ON-LINE APPENDIX

Patient Selection for Mechanical Recanalization

Our in-house standards imply that patients presenting with acute stroke symptoms are primarily surveyed by physicians of the Stroke Unit of the Department of Neurology. An NIHSS score is assessed at admission, and a CT stroke protocol (including noncontrast CCT, CT angiography, and CT perfusion) is performed. If hemorrhage is ruled out on noncontrast CCT, the time window is not exceeded (<4.5 hours), and no other contraindications are present according to the neurologic guidelines, patients receive IV thrombolysis with recombinant tissue plasminogen activator.[1] If a major vessel occlusion is found on CTA and CTP shows significant mismatch between cerebral blood flow and cerebral blood volume, indicating salvageable brain tissue, the patient is immediately transferred to the angiography suite. Mechanical endovascular recanalization therapy is performed if the occlusion is still visible on the diagnostic digital subtraction angiography series. Routinely, a microcatheter is introduced through the thrombus, and 1 microcatheter injection is performed to assure a positioning beyond the thrombus.

For CTA, CTP, and DSA, low-osmolar, nonionic contrast media (iomeprol, Imeron 300; Bracco, Milan, Italy) were used consistently.

Periprocedural Parameters and Clinical Patient Characteristics

For each patient, the following clinical and periprocedural information was derived from clinical records and the peri-interventional protocols of mechanical recanalization:

- Sex
- Age
- NIHSS score on admission
- Number of cerebrovascular risk factors (ie, arterial hypertension, diabetes mellitus, hypercholesterinemia, obesity, or smoking)
- Etiology of stroke based on the Trial of Org 10172 in Acute Stroke Treatment criteria (1 = large-artery atherosclerosis, 2 = cardioembolic, 3 = dissection, 4 = unknown etiology)[2]
- Preinterventional administration of IV thrombolysis (yes/no)
- If applicable, the amount of rtPA (milligram)
- The amount of contrast agent applied during the recanalization procedure (milliliter)
- The time interval from symptom onset until initial noncontrast CCT
- The time interval from initial noncontrast CCT until the beginning of the mechanical recanalization procedure
- The duration of interventional recanalization procedure
- The type of mechanical recanalization device (temporary stent versus other devices)
- The clinical outcome in terms of the modified Rankin Scale score 90 days after the event. An mRS of 0–3 was defined as good, and an mRS score of 4 or 5 and death were considered poor outcomes.

IMAGING PARAMETERS

All CT examinations were performed on either a 128-detector row CT scanner (SOMATOM Definition AS; Siemens, Erlangen, Germany) with whole brain perfusion (9.6-cm coverage) or a 16-detector row CT scanner (BrightSpeed; GE Healthcare, Milwaukee, Wisconsin) with 2 perfusion sections. Perfusion analysis was performed for all datasets with the vendor-provided software; by using a semiautomatic deconvolution algorithm and color-coded perfusion, parameter maps for CBF and CBV were calculated.

DSA with endovascular mechanical recanalization was performed on a biplanar DSA unit with an image matrix of 1024 × 1024 (NeuroStar; Siemens) by using a saline-flushed guide catheter under systemic heparinization.

MR imaging examinations were performed on a 1.5T MR imaging scanner (Magnetom Symphony; Siemens) including DWI, FLAIR, and T2*-weighted sequences.

Image Analysis

The pretherapeutic noncontrast CCT was analyzed to rule out any intracranial hemorrhage and to assess the presence of early signs of ischemia, namely the presence of a hyperattenuated vessel or hypoattenuation in ≥1 region of the ASPECTS. In ASPECTS topography, the MCA territory is divided into 10 regions (caudate, lentiform nucleus, internal capsule, insula, and M1–M6).[3] Regarding CTP, raters visually evaluated each ASPECTS region on the color-coded maps for relatively low CBF and CBV compared with the mirror region in the contralateral hemisphere.[4] In patients who received 2-section CTP, this analysis was done only in those cases in which all territories of the ASPECTS were displayed by the 2 available sections. Otherwise CBF and CBV ASPECTS could not be collected. Perfusion mismatch was defined as ASPECTS on the CBF map minus ASPECTS on the CBV map.

