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Association of initial imaging modality and futile recanalization after thrombectomy

Running title: MRI vs CT for thrombectomy selection

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Abstract

Objective: To test the hypothesis that selection by initial imaging modality (MRI vs CT) is associated with rate of futile recanalizations (FR) after mechanical thrombectomy (MT), we assessed this association in a multicenter, retrospective observational registry (BEYOND-SWIFT, NCT03496064).

Methods: In 2011 patients (49.7% female, median age 73 [61-81]) included between 2009 and 2017, we performed univariate and multivariate analyses regarding the occurrence of FR. FR were defined as 90 day modified Rankin Scale (mRS) 4-6 despite successful recanalization in patients selected by MRI (N=690) and CT (N=1321) with a sensitivity analysis considering only patients with mRS 5-6 as futile.

Results: MRI as compared to CT resulted in similar rates of subsequent MT (aOR 1.048, 95% CI 0.677 – 1.624). Rates of FR were as follows: 571/1489 (38%) FR mRS 4-6 including 393/1489 (26%) FR mRS 5-6. CT based selection was associated with increased rates of futile recanalizations compared to MRI (44%[41-47%] vs. 29%[25-32%], $p < 0.001$; aOR 1.77 (95%-CI: 1.25-2.51)). These findings were robust in sensitivity analysis. MRI-selected patients had a delay of approximately 30 minutes in workflow metrics in real-world university comprehensive stroke centers. However, functional outcome and mortality were more favorable in patients selected by MRI compared to patients selected with CT.

Conclusions: CT-selection for MT was associated with an increased risk of futile recanalizations as compared to MR-selection. Efforts are still needed to shorten workflow delays in MRI patients. Further research is needed to clarify the role of the initial imaging modality on FR occurrence and to develop a reliable FR prediction algorithm.

Key words: Acute ischemic stroke – MRI – CT – Futile Recanalization – Endovascular

Introduction:

Despite the overwhelming efficacy of mechanical thrombectomy (MT) for endovascular treatment of acute ischemic stroke (AIS), up to 25-50% of patients have a poor long-term outcome (modified Rankin Scale or mRS 4-6) despite successful recanalization – a phenomenon termed futile recanalization (FR) (1–3).

From a patient's perspective, being bedridden, incontinent and requiring constant nursing (mRS 5) or dead (mRS 6) can indeed be assumed to represent a futile outcome. Some, however, might consider moderately severe disability requiring assistance to attend to bodily needs or to walk (mRS 4) an acceptable, non-futile outcome. From a societal and health economics point of view, given the logistic and economic impact of endovascular treatment, there is a need to reduce FR (2,4). Known predictors of FR include age, National Institute of Health Stroke Scale (NIHSS) (2,5), procedure time (6), and leukoaraiois (7). However, the role of the initial imaging modality for patient selection on the rate of FR remains unclear (8). We hypothesized that imaging modality influences decisions regarding which patients to treat by MT hence resulting in a different rate of FR.

Therefore, the main objectives of this study were to: 1) determine the rate of FR in patients undergoing MT selected by MRI versus CT in a large multi-center registry; 2) identify relevant secondary outcomes, such as workflow metrics, sICH, mortality, and functional outcome according to initial imaging modality.

Methods

Briefly, this multi-center, retrospective, international, non-randomized observational registry was designed to investigate the safety and efficacy of a second-generation market-released neurothrombectomy device in borderline indications for treatment of AIS patients. In the 2007 period (Center Munich), this included treatment with a Solitaire AB used as retrievable Stent. Medtronic provided financial funding of the registry.

Inclusion criteria of the registry were treatment with a Medtronic market-released thrombectomy device for an intracranial large vessel occlusion with attributable neurological symptoms. Current participation in another clinical trial was the only exclusion criterion. For this analysis, we included all patients from the registry with available information on initial imaging modality. Between 26 – 90% of all patients treated by MT at each center during the study timeframe were included in this registry. Choice of imaging modality was center-specific and not specified. Four centers used mainly CT, two centers mainly MRI and the biggest center used CT and MRI in equal parts (Figure e-1: https://doi.org/ 10.5061/dryad.f4qrfj6t1). Reasons why patients underwent CT or MRI were not available as a data item in the registry, but were provided by the local principal investigator for the study timeframe (from Dryad Table 1: https://doi.org/ 10.5061/dryad.f4qrfj6t1). Local principal investigators also provided their approach for patient selection in the study timeframe (from Dryad Table 1: https://doi.org/ 10.5061/dryad.f4qrfj6t1) and all centers that had access to both modalities, based their decisions on a tissue-based approach with somewhat similar indications to perform MT. Cerebral microbleeds were no absolute contraindication for intravenous thrombolysis or endovascular treatment in the centers that used MRI as initial

imaging modality. A clear-cut intracranial hemorrhage excluded both IVT and EVT in all centers.

