JoS JOURNAL OF STROKE

Journal of Stroke 2025;27(3):390-401
https://doi.org/10.5853/jos.2025.02229

Original Article

Moving From CT-First to MRI-First Paradigm in Acute Ischemic Stroke: Treatment Rates, Time Metrics, Safety, and Outcomes

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Background and Purpose Neuroimaging is essential before intravenous thrombolysis (IVT) and endovascular treatment (EVT) for acute ischemic stroke (AIS). In May 2018, our center transitioned from computed tomography (CT) to magnetic resonance imaging (MRI) as the first-line imaging for suspected AIS. We aimed to assess the consequences of an MRI-based paradigm on patients' selection, rates of acute treatment, time metrics, safety of both IVT and EVT, and clinical outcomes.

Methods Using data from the Acute STroke Registry and Analysis of Lausanne (ASTRAL), we analyzed an equal number of patients from the CT-period (December 2012 to May 2018) and the subsequent MRI-period (May 2018 to August 2022). We performed univariable and multivariable analysis.

Results We included 2,972 consecutive AIS patients, 1,131 undergoing IVT and 662 EVT. Compared to the CT-period, the MRI-period showed similar rates of early and late IVT and EVT. The potentially missed-IVT opportunities decreased (3.1% vs. 0.8%; P_{adj}<0.01). Median door-to-needle time was longer in the MRI-period (43 min vs. 31 min, β-coefficient$_{adj}$=15, 95% confidence interval [CI]=11–27, P_{adj}<0.01), while door-to-puncture time was unchanged (β-coefficient$_{adj}$=9.95, 95% CI=-2.24–22.14, P_{adj}=0.11). Rates of symptomatic intracranial hemorrhage (SICH) were similar after IVT (5.6% vs. 3.2%, P_{adj}= 0.99) and EVT (±IVT) (6.5% vs. 4.2%, P_{adj}=0.52). Disability at 3 months was unaffected for both IVT and EVT patients (P_{adj}=0.36 and P_{adj}=0.52 respectively).

Conclusion The transition from CT to MRI as the first-line imaging reduced the rates of potentially missed IVT opportunities. While door-to-needle time increased, door-to-puncture time remained stable. Safety as measured by SICH rates and 3-month disability were unaffected by the imaging paradigm shift.

Keywords Neuroimaging; Stroke; Door-to-needle; Door-to-groin; Endovascular treatment; Intravenous thrombolysis

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Received: May 16, 2025
Revised: June 18, 2025
Accepted: August 20, 2025

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Introduction

The benefits of recanalization in acute ischemic stroke (AIS) are highly time-dependent,[1,2] therefore the emergency management of these patients requires minimizing any potential delay. Computed tomography (CT) and magnetic resonance imaging (MRI) are valid first imaging modalities for the urgent evaluation of AIS patients who may be potential candidates for revascularization treatments, yet there is no consensus among experts regarding the preferred imaging strategy for acute stroke evaluation.[3-6] CT is the most widely used approach in this setting; therefore, data on an MRI-based workflow and comparisons with CT-based acute imaging are scarce. MRI has longer acquisition times and may not be feasible in every patient; however, it could be advantageous in quantifying the ischemic core, estimating the delay of stroke onset in patients with unknown onset or wake-up stroke, and ultimately providing a better selection of revascularization treatment candidates.[6,7]

In terms of treatment delays, safety, and outcomes, the limited data about the use of MRI as first imaging modality in stroke patients eligible for revascularization treatment have shown mixed results, and most of evidence is nonrandomized.[8-15] A quasi-randomized, single-center trial showed that compared to CT, MRI-based evaluation leads to longer door-to-needle (DTN) time in patients treated with intravenous thrombolysis (IVT), without differences in the 3-month disability outcome.[10]

In our center, multimodal CT has been the first-line imaging modality for evaluating all AIS cases from 2003 till May 2018, at which point we incorporated a new MRI machine in the emergency department (ED). This transition provided us the opportunity to compare the two modalities using real-world clinical practice data. The feasibility of the MRI-first approach, its consequences on the diagnostic workflow, the diagnostic performance for AIS in the emergency setting, and the overall clinical outcome, have already been presented in a previous paper.[16] In this new analysis we focused on patients undergoing acute revascularization treatment.

The objective of this quality assurance project of the treatment practice in our hospital was to evaluate the MRI-based paradigm, when compared to the CT-based approach, with regards to (1) the selection and rates of AIS patients undergoing revascularization treatment with IVT or endovascular treatment (EVT), (2) in-hospital delays in administering these treatments (DTN for IVT and door-to-inguinal puncture [DTP] for EVT), (3) the safety of IVT and EVT, and (4) the 3-month disability outcome in treated patients.

Methods

Study population

The Acute STroke Registry and Analysis of Lausanne (ASTRAL) collects all AIS patients admitted to the stroke unit and/or intensive care unit of the Lausanne University Hospital (Centre Hospitalier Universitaire Vaudois [CHUV]) since 2003, as published previously.[17] We conducted the current study on the ASTRAL population, excluding from the analysis all secondary transfers from other hospitals, patients who had undergone brain imaging prior to arrival at our hospital, and in-hospital strokes.

We defined two time-based groups to identify the two paradigms: the MRI-paradigm including all consecutive patients satisfying the inclusion criteria admitted between May 1, 2018 (date when the MRI machine in the ED became operational) and August 31, 2022, and the CT-paradigm comparison group including an equal number of consecutive patients admitted between December 2012 and April 2018. As we aimed to conduct an intention-to-imaging study, the patients who had CT as first-imaging between May 2018 and August 2022 were kept in the MRI-paradigm group for the analysis.

Data collection

Stroke physicians and study nurses routinely collect data and parameters in a prespecified manner in ASTRAL, both in the acute hospital stay and after discharge. The variables in ASTRAL include demographics; patients' and stroke characteristics; acute and subacute brain and cervico-cerebral arterial imaging; revascularization treatments, i.e., IVT and EVT; and clinical outcome at 3 months (modified Rankin Scale [mRS]).

Patients' clinical assessment, neuroimaging protocol, and acute revascularization treatment

In our setting, every patient with suspected acute stroke admitted to the ED is evaluated by an ED physician and the on-call neurologist. The neurological evaluation consists of the National Institutes of Health Stroke Scale (NIHSS) assessment, and neuroimaging is done as soon as possible, usually within 24 hours, regardless of treatment eligibility in all suspected acute strokes with last known well (LKW) less than 24 hours. A stroke code is activated by the ED physician and the on-call neurologist based on a call with the prehospital teams for patients identified as eligible for an IVT or EVT, allowing for an immediate and simultaneous evaluation by a dedicated team on arrival at CHUV.

Both CT and MR scanners are located within the ED, in close proximity to the dedicated room where patients arriving under stroke code are initially received and evaluated. The transport distance from the area of the initial clinical evaluation to either

scanner is less than 50 m, and patient transfer typically requires no more than 1 to 2 minutes.

At least one arterial study of extra- and intracranial cerebral arteries is performed on admission, i.e., CT angiography (CTA) and MR angiography (MRA) (time-of-flight [TOF] and contrast MRA).

For multimodal CT-based imaging, we used a 64-multidetector CT scanner (LightSpeed VCT, GE Healthcare, Milwaukee, WI, USA) between December 2012 and November 2015, and a 256-multidetector CT scanner (Revolution CT, GE Healthcare, Milwaukee, WI, USA) thereafter. The institutional standard of care for patients with suspected AIS includes CT imaging protocol including non-contrast CT (NCCT), CT-perfusion (CTP), CTA, and post-contrast series (delayed venous-phase axial CT images acquired following the CTA).[18] The acquisition of this CT-based protocol including CTP usually takes 8 minutes. For MRI imaging, we use a 3-T scanner (Vida, Siemens, Erlangen, Germany) with the following sequences: sagittal T1 gradient echo, axial diffusion, axial 2D fluid attenuated inversion recovery (FLAIR), axial T2 gradient echo, TOF angiography, gadolinium-enhanced cervical MRA, post-contrast axial T1 gradient echo, and perfusion weighted imaging (PWI), as previously described.[19] Apparent diffusion coefficient (ADC) maps are generated from diffusion-weighted imaging (DWI) sequence. The duration of this MRI protocol is approximately 19 minutes.