CTA was analyzed for the presence and site of the intracranial vessel occlusion.

On the initial diagnostic angiogram series, vessel occlusion, known from CTA, was reconfirmed to exclude patients with vessel recanalization by mere IV thrombolysis. For each patient, the recanalization result was assessed on the control angiogram and was classified as successful (TICI 3 or 2b) or failed (TICI 0, 1, or 2a).[5,6]

Postinterventional CCTs were analyzed for the presence and topographic distribution of hyperattenuated lesions. We differentiated the following anatomic localizations: 1) basal ganglia; 2) cerebral cortex, sectioned according to M1–M6 of the ASPECTS; and 3) sulci of the cerebral hemispheres (Fig 1, main text). If hyperattenuated intracerebral lesions were present in the basal ganglia and/or cerebral cortex, hyperattenuated intracerebral lesion total volume and mean and maximum attenuation in Hounsfield units were assessed by manual region-of-interest measurements on axial sections by using the open-source software OsiriX (http:// www.osirix-viewer.com). Hyperattenuated lesions that were no longer discernible on the 24-hour follow-up examination were defined as contrast enhancement; hyperattenuated lesions that persisted on follow-up 1 were considered hemorrhagic lesions.[7]

Final stroke lesion volume was determined on follow-up 2 scans on the basis of the ASPECTS, also used for MR imaging, and by manual volume measurements performed with OsiriX software. If MR imaging was performed fewer than 7 days after the acute stroke, this analysis was done on the *b*1000 images of the

DWI sequence; otherwise FLAIR was analyzed. In patients in whom poor clinical condition or other MR imaging contraindications prohibited the performance of MR imaging, noncontrast CCT was used as follow-up 2. The final lesion was categorized into 3 groups: 1) no infarction, 2) pure ischemic infarction, and 3) ischemic and hemorrhagic infarction. Hemorrhagic infarction was further subdivided according to the European Cooperative Acute Stroke Study trial classifications into hemorrhagic transformation (HI1 and HI2 according to ECASS) and parenchymal hemorrhage (PH1 and PH2 according to ECASS).[8]

Statistical Analysis

Statistical analyses were performed by using the Statistical Package for the Social Sciences software (Version 17; IBM, Armonk, New York). We chose a value of $P = .05$ as a level of statistical significance. We performed univariate analyses, including Kruskal-Wallis, Fisher exact, and Mann-Whitney *U* tests. To evaluate risk factors for the incidence of hyperattenuated intracerebral lesions, we performed logistic regression analyses. Furthermore, the Fisher exact test, ORs, and 95% CIs were determined to evaluate the association of hyperattenuated lesions with the risk of hemorrhagic transformation within the first 3 weeks. In addition, logistic regression analyses were used to evaluate whether different clinical and/or imaging factors were associated with clinical outcome.

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On-line Table 1: Imaging findings on pretherapeutic CCT examination ($N = 101$ patients)

	No.[a]	No. (%)	Median	IQR
Noncontrast CCT:	101			
Any early stroke signs		85 (84.2%)		
Early stroke signs in the basal ganglia		73 (72.3%)		
Hyperattenuated vessel sign		50 (49.5%)		
ASPECTS			8	4
CT angiography	101			
MCA occlusion		81 (80.2%)		
Left side		32 (31.7%)		
Right side		49 (48.5%)		
iICA occlusion		20 (19.8%)		
Left side		10 (9.9%)		
Right side		10 (9.9%)		
CT perfusion	101			
Whole-brain perfusion available		60 (59.4%)		
Two perfusion sections available[b]		41 (40.6%)		
Degree of perfusion mismatch[b]		98[c]	4	4

Note:—iICA indicates intracranial segment of the ICA.