Indications for MRI as opposed to CT included both favorable prognostic features (low NIHSS, no contraindications such as vomiting or pacemakers) as well as unfavorable prognostic features (posterior circulation large vessel occlusion including basilar artery occlusion, intubated patients, and unknown onset time). Choice of EVT after imaging was a tissue-based approach in all participating centers putting slightly different emphasis on NIHSS, time elapsed, infarct core/ASPECTS, collaterals and overall prognosis (from Dryad Table 1: https://doi.org/ 10.5061/dryad.f4qrfj6t1).

Variables and Image analysis

Operators or independent research fellows at each center determined the site of large vessel occlusion and postinterventional recanalization according to the modified thrombolysis in cerebral infarction (mTICI) scale. Successful recanalization was defined as mTICI ≥ 2b, representing at least 50% antegrade angiographic reperfusion downstream of the initially occluded target territory (10). Tandem occlusion was defined as an intracranial large vessel occlusion coupled with an ipsilateral extracranial occlusion or a stenosis of 90% or more. For the subgroup analysis of ASPECTS, 1 point was added in MRI patients to correct for the differences in DWI-ASPECTS as compared to CT-ASPECTS (11).

Outcomes

The primary endpoint of this analysis was FR, which was defined as modified Rankin Scale (mRS) 4-6 at 90 days despite successful endovascular recanalization (mTICI ≥ 2b) (12). Secondary outcomes included a sensitivity analysis defining FR as mRS 5-6 at 90 days, all-cause mortality at 90 days, symptomatic intracranial hemorrhage (sICH), which was assessed at each center applying the European Co-operative Acute Stroke Study-II (ECASS II) criteria (13) and good functional outcome (mRS 0-2) at 90 days. The mRS score at 90 days was

obtained either in routinely scheduled clinical visits or by using standardized telephone interviews.

Statistical analysis

As the patients not undergoing MT were not collected in BEYOND-SWIFT, we sought to address the issue which parameters were associated with undergoing MT according to each imaging modality in the local database (2015 – 2018) from the biggest participating center (Bern). For this purpose, patients that had a vessel occlusion in the suspected ischemic territory presenting between 0 – 48 hours after symptom onset were compared with univariable analysis as outlined above. A backward stepwise multiple logistic regression analysis was performed to identify factors associated with performing subsequent MT. Then, age, sex and the imaging modality was added to the model to analyze, whether the imaging modality itself was associated with MT decisions.

In the BEYOND-SWIFT dataset, we compared the imaging groups (MRI versus CT) using Chi squared and and Fisher's exact tests for categorical variables, Whitney-Mann-U-Test for non-normally continuous or ordinally scaled variables, and Welsch's t-test for independent normally distributed data.

For the primary analysis of a pre-interventional model, the association of imaging type (MRI versus CT) with all outcome parameters was assessed using multivariable logistic regression adjusting for the following pre-specified confounders: age (continuous), sex (categorical), NIHSS on admission (ordinal, adjusted odds ratio [aOR] per point increase), known symptom onset (categorical), pre-stroke independence (mRS 0-2; categorical), hypertension (categorical), diabetes (categorical), smoking (categorical), previous stroke (categorical), center (categorical, contrast type: comparator; indicator: largest center), anterior vs posterior circulation (categorical), time from symptom onset to groin puncture (continuous), and intravenous thrombolysis (categorical). For the prognostic post-interventional model, the

following additional confounders were included: TICI 3 versus TICI 2b (categorical), use of balloon guiding catheter (categorical), intracranial stenting (categorical), general anesthesia (categorical), time from groin puncture to recanalization (continuous), and number of passes (ordinal, adjusted odds ratio [aOR] per pass). The rationale for both models was the combination of known predictors of FR following EVT (2,5) and baseline and interventional differences of patients with and without FR factoring in the (multi)collinearity between variables (from Dryad Table 2: https://doi.org/ 10.5061/dryad.f4qrfj6t1). In a post-hoc analysis, an ordinal shift analysis was applied using the same covariates and factors as stated above.

We excluded patients with missing data items from the multivariate analysis. For the sensitivity analysis, the same model was used to assess the association of imaging modality with FR defined as mRS 5-6 at 90 days, despite successful recanalization. We used a level of significance of 0.05. All analysis were performed with SPSS Version 25.

Standard Protocol Approvals, Registrations, and Patient Consents: Details on the registry (BEYOND-SWIFT) are registered at NCT03496064 and further details were previously published (9). Patient consent was obtained according to Good Clinical Practice and/or institutional review board and/or local or institutional policies.

Data Availability: anonymized data will be shared by request from any qualified investigator after clearance by the ethics committee.

Results:

Baseline

See Figure 1 for the registry flowchart. The rates of FR were as follows: 38% (571/1489) FR mRS 4-6 including 26% (393/1489) FR mRS 5-6 and 62% (918/1489) non-FR with mRS 0-3 at three months. 1213/1489 (81.5%) patients were included in the primary multivariable

analysis. Missing information on symptom onset to groin puncture (248) was the main missing data item.