The institutional goals for patients eligible for IVT and/or EVT are as follows: door-to-imaging delay, 15 minutes; DTN delay for IVT, 30 minutes; and DTP delay for EVT, 60 minutes. IVT is recommended for disabling stroke (defined as NIHSS ≥4, or NIHSS <4 but with a deficit deemed disabling by the treating physician) within 4.5 hours without an age limit in patients with a pre-stroke mRS score ≤3 if no clinical, radiological, or laboratory contraindications were identified. To identify later arriving and wake-up patients candidates for IVT, a significant penumbra on perfusion imaging was used since 2008, or a mismatch between FLAIR and DWI on MRI since 2018.[20,21] EVT was offered in supratentorial AIS to patients up to 6 hours with known onset if NIHSS was ≥6, proximal vessel occlusion and CTP showing >50% of penumbra until 2014. Afterwards, this latter imaging criteria was replaced by Alberta Stroke Program Early CT Score (ASPECTS) ≥5 and the lower NIHSS limit was replaced by the presence of a potentially disabling deficit.[22] Late treatment after 6 hours was offered starting in 2015 to patients with an ASPECTS ≥7 and a CTP mismatch ratio ([penumbra+core]/core) >2.0. From May 2017, patients were treated up to 8 hours without perfusion imaging, and late treatment was offered following DAWN criteria and for an NIHSS of 1–10 and ASPECTS ≥8.[23] From January 2018, late treatment alternatively followed Endovascular Therapy Following Imaging Evaluation for Ischemic Stroke 3 (DEFUSE-3) criteria[24] and was mainly DWI/PWI based. ASPECTS scores on MRI were assessed as previously described by identifying areas of acute ischemia, defined as hyperintense signal on axial DWI, and applying the ASPECTS methodology using the same topographical approach as with CT: starting from a score of 10, one point was subtracted for each region showing signs of acute ischemia.[25] Basilar artery occlusions were treated with EVT up to 6 hours until April 2017 in the absence of extensive brainstem infarct on radiology. Since May 2017, treatment window was extended to 8 hours if posterior circulation ASPECTS (pc-ASPECTS) was ≥7, and until 24 hours if no transverse irreversible brainstem ischemia was present on MRI, or if pc-ASPECTS was ≥8.[20] An expert neuroradiologist is available 24/7 for imaging interpretation.

Outcomes definition

To evaluate the consequences of an MRI-based paradigm on patients' selection and rates of acute revascularization treatment, we assessed the rates of early and late IVT and EVT treatments, both overall and specifically for posterior circulation strokes, as well as the rate of potentially missed IVT opportunities. The rates of early and late IVT treatment were calculated as the proportion of patients treated with IVT among all potential candidates, defined as patients with baseline NIHSS ≥4 arriving within 4 hours from symptoms onset or LKW for early IVT, and after 4 and 23 hours for late IVT. The 4-hour limit for LKW-to-arrival was chosen based on the conventional treatment window of 4.5 hours from symptom onset to treatment, accounting for the 30-minute in-hospital delay required to initiate treatment, which corresponds to the benchmark DTN time established in performance goals for timely care. The rates of early and late EVT treatment were calculated as the proportion of patients treated with EVT among all potential candidates, defined as patients with baseline NIHSS ≥4 and large vessel occlusion (LVO) arriving within 8 hours from symptoms onset or LKW (early EVT) and between 8 and 23 hours (late EVT). LVO was defined as an occlusion of the first segment of the anterior, middle, or posterior cerebral artery, the M2 segment of the middle cerebral artery, or the basilar artery. The rate of any revascularization treatment for posterior circulation strokes was calculated as the proportion of patients treated with IVT and/or EVT among all those with isolated posterior circulation stroke and an initial NIHSS ≥4, arriving within 23 hours from symptom onset or LKW. Finally, the rate of potentially missed IVT opportunities was defined as the proportion of acute stroke cases that met all institutional eligibility criteria for IVT (as detailed above) but were nonetheless not treated with IVT, over the total number of IVT performed in the same period.

To assess the time metrics and acute stroke workflow in the

https://doi.org/10.5853/jos.2025.02229

two paradigms, we evaluated: the median DTN time, defined as the delay in minutes from hospital arrival to start of IVT; the median DTP time, defined as the delay in minutes from hospital arrival to inguinal puncture; and the rate of successful recanalization in EVT, defined as expanded Thrombolysis in Cerebral Infarction (eTICI) score ≥2b67 at the end of the procedure.[26]

To assess the consequences of an MRI-paradigm on safety of both IVT and EVT, we measured the rates of symptomatic intracranial hemorrhage (SICH) within 36 hours, according to the European Co-operative Acute Stroke Study (ECASS-2) definition,[27] including both parenchymal SICH and subarachnoid hemorrhage (SAH), in patients treated with IVT alone and in those treated with EVT (±IVT). We also assessed the mortality at 7 days in both treatment groups.

As clinical outcomes, we assessed the 3-month disability in patients treated with IVT alone and with EVT (±IVT) and the rate of futile recanalization in patients treated with EVT (±IVT), defined as poor 3-month outcome (mRS 4–6) despite successful intracranial recanalization (eTICI ≥2b67) at the end of EVT. This analysis was performed for the overall EVT cohort, for early EVT (onset-to-inguinal puncture time ≤8 h) and late EVT (>8 h) separately.

Statistical analysis

Continuous and ordinal variables were expressed as medians (with interquartile range, IQR), and categorical variables as absolute counts (with percentage), unless stated otherwise.

Initially, we compared each outcome between MRI-paradigm and CT-paradigm groups, using unadjusted regression analyses to calculate crude odds ratio (OR) for binary outcomes and beta coefficients (β-coefficient) for continuous variables, along with 95% confidence intervals (CIs).

Next, we performed multivariable analyses for each above-mentioned outcome. Each time, we first assessed the presence and the shape of temporal trends throughout the study period. To do this we used generalized additive models to fit smooth curves for each outcome with a cubic smoothing spline term for the time variable. We chose generalized additive model given their flexibility in fitting nonlinear patterns in the data, allowing us to identify trends over time that may not have been captured using traditional linear models. Depending on whether the outcome was continuous, binary, or multicategory, we respectively used additive quantile regression model, generalized additive models with binomial distribution, and generalized additive model with ordered categorical outcome. The time variable was obtained by dividing the study period into ten consecutive periods with an equal number of consecutive patients in each period. Results of time trends were expressed as *P*-values.

