27)	0.496
Poor collateral score, n (%)	89 (31)	48 (28)	0.534
Follow-up			
Malignant MCA infarction, n (%)	35 (12)	19 (11)	0.766
Poor clinical outcome at 90 days*, n (%)	151 (53)	86 (50)	0.576

* Either parametric or non-parametric tests were performed depending on the variable distribution.

† defined as mRS≥3

ME: malignant edema, SD: standard deviation, NIHSS: National Institutes of Health Stroke Scale, tPA: tissue plasminogen activator, TIA: transient ischemic attack, MI: myocardial infarction, NCCT: non-contrast CT, ASPECTS: Alberta Stroke Program Early CT Score, CSF: cerebrospinal fluid, ICV: intracranial volume, CBV: cerebral blood volume, MTT: mean transit time, ICA: internal carotid artery, CBS: clot burden score, MCA: middle cerebral artery.

Table II. Association between potential predictors and malignant middle cerebral artery infarction

Characteristic	OR (95%-CI)
Age, per 10 years decrease	1.5 (1.2-2.0)
Male sex	1.5 (0.7-3.3)
Admission NIHSS, per point increase	1.2 (1.1-1.3)
Intravenous tPA	0.6 (0.3-1.2)
Endovascular treatment	1.7 (0.6-4.3)
Imaging findings	
Hyperdense vessel on NCCT	3.5 (1.7-8.0)
NCCT (pc-)ASPECTS score, per point decrease	1.8 (1.5-2.1)
CSF volume, per 100 mL decrease	3.1 (1.6-6.5)
CSF/ICV per 10% decrease	4.5 (1.9-11.7)
CBV (pc-)ASPECTS score, per point decrease	1.7 (1.5-2.1)
Terminal ICA/proximal M1 occlusion	7.3 (3.5-16.0)
Poor collateral score	7.3 (3.4-16.7)

OR: odds ratio, NIHSS: National Institutes of Health Stroke Scale, tPA: tissue plasminogen activator, ref: reference, TIA: transient ischemic attack, MI: myocardial infarction, NCCT: non-contrast CT, ASPECTS: Alberta Stroke Program Early CT Score, CSF: cerebrospinal fluid, ICV: intracranial volume, CBV: cerebral blood volume, MTT: mean transit time, ICA: internal carotid artery, CBS: clot burden score.

Table III. Subgroup characteristics: patients aged from 18 to 60

Characteristic	Total n=87	ME n=20 (23%)	No ME n=67 (77%)	P-value*
Age, mean±SD	50±8	48±10	50±7	0.439
Male sex, n (%)	58 (67)	14 (70)	44 (66)	0.719
Admission NIHSS, median (Q1-Q3)	12 (7-17)	16 (13-18)	12 (7-15)	0.001
Imaging findings				
CSF/ICV percentage, mean±SD	9±4	9±4	10±4	0.418
Terminal ICA/proximal M1 occlusion, n (%)	22 (25)	12 (60)	10 (15)	<0.001
Poor collateral score, n (%)	25 (29)	13 (65)	12 (18)	<0.001
Follow-up				
Poor clinical outcome at 90 days†, n (%)	43 (50)	19 (95)	24 (36)	<0.001

* Either parametric or non-parametric tests were performed depending on the variable distribution.

† defined as mRS≥3

ME: malignant edema, SD: standard deviation, NIHSS: National Institutes of Health Stroke Scale, CSF: cerebrospinal fluid, ICV: intracranial volume, ICA: internal carotid artery.

Table IV. Subgroup analysis: multivariable prediction models and the association with malignant middle cerebral artery infarction in patients aged from 18 to 60

Factor	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)
Age, per 10 years decrease	1.3 (0.7-2.7)		
Admission NIHSS, per point increase	1.2 (1.1-1.3)	1.1 (1.0-1.3)	
Terminal ICA/proximal M1 occlusion			9.6 (2.5-36.7)
Poor collateral score		5.5 (1.6-18.5)	9.6 (2.6-35.6)
CSF/ICV, per 10% decrease	2.4 (0.5-12.5)	1.7 (0.3-10.8)	1.1 (0.2-8.1)

OR: odds ratio, CI: confidence interval, NIHSS: National Institutes of Health Stroke Scale, CSF: cerebrospinal fluid, ICV: intracranial volume.

Table V. Subgroup analysis: comparison of clinical and imaging models with and without the ratio between intracranial cerebrospinal fluid volume and intracranial volume in patients aged from 18 to 60

Factor	AUROC	95% CI	P-value
Age + NIHSS	0.736	0.612-0.860	
Age + NIHSS + CSF/ICV	0.754	0.630-0.877	
Difference	0.018		0.278
NIHSS + Poor collateral score	0.800	0.690-0.910	
NIHSS+ Poor collateral score+ CSF/ICV	0.812	0.704-0.919	
Difference	0.012		0.545
ICA/proximal M1 occlusion + Poor collateral score	0.836	0.706-0.936	
ICA/proximal M1 occlusion + Poor collateral score + CSF/ICV	0.840	0.706-0.966	
Difference	0.004		0.916

AUROC: area under the receiver operating characteristic, CI: confidence interval, NIHSS: National Institutes of Health Stroke Scale, CSF: cerebrospinal fluid, ICV: intracranial volume.