[insert figure 1]

Baseline characteristics and univariate comparisons of patients according to imaging modality are presented in table 1.

[insert table 1]

Characteristics and univariate comparisons of patients with FR and without FR are presented in table 2. Patients with FR were older, had more severe stroke, were more often dependent before stroke onset, had higher glucose levels, less often witnessed symptom onset, a different cardiovascular risk profile, and more often a posterior circulation large vessel occlusion.

[insert table 2]

In the single-center analysis of the biggest participating center, patients with MRI as the initial imaging modality had a lower crude proportion of subsequent MT as compared to CT patients (61.8% vs. 80.1%, P<0.001). However, after adjustments for baseline differences, MRI as compared to CT was not associated with a lower rate of subsequent MT (aOR 1.048, 95% CI 0.677 – 1.624). Of the baseline factors, NIHSS (aOR 1.198 95% CI 1.156 - 1.241 per 1 point increase), posterior circulation large vessel occlusion (aOR 0.352 95% CI 0.228 - 0.542), preceding oral anticoagulation (aOR 2.610 95% CI 1.062 - 6.418) and treatment with intravenous thrombolysis (aOR 0.296 95% CI 0.203 - 0.432) were significantly associated with subsequent MT.

Univariate Analysis

Univariate outcomes are presented in table 3. Patients selected by MRI as compared to CT had lower rates of futile recanalization (28.6% [25-32%] vs 43.8% [41-47%], P<0.001). This

finding remained consistent when only considering successfully recanalized patients with mRS 5-6 as FR (18.6% [15-22%] vs 30.7% [28-34%], P<0.001).

[insert table 3]

Multivariate analysis

According to the multivariable binary logistic regression analysis adjusting for prespecified confounders outlined in the methods section, CT was associated with increased odds for FR (aOR 1.770, 95%-CI 1.251 – 2.506, Figure 2) as compared to MRI selection. This finding was consistent when using an ordinal shift analysis (aOR for the association of MRI with mRS 0.689, 95% CI 0.556 – 0.854). In the sensitivity analysis considering patients with mRS 5-6 as futile, the point estimate was very similar (aOR 1.758, 95%-CI 1.197– 2.583).

Of the prespecified confounders, age (per 1 year aOR 1.043, 95%-CI 1.031 – 1.055), NIHSS on admission (per 1 point aOR 1.087, 95%-CI 1.066 – 1.109), pre-stroke-independence (aOR 0.239, 95%-CI 0.138 – 0.414), diabetes (aOR 1.782, 95%-CI 1.254 – 1.532) and arterial hypertension (aOR 0.727, 95%-CI 0.530 – 0.997) were associated with FR.

[insert figure 2]

Postinterventional model

Also in the postinterventional multivariate model adjusting for additional interventional confounders, CT significantly increased the odds of having FR as compared to MRI selection (aOR 1.858, 95%-CI 1.285 – 2.687). Also in this model, the results were consistent when using an ordinal shift analysis (aOR for the association of MRI with mRS 0.639, 95% CI 0.494 – 0.827). Of the periinterventional confounders, complete recanalization TICI 3 (aOR 0.607, 95%-CI 0.432 – 0.853), intracranial stenting (aOR 2.620 ,95%-CI 1.071 - 6.406) and maneuver count (per 1 pass aOR 1.253, 95%-CI 1.077 – 1.457) were associated with FR.

Subgroup analyses

Our main finding of an increased risk of futile recanalization in patients selected by CT were consistent throughout subgroups according to centers, anterior as compared to posterior circulation (p for interaction P=0.862), occlusion site and low and high ASPECTS score (Figure 3 and from Dryad Table 3: https://doi.org/ 10.5061/dryad.f4qrfj6t1). When restricting the analysis to patients with known time of symptom onset, the increased risk of futile recanalization in patients selected by CT was robust also in patients presenting 0-6 hours after known symptom onset (aOR 1.757, 95% CI 1.168 – 2.644) and the point estimate suggested an ever more pronounced association for patients presenting beyond 6 hours (aOR 24.6, 95% CI 0.557 – 1087), without reaching significance in this small subgroup. In patients with known symptom onset, there was no interaction of imaging type and presentation within 6 hours (P=0.782).

Secondary outcomes:

There was no difference in time from symptom onset to hospital admission between the imaging modalities (Table 4). However, there was a time delay of 24 minutes from admission to groin puncture and 37 minutes from onset of symptoms to IVT needle in patients undergoing MRI. Rates of sICH were higher in patients selected with CT (7.0% vs 4.4%, P = 0.018), although this was non-significant after adjustments (aOR 1.087, 95%-CI 0.552 – 2.141). Rates of good functional outcome (mRS 0-2) were lower on univariate (39.5% vs 50.1%, P<0.001) and multivariable analysis (aOR 0.539, 95%-CI 0.395 – 0.735) in patients selected with CT as compared to MRI. Fittingly, mortality at three months was higher in patients selected with CT on univariate (28.1% vs 20.5%, P<0.001) and multivariable analysis (aOR 1.613, 95%-CI 1.153 – 2.257). Additional analysis regarding influence of imaging modality on subsequent MT and pattern of vessel occlusions according to imaging modality

and occurrence of FR are available from Dryad (Tables 4-7: https://doi.org/ 10.5061/dryad.f4qrfj6t1).