Then we added to the models for each outcome the imaging paradigm variable together with potential confounders based on clinical plausibility and the time trend variable (when significant in the previous analysis) to obtain adjusted OR (or adjusted β-coefficients for continuous outcome variables) and 95% CIs. The potential confounders entered as model covariates for each outcome analysis are described as follows. The models for the rates of early and late IVT and EVT were adjusted for age, sex, baseline NIHSS, onset known, onset-to-door delay, and pre-stroke mRS. The same covariates were entered in the models for the rate of IVT and EVT in posterior circulation strokes, the rate of potentially missed IVT, DTN, and DTP. The DTP model also included as covariate IVT prior to EVT. The models for the rates of successful and futile recanalization in EVT were adjusted for the same factors as above, with the addition of stroke mechanism and site of intracranial occlusion. The rate of SICH in the IVT cohort was adjusted for age, baseline NIHSS, sex, baseline blood glucose, onset-to-IVT delay (min), mechanical thrombectomy (yes/no), any antiplatelet, pre-stroke anticoagulants, and baseline ASPECTS. The same factors for adjustment were used for the rate of SICH in the EVT cohort, plus DTP delay (min) and thrombectomy device passes. The disability at 3-month (mRS) and mortality at 7 days in both IVT and EVT cohorts were adjusted for age, baseline NIHSS, sex, pre-stroke mRS, onset-to-IVT delay (min), mechanical thrombectomy, baseline ASPECTS, and type of acute treatment received, plus active cancer for mortality analyses.

The statistical analysis was performed with R version 3.4.2 software or above (R Foundation for Statistical Computing, Vienna, Austria).

Standard protocol approvals, registrations, and patient consents

ASTRAL follows institutional regulations for clinical and research databases. Data were collected from routine clinical and radiological management and anonymized before analysis. Because only anonymized data were used, neither ethics committee approval nor patient consent was required according to the Swiss Human Research Act (HRA) and applicable data protection legislation. The status of patient consent also did not need to be considered, as this was primarily a quality assurance project of treatment practice in our institutions, which is not covered by the HRA.

Results

A total of 2,972 consecutive patients were included, half in the CT-paradigm and half in the MRI-paradigm. The median age was 76 years (IQR 65–84), and 46% were female (n=1,361). IVT was administered in 1,131 patients, and 662 underwent EVT. Further

details on the study cohort are displayed in Supplementary Table 1 and in our previous work on the diagnostic impact of the imaging paradigm change.[16] After shifting to the MRI-paradigm, MRI was attempted as the first imaging modality in 80% of patients (n=1,192/1,486), of whom 97.3% (n=1,160/1,192) had a complete exam of sufficient quality. The reasons for not performing MRI as the first imaging modality during the MR-first period were primarily patient-related, including contraindications such as pacemakers, metallic implants or devices, severe agitation, or clinical instability (a complete list is provided in Supplementary Figure 1 and in our previous work the diagnostic performance of the MRI-first paradigm[16]).

Acute treatment rates

Through the study period, of 1,843 potential candidates for IVT (NIHSS ≥4), 52% (n=954) received the treatment, with rates of 75.9% (n=842/1,110) in the early time window and 15.3% (n=112/733) in the late time window (Table 1). Time trend analysis showed a decrease in early IVT rates following the introduction of MRI, while the rate of late IVT progressively increased already during the CT period and reached a plateau during the MRI period (Figure 1A and B). Although this resulted in a reduction of early IVT rate from 78.1% in the CT period to 72.6% in the MRI period, and an increase of late IVT rate from 9.0% to 20.9%, the multivariable regression analysis adjusted for time trend and other potential confounders showed no significant association between the imaging paradigm and early or late IVT rates (Table 1).

Of 829 potential candidates for EVT (NIHSS ≥4, presence of LVO), 64% (n=537) received the treatment. The rates of early and

Table 1. Outcomes of the overall cohort and the two groups of interest, CT-paradigm, and MRI-paradigm

	Overall population (n=2,972)	CT-paradigm (n=1,486)	MRI-paradigm (n=1,486)	OR (95% CI)	P_{univ}	aOR (95% CI)	P_{adj}
Acute treatment rates in potentially eligible patients*							
Early IVT	842/1,110 (75.9)	511/654 (78.1)	331/456 (72.6)	0.74 (0.56–0.98)	0.03	0.79 (0.59–1.05)	0.11
Late IVT	112/733 (15.3)	31/345 (9.0)	81/388 (20.9)	2.67 (1.72–4.16)	<0.01	0.91 (0.25–3.32)	0.88
Early EVT	451/653 (69.1)	225/391 (57.5)	226/262 (86.3)	4.63 (3.09–6.94)	<0.01	0.78 (0.27–2.25)	0.65
Late EVT	86/176 (48.9)	19/89 (21.4)	67/87 (77.0)	12.34 (6.06–25.15)	<0.01	2.15 (0.39–12.04)	0.38
IVT or EVT in posterior circulation strokes	191/334 (57.2)	91/172 (52.9)	100/162 (61.7)	1.44 (0.93–2.22)	0.10	1.97 (0.66–5.88)	0.23
Missed IVT opportunities	27/1403 (1.9)	21/679 (3.1)	6/724 (0.8)	0.26 (0.11–0.65)	<0.01	0.22 (0.09–0.57)	<0.01
IVT cohort outcomes							
Door-to-needle time (min)†	37 (27–53)	31 (24–48)	43 (33–58)	12 (9.64–14.36)	<0.01	15.63 (11.27–20.0)	<0.01
SICH	50/1,131 (4.4)	33/593 (5.6)	17/538 (3.2)	0.55 (0.30–1.01)	0.05	1.00 (0.29–3.40)	0.99
7-day mortality	66/1,131 (5.8)	33/593 (5.6)	33/538 (6.1)	1.11 (0.67–1.82)	0.68	0.51 (0.16–1.56)	0.23
3-month mRS	2 (1–3)	2 (1–4)	2 (1–3)	1.37 (1.10–1.72)	<0.01	1.26 (0.77–2.06)	0.36
EVT cohort outcomes							
Door-to-puncture time (min)†	102 (88–124)	101 (90–121)	104 (85–129.1)	-3 (-7.66–1.66)	0.21	9.95 (-2.24–22.14)	0.11
SICH	34/662 (5.1)	18/278 (6.5)	16/384 (4.2)	0.63 (0.31–1.25)	0.19	0.62 (0.14–2.68)	0.52
Successful recanalization (eTICI ≥2b67)	556/651 (85.4)	223/274 (81.4)	333/377 (88.3)	1.73 (1.12–2.68)	0.01	0.74 (0.28–1.91)	0.53
7-day mortality	46/662 (6.9)	14/278 (5.0)	32/384 (8.3)	1.71 (0.90–3.28)	0.10	0.96 (0.24–3.78)	0.95
3-month mRS	2 (2–4)	2 (1–4)	2 (2–4)	0.78 (0.59–1.05)	0.10	1.22 (0.66–2.26)	0.52
Futile recanalization, all EVT	140/527 (26.6)	50/219 (22.8)	90/308 (29.2)	1.40 (0.94–2.08)	0.10	1.03 (0.41–2.56)	0.95
Futile recanalization, early EVT	112/441 (25.4)	44/197 (22.3)	68/244 (27.9)	1.34 (0.87–2.08)	0.18	0.97 (0.34–2.71)	0.95
Futile recanalization, late EVT	28/86 (32.6)	6/22 (27.3)	22/64 (34.4)	1.40 (0.48–4.08)	0.54	0.33 (0.01–11.27)	0.54

Continuous and ordinal variables are expressed as medians (interquartile range), and categorical variables as absolute counts (percentage). Odds ratios and *P*-values are given for the unadjusted (OR and P_{univ}) and adjusted (aOR and P_{adj}) analyses. For continuous outcome variables, β coefficients and 95% CIs are reported.

CT, computed tomography; MRI, magnetic resonance imaging; OR, odds ratio; aOR, adjusted odds ratio; CI, confidence interval; IVT, intravenous thrombolysis; EVT, endovascular treatment; SICH, symptomatic intracranial hemorrhage; mRS, modified Rankin Scale; eTICI, expanded Thrombolysis in Cerebral Infarction; NIHSS, National Institutes of Health Stroke Scale.