[a] No. indicates number of patients in whom the parameter was available in this retrospective study.

[b] The degree of perfusion mismatch was determined as ASPECTS on the CBF map minus ASPECTS on the CBV map.

[c] In 3 of 41 cases with 2-section CTP, ASPECTS of CBF and CBV was not determined because not all ASPECTS territories were fully displayed; thus, the degree of perfusion mismatch was not assessed.

On-line Table 2: Details on acute stroke treatment

	No.[a]	No. (%)	Median	IQR
IV thrombolysis (rtPA)				
Yes	101	74 (73.3%)		
Amount (mg rtPA)	58		63	16
Time interval from symptom onset to initial CCT (min)	55		129	75
Time interval from initial CCT to start of mechanical recanalization procedure (min)	101		60	45
Procedures of mechanical recanalization	101			
Duration (min)			125	65
Amount of contrast agent (mL)			200	50
Recanalization device				
Temporary stent alone		86 (85.1%)		
Temporary stent + other[b]		10 (9.9%)		
Other[c] alone		5 (5%)		
Successful recanalization (TICI 3 or 2b)		78 (77.2%)		
TICI 3		49 (48.5%)		
TICI 2b		29 (28.7%)		
No successful recanalization (TICI 0, 1, or 2a)		23 (22.8%)		
TICI 0		8 (7.9%)		
TICI 1		7 (6.9%)		
TICI 2a		8 (7.9%)		

[a] No. indicates number of patients in whom the parameter was available in this retrospective study.

[b] We used the following other recanalization devices: 8× Penumbra aspiration system (Penumbra, Alameda, California), 1× goose neck snare (Amplatz; Microvena, White Bear Lake, Minnesota), and 1× Phenox clot retriever (phenox, Bochum, Germany).

[c] We used the following other recanalization devices: 1× goose neck snare alone, 1× Merci clot retriever (Stryker; Kalamazoo, Michigan) + goose neck snare, 3× permanent stent.

On-line Table 3: Characteristics of patients with and without hyperattenuating lesions on postinterventional CCT

	Patients without HCLs (Total: *n* = 16)[b]	Patients with HCLs (Total: *n* = 85)[b]	*P* Value[a]
Age (yr)	73.5/15.25[c]	70/22[c]	.37
Sex (No.)			.08
Men	9	29	
Women	7	56	
No. of CVRFs	1/1 ($n = 14$)[b]	11 ($n = 67$)[b]	.90
NIHSS score on admission	12/3 ($n = 15$)[b]	16/6 ($n = 83$)[b]	.007[a]
Etiology of stroke (No.)			.5
TOAST 1	1	16	
TOAST 2	12	51	
TOAST 3	0	5	
TOAST 4	3	13	
Pretherapeuthic imaging findings			
ASPECTS	8.5/4[c]	8/4[c]	.61
Degree of perfusion mismatch based on ASPECTS[d]	5.5/4.5[c]	4/4[c] ($n = 82$)[b]	.30
Occlusion site			.43
MCA (left/right)	2/9	30/40	
iICA (left/right)	3/2	7/8	
Treatment-related parameters			
IV thrombolysis			
Yes (No.)	15	59	.06
Amount (mg rtPA)	63/18.5[c] ($n = 14$)[b]	63/12.5[c] ($n = 45$)[b]	.40
Amount of contrast agent (mL)	150/100[c]	200/50[c]	.014[a]
Time from symptom onset to start of IV thrombolysis (min)	120/57.5[c] ($n = 9$)[b]	112.5/88.8[c] ($n = 46$)[b]	.76
Time from IV thrombolysis to start of mechanical recanalization procedure (min)	60/27.5[c]	70/50[c]	.96
Duration of mechanical recanalization procedure (min)	105/48.8[c]	135/75[c]	.023[a]
Recanalization device			.78
Temporary stent (No.)	11	54	
Other (No.)	5	31	
Recanalization success			.11
No (TICI 0, 1, 2a) (No.)	1	22	
Yes (TICI 2b, 3) (No.)	15	63	
Clinical outcome			.77
Good (mRS $\leq$ 3)	6	28	
Poor (mRS $\geq$ 4)	9	55	