[insert table 4]

[insert figure 3]

Discussion:

The main findings concerning the initial imaging selection modality for endovascular treatment in patients with acute ischemic stroke based on this multi-center registry analysis are:

(1) As compared to patients selected with CT, use of MRI was associated with a decreased risk of futile recanalization. (2) Patients selected by MRI have an unadjusted delay of roughly half an hour in workflow metrics in real-world university comprehensive stroke centers. (3) Nonetheless, as compared to patients selected with CT, functional outcome and mortality were more favorable in patients selected by MRI even after multivariable adjustments.

Despite the effectiveness of endovascular stroke treatment, the rate of FR remains very high (2). Hence, there is a need to reduce futile interventions (4) to protect patients' autonomy and limit healthcare costs. Whether selection by MRI as opposed to CT actually results in a higher (8,14) or a lower indication rate for EVT (15) depends on the detailed imaging protocol, time from symptom onset to imaging and decision algorithm. In our analysis, there was no influence of the initial imaging modality on MT rates.

In our analysis, MRI as the initial imaging modality compared to triage with CT was associated with a reduced rate of FR in high-volume comprehensive stroke centers. Several factors may explain this finding. Firstly, MRI often provides more clear-cut information compared to CT ASPECTS and may facilitate treatment decisions in complex clinical scenarios. Diffusion weighted imaging as compared to CT-perfusion, in particular, may provide a different estimate of the ischemic core translating into improved individual patient selection in real-world clinical conditions (8,16,17). Moreover, MRI-selected patients seem to

have a lower rate of sICH, as also shown in a recent Korean study (18) (see below) which may explain the lower frequency of FR, given the association between sICH and poor outcome.

Since the breakthrough of endovascular stroke therapy, indications to perform MT are constantly expanding which may increase the rate of FR. Given the benefit of MT in almost all subgroup analyses, the role of imaging – at least in the early phase – is gradually shifting from selecting patients to deselecting patients. According to our results, MRI might be the more useful tool to identify patients who will most likely not benefit from EVT even in case of successful recanalization. Combining clinical factors like advanced age, pre-stroke dependency, high stroke severity and expected time to recanalization with MR-specific factors, such as large ischemic core volume might lead to a predictive FR score in the future, which remains beyond the scope of the present study. We think the main concern in this context is, that the use of MRI may lead to supraselection of eligible AIS patients benefitting from MT. Machine learning and artificial intelligence represent promising tools to precisely determine whether MT will be beneficial or futile on an individual basis for AIS patients (19,20), but until then the positive predictive value of any simple "FR algorithm" should be as high as possible to avoid withholding an evidence-based treatment from otherwise suitable patients for endovascular recanalization therapies.

In randomized controlled trials, no significant in-center delay was noted for patients undergoing MRI as compared to CT (21,22), although perfusion imaging was performed only in a minority of subjects (22). Despite longer imaging duration, no impact on onset-to-needle and onset-to-groin time was seen in those trials - possibly because of facilitated treatment decisions by DWI images with clear-cut signal changes. The roughly 30 minutes delay from admission to groin puncture in MRI-selected patients fits well with the reported data in real-world patients (18) and underscore the importance to shorten in-hospital delays for MRI

patients. However, one has to bear in mind, that MRI patients were less severely affected and hence had less clear indications for MT like more distal occlusions.

In our dataset, there was a non-significant trend for sICH occurring less frequently in patients selected with MRI. A lower percentage of MRI-selected patients received IVT before MT, a finding which was non-significant in our registry, although significant in another recent observational study (18). After adjusting for possible confounders including the lower rate of IVT in MRI-selected patients, this association was non-significant in our registry, but remained significant in the study by Kim et al. Overall, in parallel to IVT, MRI-selected MT patients appear to have an improved safety profile concerning sICH (23,24) compared to those selected with CT. This might be explained by MRI being more sensitive to detect subtle hemorrhagic changes within the ischemic lesion (25) or very severe white matter changes, and better estimation of the time elapsed in unknown or unwitnessed onsets, thereby allowing to withhold IVT in patients with higher risk to develop sICH.