*Potentially eligible patients for IVT defined as all patients with baseline NIHSS ≥4, and for EVT as all patients with baseline NIHSS ≥4 and large vessel occlusion; †β-coefficients and 95% CIs.

https://doi.org/10.5853/jos.2025.02229

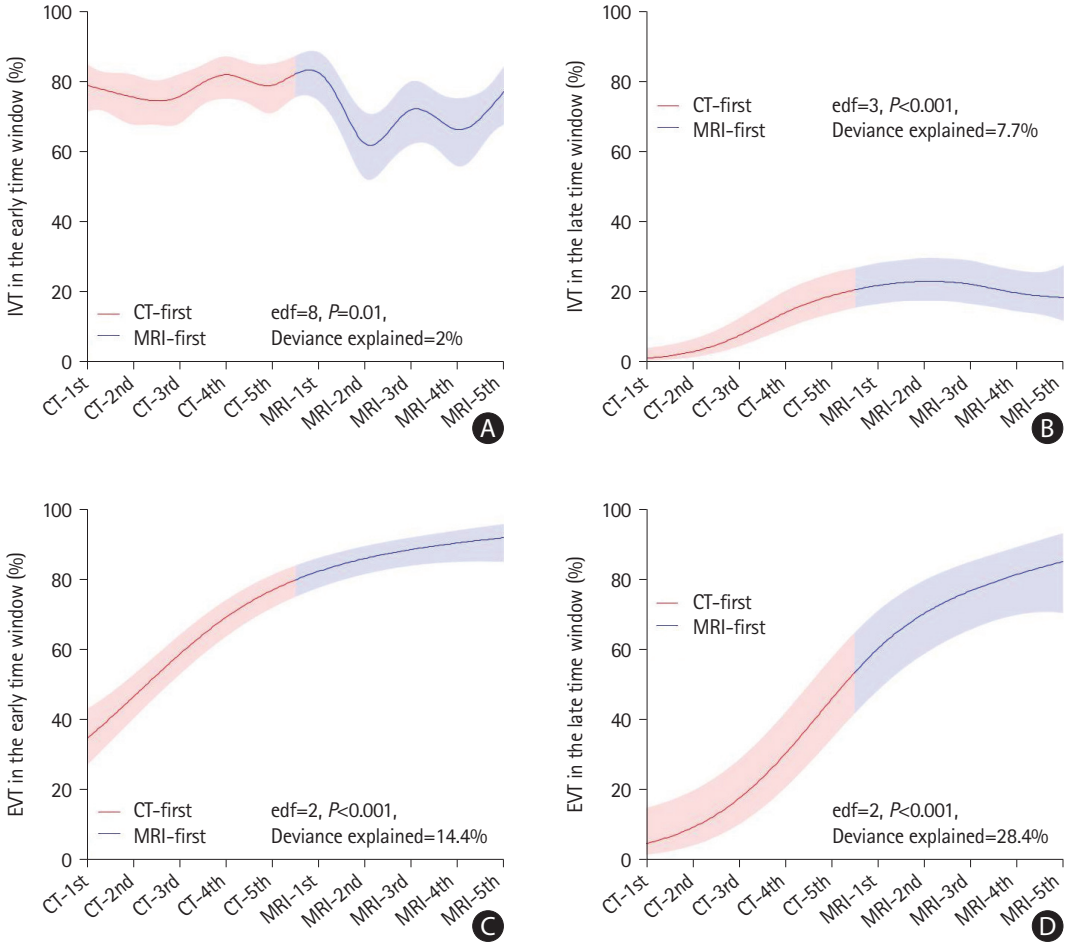

Figure 1. Time trend analyses of (A) IVT in the early time window; (B) IVT in the late time window; (C) EVT in the early time window; and (D) EVT in the late time window. Red lines and shaded areas represent the estimate and 95% CI for the CT-paradigm, while blue lines and shaded areas represent the estimate and 95% CI for the MRI-paradigm. The time variable was obtained by dividing the study period into ten consecutive groups, each containing an equal number of patients (approximately 300). CT 1st, 2nd, etc. = first, second, etc. groups in the CT-paradigm; MRI 1st, 2nd, etc. = first, second, etc. groups in the MRI-paradigm. CT, computed tomography; MRI, magnetic resonance imaging; IVT, intravenous thrombolysis; EVT, endovascular treatment; CI, confidence interval; edf, estimated degrees of freedom.

late EVT among potential candidates progressively increased throughout the study period, reaching a plateau in later years (Figure 1C and D). This trend remained unaffected by the imaging paradigm shift, as shown by both visual assessment of the time trend curves and multivariable regression analyses (Table 1). Among patients with isolated posterior circulation strokes, the rate of any IVT and/or EVT within 24 hours remained stable, with no significant difference between the CT and MRI paradigms (52.9% in CT-paradigm vs. 61.7% in MRI-paradigm, OR_{adj} 1.97, 95% CI 0.66–5.88, P_{adj}=0.23) (Table 1 and Figure 2A).

The rate of potentially missed IVT opportunities (defined as the proportion of acute strokes not treated by IVT despite having the criteria, over the total number of IVT performed in the same period) was higher during the CT-paradigm (3.1%) compared to the MRI-paradigm (0.8%), a difference that remained significant after multivariable adjustment for confounders (OR_{adj} 0.22, 95% CI 0.09–0.57, P_{adj}<0.01) (Table 1 and Figure 2B).

Time metrics and acute workflow

The median DTN time for IVT-treated patients increased from 31 minutes (IQR=24–48) during the CT-paradigm to 43 minutes (IQR=33–58) during the MRI-paradigm, a difference that remained significant after multivariable adjustment (β coefficient 15.63 (95% CI 11.27–20.0, P_{adj}<0.01) (Table 1 and Figure 2C). The median DTP time for EVT-treated patients decreased in the initial study years and then remained stable (Figure 2D), with no significant difference between the CT (101 min, IQR= 90–121) and MRI paradigms (104 min, IQR=85–129) after multivariable adjustment (β coefficient 9.95, 95% CI -2.24–22.14, P_{adj}=0.11) (Table 1).

The rate of successful recanalization (eTICI ≥2b67) in EVT (±IVT) patients was similar within the two imaging paradigms (81.4% in CT vs. 88.3% in MRI, OR_{adj} 0.74, 95% CI 0.28–1.91, P_{adj}=0.53) (Table 1 and Supplementary Figure 2A).