Note:—HCLs indicate hyperattenuated intracerebral lesions; CVRF, cardiovascular risk factors; Trial of Org 10172 in Acute Stroke Treatment (TOAST) 1, large-artery atherosclerosis; 2, cardioemboly; 3, dissection; 4, unknown etiology; iICA, intracranial segment of the ICA.

[a] Statistically significant results in the univariate analysis ($P < .05$).

[b] If the respective parameter was not available in all patients, the number of patients available for analysis is given in parentheses.

[c] Numbers indicate median/IQR.

[d] Calculated as described in the On-line Appendix.

On-line Table 4: Characteristics of patients with good-versus-poor clinical outcome

	Patients with Good Clinical Outcome (n = 34)[a]	Patients with Poor Clinical Outcome (n = 64)[a]	P Value[b]
Age (yr)	67.5/26.8[c]	73.5/18.5[c]	.014[b]
Sex			.39
Men (No.)	15	23	
Women (No.)	18	41	
No. of CVRFs	1/1[c] (n = 31)[a]	1/1[c] (n = 49)[a]	.14
NIHSS score on admission	14/6[c]	16/6[c] (n = 63)[a]	.003[b]
Etiology of stroke (No.)			.32
TOAST 1	4	13	
TOAST 2	20	41	
TOAST 3	3	2	
TOAST 4	7	8	
Imaging findings			
Pretherapeuthic ASPECTS	9/4[c]	6.5/4.8[c] (n = 63)[a]	.035[b]
Degree of perfusion mismatch based on ASPECTS[d]	5.5/3.3[c]	3/4[c] (n = 61)[a]	.001[b]
Occlusion site (No.)			.41
MCA (left/right)	9/20[c]	23/26[c]	
iICA (left/right)	2/3[c]	8/7[c]	
pCCT findings			.28
No HCLs	6	9	
CE	15	20	
HL	13	35	
Treatment-related parameters			
IV thrombolysis			
Yes (No.)	29	43	
Amount (mg rtPA)	59/27[c] (n = 27)[a]	56/64[c] (n = 57)[a]	.25
Amount of contrast agent (mL)	200/100[c]	200/50[c]	.49
Time from symptom onset to start of IV thrombolysis (min)	100/73.8[c] (n = 20)[a]	120/92,5[c] (n = 34)[a]	.59
Time from IV thrombolysis to start of mechanical recanalization procedure (min)	57.5/56.3[c]	75/45[c]	.044[b]
Duration of mechanical recanalization procedure (min)	120/76.3[c]	135/75[c]	.36
Recanalization device			.11
Temporary stent	26	38	
Other	8	26	
Recanalization success			.0003[b]
No (TICI 0, 1, 2a)	1	22	
Yes (TICI 2b, 3)	33	42	

Note:—CVRF indicates cardiovascular risk factors; Trial of Org 10172 in Acute Stroke Treatment (TOAST) 1, large-artery atherosclerosis; 2, cardioemboly; 3, dissection; 4, unknown etiology; pCCT, postinterventional cranial CT; HCLs, hyperattenuating intracerebral lesions, CE, contrast enhancement; HL, hemorrhagic lesion; iICA, intracranial segment of the ICA.

[a] If respective parameter was not available in all patients, the number of patients available for analysis is given in parenthesis.

[b] Statistically significant results in the univariate analysis ($P < .05$).

[c] Numbers indicate median/IQR.

[d] Calculated as described in the On-line Appendix.