Our finding of improved functional outcome at three months for MRI-selected patients is in line with data from the mostly early time window HERMES collaboration (26) and late time window DEFUSE-3 trials (27). Moreover, in SWIFT PRIME, MRI-selected patients had similar clinical and imaging outcomes as compared to CTP-selected patients, despite worse prognostic characteristics (21). Nevertheless, assignment bias might have influenced those findings, since the choice of imaging was not randomized in any of the aforementioned trials. It is noteworthy that real-world studies have found no relevant difference in functional outcome (18,21,22,27) between MRI- and CT-selected patient. Upcoming randomized controlled trials on this issue are on the horizon and will hopefully soon elucidate whether the type of imaging modality significantly influences outcome (NCT03745391).

However, the main aim of this study was to sensitize stroke physicians that apparently the imaging modality influences their decisions regarding which patients to treat by MT. Whether

this results in an overall better, worse or equal outcome can only be judged by upcoming randomized controlled trials on this issue (NCT03745391).

Given the large sample size and good quality data, we were able to include many pre- and post-interventional confounders in our model. Despite potential overadjustment, the association of MRI and reduced FR remained significant arguing for a real effect. Of course, this study has the limitations of a multicenter, single-arm, retrospective registry of a highly selected patient population. Most importantly, patient triage with MRI or CT was center-specific; reasons to prefer one imaging modality in individual patients was not available, and no medical comparison group was available. Hence inference on the overall influence of the imaging modality on the subsequent indication rate for MT are not possible. We sought to address this issue by including the treating center as categorical factor in the multivariable analysis. A major limitation of our study is the absence of core-lab adjudicated recanalization grade, as well as pre- and post-interventional infarct volumes, among other factors. Moreover, the percentage of advanced perfusion studies and predictors shown to be associated with FR after EVT, including leukoaraiosis (7), were lacking. Additionally, no information was available on the rate of angiography, although all centers confirmed, that angiography was always intended and only skipped in cases of clinical problems (vomiting, agitation, …). Furthermore, more detailed workflow timepoints (admission to imaging time, imaging to puncture time, etc.) were not available, which hampers understanding differences in the workflow-related effects of each imaging modality. The date of the intervention was not known. However, the use of each imaging technique was consistent during the study period at each center and it is unclear how the expansion of indications for MT (e.g. more distal occlusions) might have influenced the occurrence of FR by each imaging modality. Finally – given the overall favorable prognostic profile of MRI patients - it remains possible that initial CT imaging might represent a surrogate marker of other residual confounding variables (frailty, off-hour treatment, poor general condition, and patients with pacemakers) and

selection bias might be present representing the true reason for increased rates of FR in those patients. Hence, our results need to be replicated by other groups and verified by upcoming randomized controlled trials on this issue (NCT03745391).

Conclusion

Patient selection for MT by CT was associated with an increased risk of FR compared to MRI selection. Further research is needed to clarify the role of the initial imaging modality on FR occurrence and to develop a reliable FR prediction algorithm which could be included into shared decision-making and elucidation of patient preferences. Efforts are still needed to shorten workflow delays in MRI patients. If confirmed in upcoming RCTs, cost-effectiveness analyses comparing CT with MR as the best initial imaging modality for MT seem warranted due to the ambivalence between MR-related costs and those associated with futile recanalization.

Appendix. Authors

Name	Location	Contribution
Thomas Raphael Meinel, MD*	Department of Neurology, Inselspital, Bern University Hospital, University of Bern, Switzerland	Drafting the manuscript, study concept and design, analysis and interpretation of data, acquisition of data, statistical analysis.
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Tables

	MRI, N=690	**CT N=1321**	**Available** of N=2011	**P**
Clinical items				
Age (years)	72 (60-80)	74 (62-82)	2011	0.003
Sex (female)	351 (50.9%)	648 (49.1%)	2011	0.452
NIHSS on admission	15 (9-19)	17 (12-21)	1983	<0.001
Transfer from another hospital	171 (24.9%)	547 (41.4%)	2009	<0.001
Stroke onset - witnessed - unwitnessed	 550 (79.7%) 140 (20.3%)	 1080 (81.8%) 241 (18.2%)	2011	0.281
Wake up Stroke	67 (11.3%)	92 (7.1%)	1894	0.003
Pre stroke independence (mRS 0-2)	645 (95.1%)	1206 (91.9%)	1990	0.007
Blood pressure systolic (mmHg)	153 (134 – 173)	148 (130 – 165)	1447	<0.001
Blood pressure diastolic (mmHg)	81 (70 – 95)	80 (70 – 90)	1446	0.030
Admission glucose (mmol/L)	6.6 (5.7-7.9)	6.8 (5.8-8.3)	1487	0.021
Medication				
Antiplatelet - Mono - Dual	 187 (32.1%) 8 (1.4%)	 367 (28.1%) 18 (1.4%)	1887	0.209
Statin	133 (27.1%)	377 (31.0%)	1706	0.115
Anticoagulation - VKA - DOAC	 43 (7.4%) 18 (3.1%)	 175 (13.4%) 55 (4.2%)	1888	<0.001
Etiology				
TOAST - Large artery - Cardioembolism - Other specific - Unknown	 83 (12.2%) 269 (39.4%) 44 (6.5%) 286 (41.9%)	 194 (15.0%) 644 (49.7%) 97 (7.5%) 360 (27.8%)	1977	<0.001
Risk factors				
Diabetes	117 (17.3%)	234 (17.8%)	1991	0.804
Arterial Hypertension	443 (65.3%)	870 (66.4%)	1989	0.653
Dyslipidemia	356 (52.8%)	636 (48.8%)	1977	0.097
Smoking	198 (29.6%)	353 (28.3%)	1918	0.561
Previous stroke	84 (12.3%)	184 (14.0%)	1996	0.333
Imaging				
CT-/DWI-ASPECTS	8 (5-9)	9 (7-10)	1698	<0.001
Tandem Occlusion	99 (14.4%)	207 (15.7%)	2009	0.472
Location - Anterior - Posterior	 638 (92.5%) 52 (7.5%)	 1159 (88.2%) 155 (11.8%)	2004	0.003