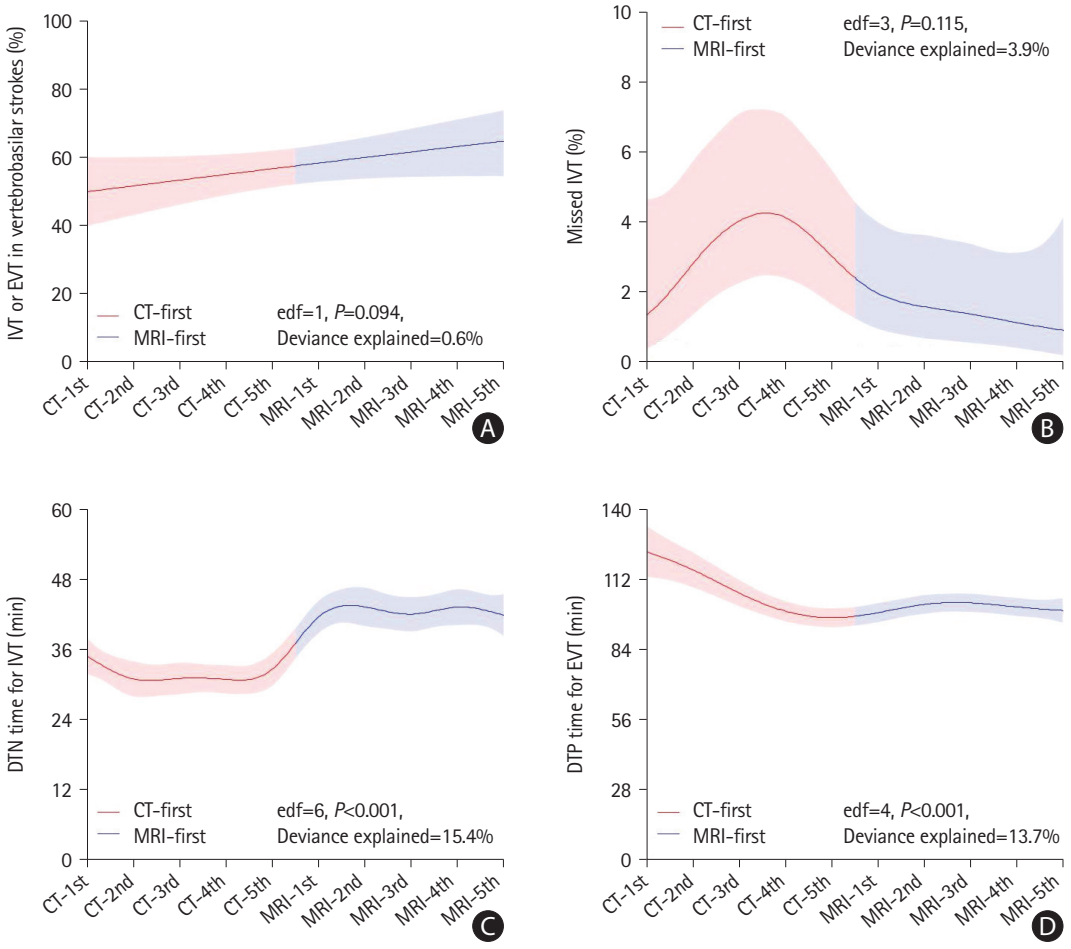

Figure 2. Time trend analyses of (A) IVT or EVT in vertebrobasilar strokes; (B) missed IVT opportunities; (C) DTN; and (D) DTP times. Red lines and shaded areas represent the estimate and 95% CI for the CT-paradigm, while blue lines and shaded areas represent the estimate and 95% CI for the MRI-paradigm. The time variable was obtained by dividing the study period into ten consecutive groups, each containing an equal number of patients (approximately 300). CT 1st, 2nd, etc. = first, second, etc. groups in the CT-paradigm; MRI 1st, 2nd, etc. = first, second, etc. groups in the MRI-paradigm. CT, computed tomography; MRI, magnetic resonance imaging; IVT, intravenous thrombolysis; EVT, endovascular treatment; DTN, door-to-needle; DTP, door-to-inguinal puncture; CI, confidence interval; edf, estimated degrees of freedom.

Safety of both IVT and EVT

The rate of SICH after IVT was characterized by slight linear reduction over time (Figure 3A), resulting in a lower rate in the MRI-paradigm (5.6% vs. 3.2%); however, this difference was not significant in the multivariable analysis (OR_{adj} 1.00, 95% CI 0.29–3.40, P_{adj}=0.99). The rate of SICH after EVT (±IVT) was similar across both paradigms (6.5% vs. 4.2%, OR_{adj} 0.62, 95% CI 0.14–2.68, P_{adj}=0.52) (Table 1 and Figure 3B).

Mortality rate at 7 days among IVT-only patients was comparable between paradigms (5.6% vs. 6.1%, OR_{adj} 0.51, 95% CI 0.16–1.56, P_{adj}=0.23) (Table 1 and Supplementary Figure 2B). Mortality at 7 days after EVT showed a significant constant linear increase over the course of the study (Supplementary Figure 2C), resulting in a higher rate in the MRI paradigm (5.0% vs. 8.3%). However, this difference appeared to reflect the underlying temporal trend rather than an effect of the imaging paradigm change, which was not significant in the multivariable analysis (OR_{adj} 0.96, 95% CI 0.24–3.78, P_{adj}=0.95) (Table 1).

Clinical outcomes

Disability in IVT patients decreased over time (Figure 3C), though no clear association with imaging paradigm was found in multivariable analysis (OR_{adj} for favourable mRS shift, MRI vs. CT= 1.26, 95% CI=0.77–2.06, P_{adj}=0.36) (Table 1). Among EVT-treated patients, disability remained stable over time and across imaging paradigm (OR_{adj}=1.22, 95% CI=0.66–2.26, P_{adj}=0.52) (Table 1 and Figure 3D).

The rate of futile recanalization (defined as 3-month mRS= 4–6 despite eTICI ≥2b67) in EVT patients was similar between the two paradigms (22.8% vs. 29.2%, OR_{adj} 1.03; 95% CI 0.41–2.56, P=0.95), with similar findings when analyzing early and late time windows separately (Table 1 and Supplementary Figure 2D).