Table VI. Subgroup characteristics: patients with NIHSS of 16 or greater

Characteristic	Total n=95	ME n=21 (22%)	No ME n=74 (78%)	P-value*
Age, mean±SD	68±15	61±19	69±13	0.084
Male sex, n (%)	46 (48)	12 (57)	34 (46)	0.365
Admission NIHSS, median (Q1-Q3)	18 (17-20)	19 (18-22)	18 (17-20)	0.042
Imaging findings				
CSF/ICV percentage, mean±SD	13±4	12±5	13±4	0.119
Terminal ICA/proximal M1 occlusion, n (%)	33 (35)	12 (57)	21 (28)	0.015
Poor collateral score, n (%)	47 (50)	17 (81)	30 (41)	0.001
Follow-up				
Poor clinical outcome at 90 days†, n (%)	74 (79)	21 (100)	53 (73)	0.007

* Either parametric or non-parametric tests were performed depending on the variable distribution.

† defined as mRS≥3

ME: malignant edema, SD: standard deviation, NIHSS: National Institutes of Health Stroke Scale, CSF: cerebrospinal fluid, ICV: intracranial volume, ICA: internal carotid artery.

Table VII. Subgroup analysis: multivariable prediction models and the association with malignant middle cerebral artery infarction in patients with NIHSS of 16 or greater

Factor	Model 1 OR (95% CI)	Model 2 OR (95% CI)	Model 3 OR (95% CI)
Age, per 10 years decrease	1.4 (0.9-2.0)		
Admission NIHSS, per point increase	1.2 (1.0-1.5)	1.2 (1.0-1.4)	
Terminal ICA/proximal M1 occlusion			3.7 (1.2-11.3)
Poor collateral score		5.7 (1.7-19.6)	7.0 (2.0-24.9)
CSF/ICV, per 10% decrease	1.9 (0.5-7.8)	3.5 (0.9-13.0)	3.1 (0.9-11.0)

OR: odds ratio, CI: confidence interval, NIHSS: National Institutes of Health Stroke Scale, CSF: cerebrospinal fluid, ICV: intracranial volume.

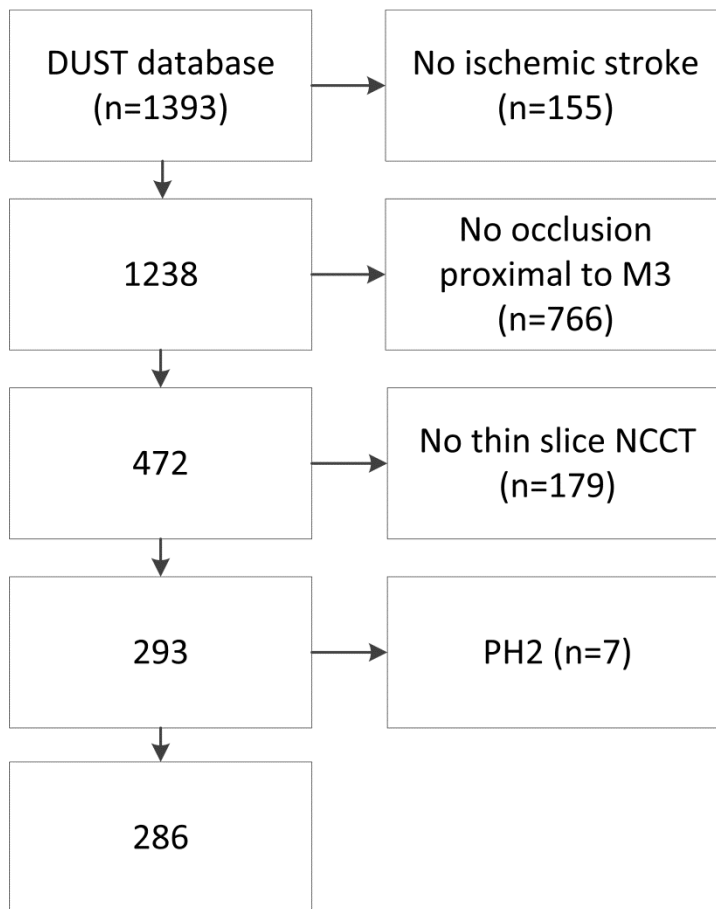
Table VIII. Subgroup analysis: comparison of clinical and imaging models with and without the ratio between intracranial cerebrospinal fluid volume and intracranial volume in patients with NIHSS of 16 or greater

Factor	AUROC	95% CI	P-value
Age + NIHSS	0.674	0.537-0.811	
Age + NIHSS + CSF/ICV	0.714	0.586-0.841	
Difference	0.040		0.355
NIHSS + Poor collateral score	0.753	0.645-0.860	
NIHSS+ Poor collateral score+ CSF/ICV	0.777	0.650-0.905	
Difference	0.024		0.047
ICA/proximal M1 occlusion + Poor collateral score	0.767	0.634-0.898	
ICA/proximal M1 occlusion + Poor collateral score + CSF/ICV	0.796	0.648-0.944	
Difference	0.029		0.070

AUROC: area under the receiver operating characteristic, CI: confidence interval, NIHSS: National Institutes of Health Stroke Scale, CSF: cerebrospinal fluid, ICV: intracranial volume.

Supplemental Figures

Figure I. Flowchart of patient selection



Legends: DUST: Dutch acute stroke study, NCCT: non-contrast CT, PH2: parenchymal hemorrhage type 2 according to ECASS classification.