Table 1 - Baseline characteristics of patients according to initial imaging modality.

Results are presented as median (interquartile range) or absolute number (percentage). MRI: magnetic resonance imaging, CT: computer tomography, NIHSS: National Institute of Health Stroke Scale, mRS: modified Rankin Scale, VKA: vitamin K antagonist, DOAC: direct oral anticoagulant, TOAST: Trial of ORG 10172 in Acute Stroke Treatment, DWI: diffusion weighted imaging; ASPECTS: Acute Stroke Prognosis Early Computed Tomography Score

	Futile, N=571	Non-Futile N=918	Available of N=1489	P
Clinical items				
Age (years)	77 (67-84)	70 (58-79)	1489	<0.001
Sex (female)	279/571 (48.9%)	438/918 (47.7%)	1489	0.670
NIHSS on admission	18 (14-22)	14 (9-18)	1472	<0.001
Transfer from another hospital	198/571 (34.7%)	299/917 (32.6%)	1488	0.429
Known time of symptom onset	438/571 (76.7%)	768/918 (83.7%)	1489	0.001
Wake up Stroke	52/539 (9.6%)	65/858 (7.6%)	1397	0.197
Pre stroke independence	491/568 (86.4%)	885/910 (97.3%)	1478	<0.001
Blood pressure systolic (mmHg)	152, SD 31	149, SD 27	1083	0.080
Blood pressure diastolic (mmHg)	80, SD 19	82, SD 19	1082	0.097
Admission glucose (mmol/L)	7.2 (6.1-8.8)	6.5 (5.7-7.6)	1117	<0.001
Medication				
Antiplatelet - Mono - Dual	 166/541 (30.7%) 8/541 (1.5%)	 232/862 (26.9%) 10/862 (1.2%)	1403	0.257
Statin	153/485 (31.5%)	211/770 (27.4%)	1255	0.125
Anticoagulation - VKA - NOAC	 64/544 (11.8%) 28/544 (5.1%)	 84/861 (9.8%) 34/861 (3.9%)	1405	0.251
Etiology				
TOAST - Large artery - Cardioembolism - Other specific - Unknown	 81/566 (14.3%) 279/566 (49.3%) 31/566 (5.5%) 175/566 (30.9%)	 128/906 (14.1%) 415/906 (45.8%) 75/906 (8.3%) 288/906 (31.8%)	1472	0.188
Risk factors				
Diabetes	120/564 (21.3%)	116/910 (12.7%)	1474	<0.001
Arterial Hypertension	388/565 (68.7%)	572/910 (62.9%)	1475	0.025
Dyslipidemia	273/561 (48.7%)	459/907 (50.6%)	1468	0.485
Smoking	135/539 (25.0%)	277/880 (31.5%)	1419	0.010
Previous stroke	87/563 (15.5%)	105/914 (11.5%)	1477	0.031
Modality				
- MRI - CT	152/571 (26.6%) 419/571 (73.4%)	380/918 (41.4%) 538/918 (58.6%)	1489	<0.001
CT/MRI-ASPECTS	8 (6-9)	8 (7-10)	1247	0.001
Tandem Occlusion	80/570 (14.0%)	135/917 (14.7%)	1487	0.762
Location - Anterior - Posterior	 489/569 (85.9%) 80/569 (14.1%)	 831/915 (90.8%) 84/915 (9.2%)	 1484 1484	0.004
Treatment				
IVT use	253/571 (44.3%)	467/918 (50.9%)	1489	0.014
Time from onset of symptoms to IVT needle (min)	131 (90-180)	125 (89-175)	419/720	0.470
Time from onset of symptoms to admission (min)	156 (75-265)	129 (70-239)	1317	0.007
Procedure				
Additional intraarterial thrombolytics	45/537 (8.4%)	62/852 (7.3%)	1389	0.470
Balloon guiding catheter	251/539 (46.6%)	425/857 (49.6%)	1396	0.272
Number of thrombectomy passes	2 (1-2)	1 (1-2)	1029	<0.001
Intracranial stenting	30/570 (5.3%)	20/916 (2.2%)	1486	0.002
Extracranial stenting	64/571 (11.2%)	102/916 (11.1%)	1487	1.000