https://doi.org/10.5853/jos.2025.02229

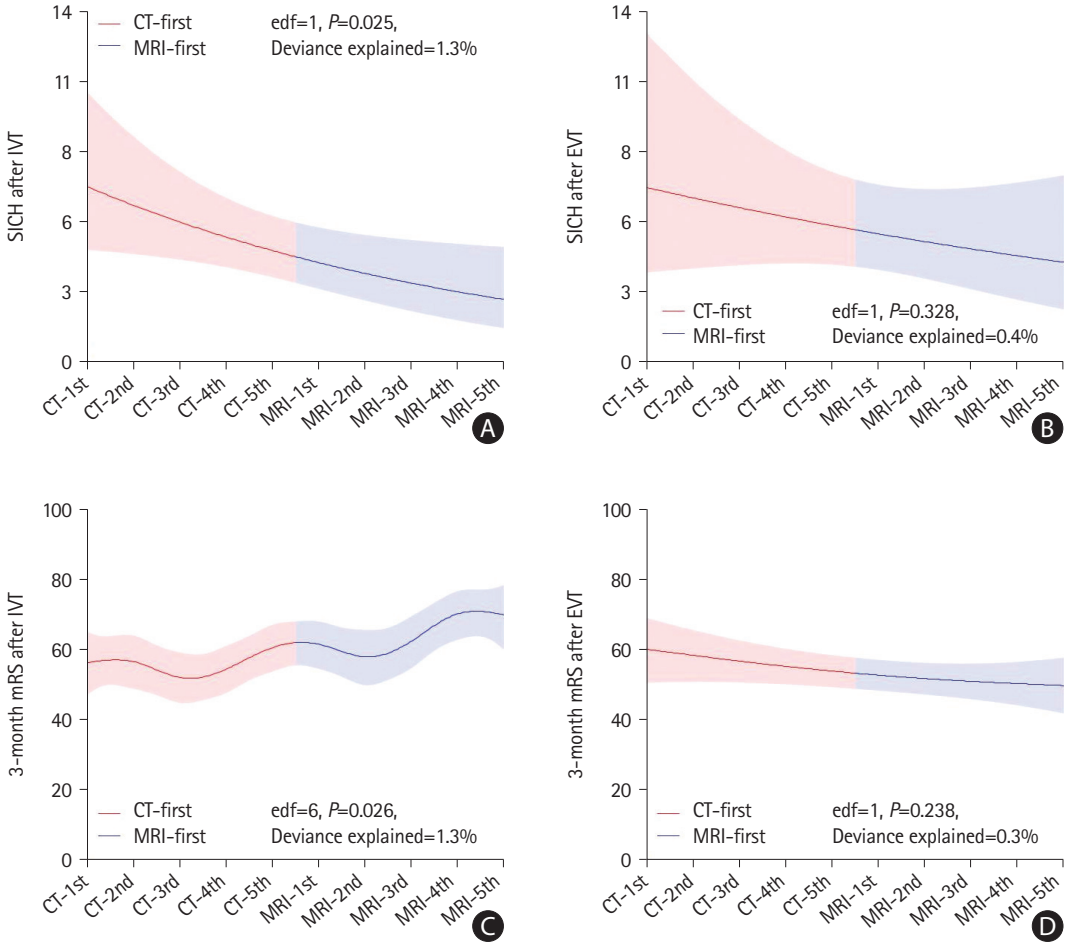

Figure 3. Time trend analyses of (A) SICH after IVT; (B) SICH after EVT; (C) 3-month mRS after IVT; and (D) 3-month mRS after EVT. Red lines and shaded areas represent the estimate and 95% CI for the CT-paradigm, while blue lines and shaded areas represent the estimate and 95% CI for the MRI-paradigm. The time variable was obtained by dividing the study period into ten consecutive groups, each containing an equal number of patients (approximately 300). CT 1st, 2nd, etc. = first, second, etc. groups in the CT-paradigm; MRI 1st, 2nd, etc. = first, second, etc. groups in the MRI-paradigm. CT, computed tomography; MRI, magnetic resonance imaging; SICH, symptomatic intracranial hemorrhage; IVT, intravenous thrombolysis; EVT, endovascular treatment; mRS, modified Rankin Scale; CI, confidence interval; edf, estimated degrees of freedom.

Non-feasibility of MRI during the MRI-paradigm

Among patients in the MRI-paradigm, those who underwent CT due to MRI non-feasibility were older, had more vascular risk factors, more severe strokes (higher NIHSS), more frequent vigilance alterations at baseline, and arrived earlier at the hospital (onset-to-door time: median 173 min, IQR 73–605 vs. 219 min, IQR 83–640; $P<0.001$) (Supplementary Table 2). The proportion of IVT administration was similar between groups, while EVT was more frequently performed in patients who did not undergo MRI—likely reflecting their more severe clinical profile. Despite similar median values, these patients exhibited a distribution shifted toward shorter treatment delays. Specifically, DTN for IVT was 43 minutes (IQR 29.7–60.7) vs. 43 minutes (IQR 34.0–57.3) in patients who underwent MRI ($P<0.001$), and DTP for EVT was 96 minutes (IQR 80.0–116.2) vs. 102 minutes (IQR 91.0–122.1), respectively ($P<0.001$).

Effect of COVID-19 pandemic

The study period included two COVID-19 waves, both occurring during the MRI period and significantly impacting hospital care and workflow. The first wave lasted from February 25 to April 20, 2020, and the second from October 7 to November 30, 2020. During these periods, we observed a significant decline in weekly admissions for AIS, from 6.5 to 5.2 patients per week (t=2.295, $P=0.03$). The 94 patients admitted during the two COVID-19 waves, beside younger age distribution, had baseline characteristics comparable to those admitted outside these periods, and rates of IVT and EVT administration remained unchanged (Supplementary Table 3). Patients admitted during the COVID-19 waves presented later to the hospital (median onset-to-door time: 338 [118.8–793.1] min vs. 210 [82–642.5] min), but in-hospital workflow metrics were unaffected, except for a slightly shorter DTN time for IVT during the COVID period (median 41 [31.7–51.7] min vs. 43 [33–59.3] min, $P<0.001$).

Discussion

In this single-center, observational study comparing MRI-first and CT-first imaging paradigms for AIS across several acute revascularization outcomes, the MRI-paradigm was associated with lower rates of potentially missed-IVT opportunities, while treatment rates, safety (SICH, 7-day mortality), and clinical outcomes (3-month mRS) for both IVT and EVT were not different between the two paradigms. While the MRI-paradigm was associated with a 12-minute increase in DTN time, DTP time remained stable. Similarly, the MRI-paradigm did not influence other EVT-specific outcomes, such as successful or futile recanalization.

The lack of significant differences in early and late IVT and EVT rates between the paradigms suggests that both approaches effectively identify indications and contraindications for these treatments. Notably, we observed an increase in late IVT and EVT rates even before the MRI-paradigm was implemented, likely reflecting evolving guidelines and new evidence. Importantly, this increase did not lead to higher rates of futile recanalization by EVT, suggesting appropriate treatment decisions independent of the imaging modality. The trend toward higher rates of IVT and/or EVT within 24 hours for posterior circulation strokes during the MRI-paradigm, though not statistically significant, aligns with MRI's increased sensitivity for detecting smaller posterior circulation lesions.[28] Two factors may explain why this trend did not reach significance: (1) our center frequently used perfusion imaging during the CT-paradigm, which improves detection of posterior circulation strokes compared to non-contrast CT,[29-31] and (2) our high revascularization rates for posterior circulation strokes even before MRI implementation (52% within 24 h in the CT-paradigm).

The reduction in the proportion of IVT-eligible, but untreated AIS cases (potentially missed-IVT opportunities) can likely be attributed to the superior sensitivity of MRI in detecting AIS, which proves particularly useful in cases with diagnostic uncertainty based on clinical history and neurological examination.[5] At our stroke center, IVT is recommended only for disabling strokes, defined as NIHSS ≥4 or NIHSS <4 with a deficit considered disabling by the treating physician, regardless of imaging evidence of ischemia. Therefore, patients with non-disabling symptoms are not considered for IVT even if small ischemic lesions are detected on MRI, whereas patients with disabling symptoms may receive IVT even in the absence of visible ischemia. Accordingly, our calculation of missed IVT opportunities was based only on patients meeting the institutional criteria for IVT and therefore did not include minor, non-disabling strokes. Given this clinical decision-making process, the reduction of missed-IVT opportunities observed with MRI likely does not reflect overtreatment of minor, non-disabling strokes based on DWI findings alone, but rather improved diagnostic certainty in patients with disabling deficits who otherwise met clinical criteria for treatment.

Regarding in-hospital time metrics, while MRI has a longer scan duration than CT—resulting in increased DTN times in our study—IVT was still efficiently administered within international benchmark times (DTN <60 min), as also demonstrated in previous studies.[9,11] Notably, DTP time was not increased, consistent with findings from two randomized controlled trials and data from the Swiss Stroke Registry.[6,8,11]

Safety outcomes were comparable between paradigms. While we observed a numerical reduction in SICH after IVT in the MRI-paradigm, this difference was not statistically significant. Earlier studies suggested that MRI-based IVT might be safer,[7] particularly in late-window patients, though subsequent analyses found no safety differences despite longer DTN times with MR.[11,32]

As expected, the initial imaging modality did not affect the rate of successful recanalization with EVT, given that this outcome depends on procedural factors rather than the initial imaging modality. The rate of futile recanalization was also similar between paradigms. While previous studies have reported higher rates of futile recanalization with CT-based EVT in the early time window,[11,33] potentially due to higher SICH rates in CT-selected patients despite shorter DTP, we observed no significant differences in our cohort. The DTP time remained consistent across paradigms, and SICH rates after EVT were similar, further supporting the equivalence of imaging approaches in terms of futile procedures. For late EVT, prior studies found no association between the imaging modality and futile recanalization rates, consistent with our findings.[11]

Functional outcomes at 3 months (mRS) were not significantly associated with the initial imaging modality in either the IVT or EVT cohorts after adjusting for confounders. Previous studies have reported mixed results, with some associating MRI-based IVT with better outcomes or reduced mortality,[7,11,32] while others found no differences.[11,12,15] Large randomized trials directly comparing initial imaging modalities are needed to address potential biases in patient selection for revascularization.

In addition to clinical outcomes, imaging strategies also carry economic implications. Regarding patient billing, all patients included in this study were hospitalized. As per the Swiss healthcare system, imaging costs are covered within a Diagnosis-Related Group (DRG) reimbursement package, which is determined primarily by the final diagnosis category and is not influenced by the specific imaging modalities performed. Therefore, there was no direct financial impact on patient billing. Regarding institutional costs, performing a CT scan with a stroke protocol is estimated to cost CHF 708.01 (approximately USD 790), while

https://doi.org/10.5853/jos.2025.02229

an MRI is estimated at CHF 1105.21 (approximately USD 1,235). A detailed cost-effectiveness analysis comparing CT and MRI would provide important insights into the economic implications of different imaging strategies and remains a relevant question for future investigations.

This study has limitations. It was a retrospective, single-center study focused primarily on elderly, predominantly Caucasian population, limiting generalizability to other demographics. Patients were treated at a specialized stroke center associated with a tertiary university hospital, potentially introducing referral bias. Furthermore, the study spanned 10 years, a period marked by advancements in stroke treatments and awareness, which may have influenced outcomes independently of the imaging modality. While we adjusted analyses for temporal trends to address this, multicenter studies with harmonized protocols would be valuable to better assess the impact of an MRI-first paradigm. Additionally, the analysis was restricted to confirmed AIS cases registered in the ASTRAL database, excluding patients with other diagnoses (e.g., intracranial hemorrhage, epilepsy) seen in the ED. This precluded any assessment of the impact of an MRI-first strategy on the broader population of patients evaluated for suspected stroke, in whom the choice of imaging modality might have an equal or even greater effect on diagnosis and management. A more comprehensive assessment of the impact of an MRI-first paradigm would ideally include all patients with suspected stroke, regardless of final diagnosis, and incorporate a cost-effectiveness analysis. However, such an analysis would require comprehensive data on hospital-wide resource utilization, which could not be evaluated for this study. While we acknowledge the relevance of this aspect, it was beyond the scope of the present work but may be addressed in future studies.

Despite its limitations, this study systematically evaluated the impact of an MRI-first approach on AIS workflow and outcomes, providing insights into real-world clinical practice. Rather than directly comparing CT and MRI efficacy, the study focused on imaging paradigms, reflecting the complexities of clinical decision-making.

Conclusions

In conclusion, in patients undergoing revascularization treatments, we observed comparable outcomes regardless of the initial imaging modality. The MRI-paradigm had the advantage of reducing potentially missed IVT opportunities but the drawback of slightly longer DTN times. Both imaging approaches are feasible, safe, and effective for AIS management without major advantages or disadvantages. Until further evidence from randomized clinical trials is available, the choice of imaging paradigm should be tailored to each center's specific needs, workflow, and resources.

Supplementary materials

Supplementary materials related to this article can be found online at https://doi.org/10.5853/jos.2025.02229.

Funding statement

Dr Rapillo acknowledges the European Academy of Neurology (EAN) for the 6-month research fellowship received.

Conflicts of interest

The authors have no financial conflicts of interest.

Author contribution

Conceptualization: CMR, PM, DS. Study design: CMR, PM, DS. Data collection: CMR, DS, PM, VDu, AS, VDa, BB, FP, SDH, GS. Statistical analysis: DS. Writing—original draft: CMR, DS. Writing—review & editing: CMR, DS, PM, VDu, AS, VDa, BB, SDH, GS. Funding acquisition: CMR, PM, DS. Approval of final manuscript: all authors.

Acknowledgments

Dr. Costanza Maria Rapillo acknowledges the European Academy of Neurology for the EAN Research Fellowship funding received in 2022 for her 6 months fellowship at CHUV, Lausanne.

Data are available upon reasonable request to the corresponding author, Dr. Davide Strambo.

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Supplementary Table 1. Patient characteristics of the overall cohort and the two groups of interest

	Overall population (n=2,972)	CT-paradigm (n=1,486)	MRI-paradigm (n=1,486)
Age (yr)	75.9 (64.9–84.1)	76.2 (65.7–84.0)	75.8 (63.5–84.1)
Female sex	1,361/2,972 (45.8)	684/1,486 (46.0)	677/1,486 (45.6)
Hypertension	2,291/2,972 (77.1)	1,154/1,486 (77.7)	1,137/1,486 (76.5)
Diabetes	598/2,972 (20.1)	301/1,486 (20.3)	297/1,486 (20.0)
Dyslipidemia	2,389/2,972 (80.4)	1,217/1,486 (81.9)	1,172/1,486 (78.9)
Smoking	1,346/2,957 (45.5)	646/1,471 (43.9)	700/1,486 (47.1)
Atrial fibrillation	917/2,971 (30.9)	493/1,485 (33.2)	424/1,486 (28.5)
Pre-stroke mRS			
0	1,317/2,970 (44.3)	676/1,486 (45.5)	641/1,484 (43.2)
1	712/2,970 (24.0)	349/1,486 (23.5)	363/1,484 (24.5)
2	499/2,970 (16.8)	241/1,486 (16.2)	258/1,484 (17.4)
≥3	442/2,970 (14.9)	220/1,486 (14.8)	222/1,484 (15.0)
Onset known	1,966/2,972 (66.2)	1,004/1,486 (67.6)	962/1,486 (64.7)
Onset-to-door delay (min)	191 (83–639)	175 (84–608)	217 (83–653)
Arterial territory			
Posterior circulation only	776/2,972 (26.1)	372/1,486 (25.0)	404/1,486 (27.2)
Anterior or multiple or undetermined	2,196/2,972 (73.9)	1,114/1,486 (75.0)	1,082/1,486 (72.8)
Baseline NIHSS	5 (2–12)	6 (3–13)	4 (2–10)
Baseline ASPECTS	9 (8–10)	10 (9–10)	9 (7–9)
Acute treatment			
No	1,592/2,972 (53.6)	827/1,486 (55.6)	765/1,486 (51.5)
IVT only	718/2,972 (24.2)	381/1,486 (25.6)	337/1,486 (22.7)
EVT only	249/2,972 (8.4)	66/1,486 (4.4)	183/1,486 (12.3)
IVT+EVT	413/2,972 (13.9)	212/1,486 (14.3)	201/1,486 (13.5)
Stroke mechanism			
Large artery atherosclerosis	432/2,972 (14.5)	205/1,486 (13.8)	227/1,486 (15.3)
Cardioembolic	871/2,972 (29.3)	466/1,486 (31.4)	405/1,486 (27.2)
Small vessels disease	295/2,972 (9.9)	143/1,486 (9.6)	152/1,486 (10.2)
Other rare, including dissections	215/2,972 (7.2)	103/1,486 (6.9)	112/1,486 (7.5)
Patent foramen ovale	64/2,972 (2.1)	35/1,486 (2.4)	29/1,486 (2.0)
Multiple causes	210/2,972 (7.1)	118/1,486 (7.9)	92/1,486 (6.2)
Undetermined	757/2,972 (25.5)	339/1,486 (22.8)	418/1,486 (28.1)
Undetermined after incomplete work-up	128/2,972 (4.3)	77/1,486 (5.2)	51/1,486 (3.4)
Other comorbidities			
Coronary disease	562/2,967 (18.9)	275/1,481 (18.6)	287/1,486 (19.3)
Cardiac failure	141/2,951 (4.8)	77/1,467 (5.2)	64/1,484 (4.3)
Active cancer	171/2,966 (5.8)	78/1,484 (5.3)	93/1,482 (6.3)
Pre-stroke treatment			
Antiplatelets	1,589/2,932 (54.2)	758/1,447 (52.4)	831/1,485 (56.0)
Anticoagulants	431/2,969 (14.5)	204/1,485 (13.7)	227/1,484 (15.3)
Leukoaraiosis	987/2,158 (45.7)	519/1,326 (39.1)	468/832 (56.2)
Baseline decreased vigilance	294/2,971 (9.9)	175/1,486 (11.8)	119/1,485 (8.0)
Baseline systolic BP (mm Hg)	151 (134–168)	152 (135–169)	150 (133–167)
Baseline diastolic BP (mm Hg)	82 (72–92)	82 (71–92)	82 (73–92)
Baseline blood glucose (mmol/L)	6.6 (5.7–8.0)	6.5 (5.7–8.0)	6.6 (5.8–8.0)

Supplementary Table 1. Continued

	Overall population (n=2,972)	CT-paradigm (n=1,486)	MRI-paradigm (n=1,486)
Imaging performed <24 h after stroke onset	2,894/2,972 (97.4)	1,438/1,486 (96.8)	1,456/1,486 (98.0)
CT as first imaging		1,421/1,486 (95.6)	264/1,486 (17.8)
MRI as first imaging		17/1,486 (1.1)	1,192/1,486 (80.2)

Continuous and ordinal variables were expressed as medians (interquartile range), and categorical variables as absolute counts (percentage), unless stated otherwise. Since proportions are calculated on the total number of patients with data available, some variables may display different denominators depending on the number of missing data.
CT, computed tomography; MRI, magnetic resonance imaging; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; ASPECTS, Alberta Stroke Program Early CT Score; IVT, intravenous thrombolysis; EVT, endovascular treatment; BP, blood pressure.