Time from onset of symptoms to groin puncture (min)	230 (167–332)	222 (160-315)	1289	0.149
Time from groin to recanalization	47 (31-78)	41 (28-65)	1463	<0.001
General anesthesia	330/537 (61.5%)	458/857 (53.4%)	1394	0.004
Interventional complication, any	67/570 (11.8%)	85/916 (9.3%)	1486	0.135
TICI 3	301/571 (52.7%)	532/918 (58.0%)	1489	0.053

Table 2 – Baseline and interventional characteristics of patients according to futility of recanalization.

Results are presented as median (interquartile range), mean with standard deviation when indicated by SD, or absolute number (percentage). NIHSS: National Institute of Health Stroke Scale, VKA: vitamin K antagonist, DOAC: direct oral anticoagulant, TOAST: Trial of ORG 10172 in Acute Stroke Treatment, MRI: magnetic resonance imaging, CT: computer tomography, ASPECTS: Acute Stroke Prognosis Early Computed Tomography Score, TICI: thrombolysis in cerebral infarction classification of recanalization.

Outcome	**MRI**	**CT**	**Available**	**P**
Futile recanalization (mRS 4-6)	152/532 (28.6%)	419/957 (43.8%)	1489/1676	<0.001
Futile recanalization (mRS 5-6)	99/532 (18.6%)	294/957 (30.7%)	1489/1676	<0.001
sICH ECASS II	30/688 (4.4%)	92/1309 (7.0%)	1997/2011	0.018
mRS 0-3	424/665 (63.8%)	602/1130 (53.3%)	1795/2011	<0.001
mRS 0-2	333/665 (50.1%)	446/1130 (39.5%)	1795/2011	<0.001
mRS 0-1	218/665 (32.8%)	275/1130 (24.3%)	1795/2011	<0.001
Mortality	136/665 (20.5%)	318/1130 (28.1%)	1795/2011	<0.001

Table 3 – Outcome data comparing patients according to initial imaging modality on univariate $\chi 2$ analysis.

MRI: magnetic resonance imaging, CT: computed tomography, sICH ECASS II: symptomatic intracranial hemorrhage according to the European Co-operative Acute Stroke Study-II definition, mRS: modified Rankin Scale.

	MRI, N=690	**CT N=1321**	**Difference in minutes**	**Available** of N=2011	**P**
Workflow metrics					
Time from onset of symptoms to admission (min)	133 (73-274)	150 (75-245)	17	1754	0.657
Time from onset of symptoms to IVT needle (min)	150 (110-180)	113 (69-165)	37	552/964	<0.001
Time from admission to groin puncture (min)	100 (82-123)	76 (46-107)	24	1577	<0.001
Time from onset of symptoms to groin puncture (min)	240 (174 -359)	228 (165 – 314)	12	1727	0.001
Time from groin to recanalization	48 (30-80)	45 (30-74)	3	1872	0.086
Time from symptom onset to recanalization	300 (225-409)	282 (215-375)	18	1619	0.005

Table 4 – Workflow metrics of patients according to initial imaging modality.

MRI: magnetic resonance imaging, CT: computer tomography.

Figure Legends

Figure 1 – Registry flowchart.

Figure 1 - TICI: thrombolysis in cerebral infarction recanalization score, mRS: modified Rankin Scale.

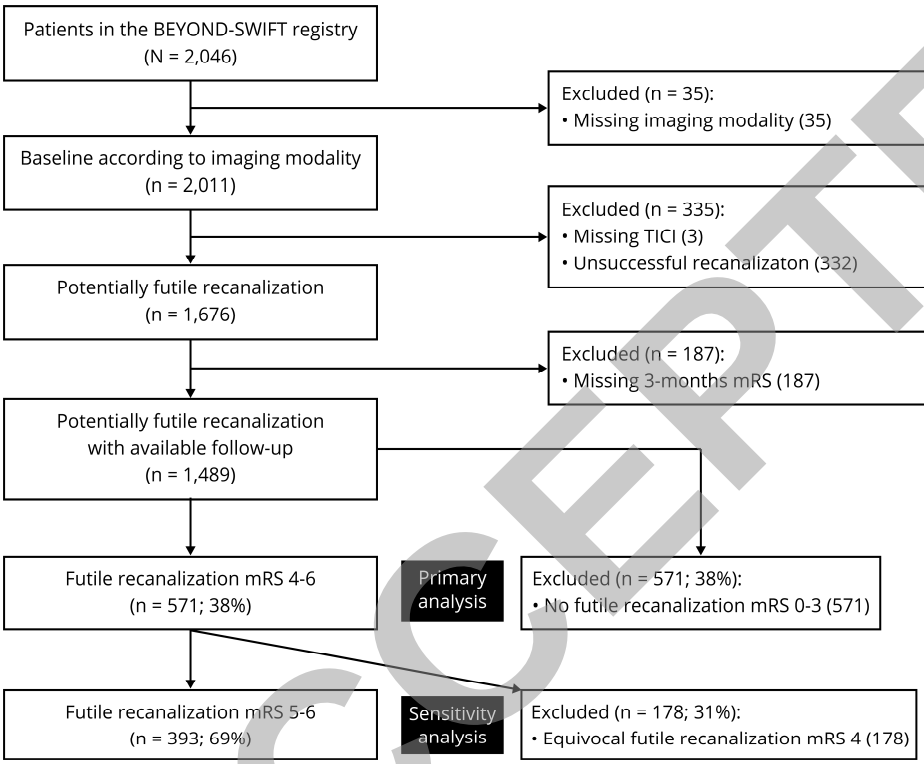


Figure 2 – Unadjusted and adjusted odds ratios of outcomes for initial imaging selection with CT as compared to MRI.

Figure 2 - FR: futile recanalization; mRS: modified Rankin Scale; sICH: symptomatic intracranial hemorrhage.

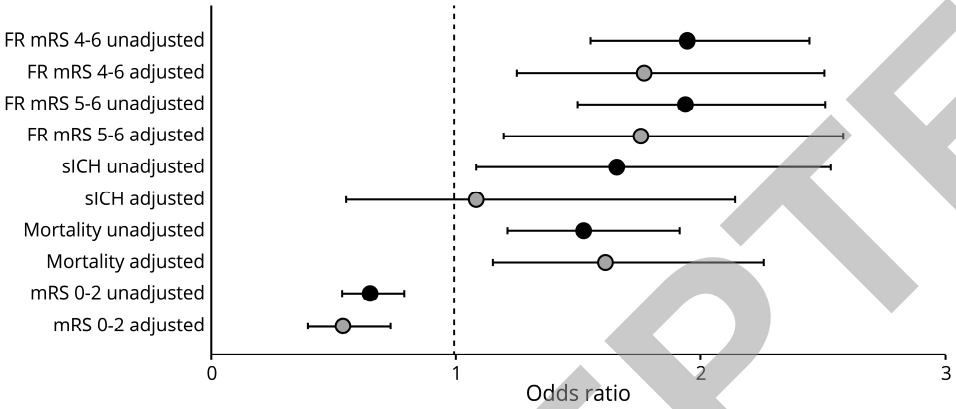
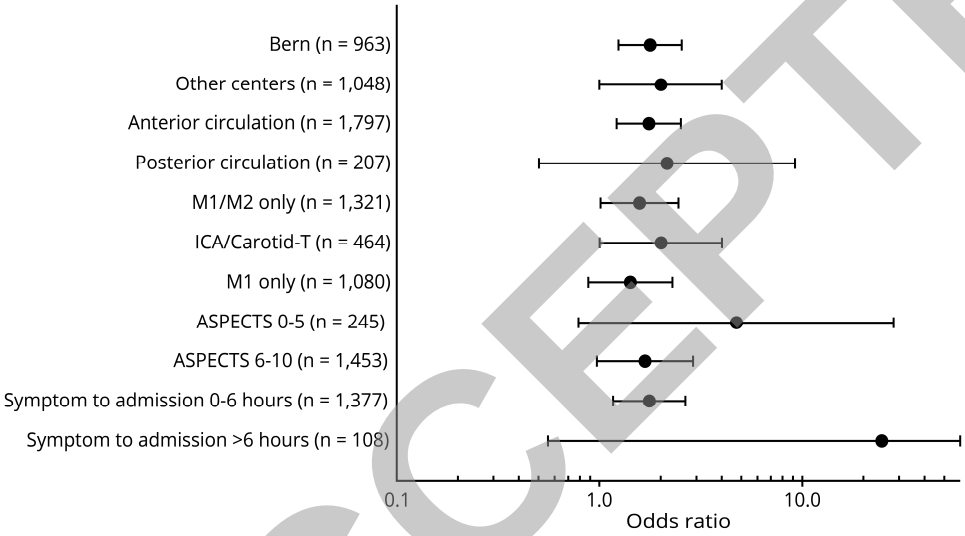


Figure 3 – Subgroup analyses: adjusted odds ratios of the multiple regression analysis for association of CT versus MRI with the primary outcome of futile recanalization.

Figure 3 - M1: Middle cerebral artery 1st segment, M2: Middle cerebral artery 2nd segment, ICA: internal carotid artery, ASPECTS: Alberta stroke program early CT score (1 point was added for MRI patients to control for the difference in DWI-ASPECTS as compared to CT-ASPECTS).



Association of initial imaging modality and futile recanalization after thrombectomy

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