Supplementary Table 2. Patient characteristics, acute treatment, and time metrics of patients in the MRI paradigm actually undergoing MRI vs. patients having CT because MRI was not possible

Variables	First imaging modality performed		*P*
	CT (n=264)	MRI (n=1,192)	
Age (yr)	81.4 (69.8–88.4)	74.7 (62.2–83)	<0.001
Female sex	121/264 (45.8)	540/1,192 (45.3)	0.929
Pre-stroke mRS			
0	86/264 (32.6)	543/1,190 (45.6)	<0.001
1	65/264 (24.6)	293/1,190 (24.6)	>0.999
2	51/264 (19.3)	200/1,190 (16.8)	0.375
≥3	62/264 (23.5)	154/1,190 (12.9)	<0.001
Vascular risk factors			
Hypertension	217/264 (82.2)	897/1,192 (75.2)	0.020
Diabetes	55/264 (20.8)	237/1,192 (19.9)	0.792
Atrial fibrillation	119/264 (45.1)	298/1,192 (25.0)	<0.001
Chronic renal failure	56/264 (21.2)	143/1,189 (12.0)	<0.001
Clinical presentation			
Baseline NIHSS	8 (3–19)	4 (2–9)	<0.001
Baseline decreased vigilance	50/264 (18.9)	65/1,191 (5.5)	<0.001
Vertebrobasilar stroke (vs. anterior circulation)	62/264 (23.5)	328/1,192 (27.5)	0.207
Acute treatment and time metrics			
IVT	101/264 (38.3)	437/1,192 (36.7)	0.678
EVT	85/264 (32.2)	299/1,192 (25.1)	0.022
Missed IVT	1/143 (0.7)	5/581 (0.9)	>0.999
Onset known	164/264 (62.1)	778/1,192 (65.3)	0.370
Onset-to-door delay (min)	173 (73–605)	219 (83–640)	<0.001
Door-to-imaging delay (min)	28 (18–99)	27 (19–146)	>0.999
Door-to-IVT delay (min)	43 (30–61)	43 (34–57)	<0.001
Door-to-groin puncture delay (min)	96 (80–116)	102 (91–122)	<0.001

Continuous and ordinal variables were expressed as medians (interquartile range), and categorical variables as absolute counts (percentage), unless stated otherwise. Since proportions are calculated on the total number of patients with data available, some variables may display different denominators depending on the number of missing data.
CT, computed tomography; MRI, magnetic resonance imaging; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; IVT, intravenous thrombolysis; EVT, endovascular treatment.

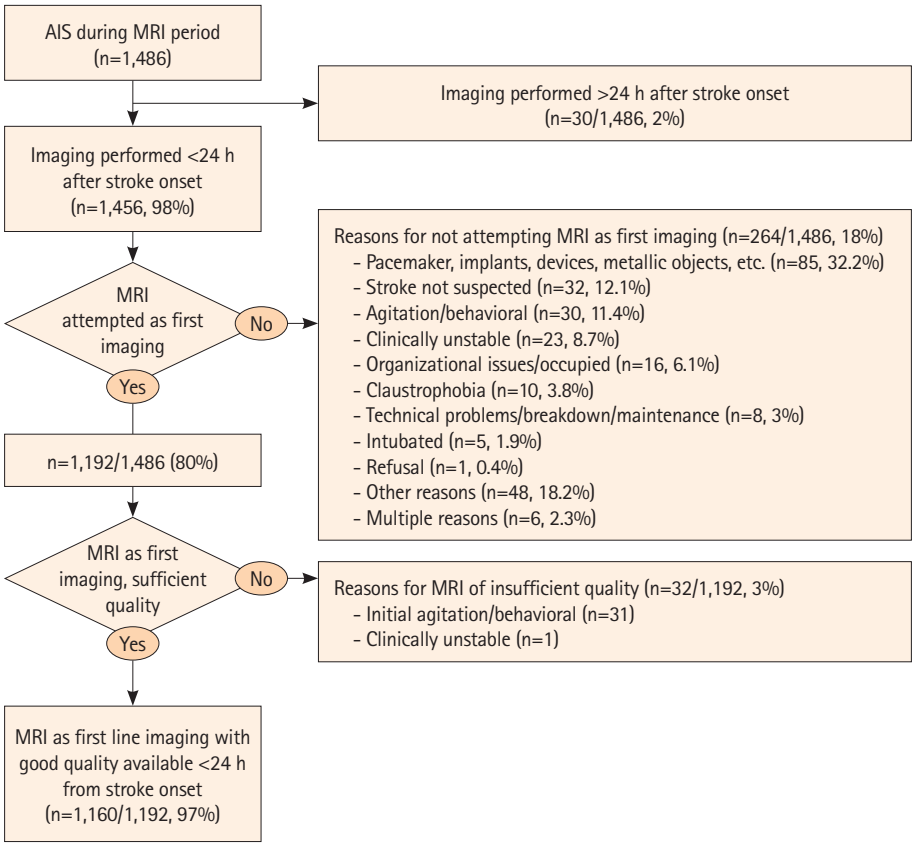
https://doi.org/10.5853/jos.2025.02229

Supplementary Table 3. Patient characteristics, acute treatment, and time metrics of patients within the MRI paradigm comparing patients during vs. outside the COVID-19 period

Variables	Arrival outside COVID-19 period (n=1,392)	Arrival during COVID-19 period (n=94)	*P*
Age (yr)	75.8 (63.7–84.1)	75.1 (59.9–83.1)	<0.001
Female sex	642/1,392 (46.1)	35/94 (37.2)	0.117
Pre-stroke mRS			
0	605/1,390 (43.5)	36/94 (38.3)	0.377
1	334/1,390 (24.0)	29/94 (30.9)	0.172
2	241/1,390 (17.3)	17/94 (18.1)	0.965
≥3	210/1,390 (15.1)	12/94 (12.8)	0.641
Vascular risk factors			
Hypertension	1,061/1,392 (76.2)	76/94 (80.8)	0.369
Diabetes	278/1,392 (20.0)	19/94 (20.2)	>0.999
Atrial fibrillation	398/1,392 (28.6)	26/94 (27.7)	0.940
Chronic renal failure	190/1,389 (13.7)	18/94 (19.1)	0.185
Clinical presentation			
Baseline NIHSS	4 (2–10)	5 (2–11)	>0.999
Baseline decreased vigilance	109/1,391 (7.8)	10/94 (10.6)	0.440
Vertebrobasilar stroke	375/1,392 (26.9)	29/94 (30.9)	0.481
First acute imaging modality			
None	27/1,392 (1.9)	3/94 (3.2)	0.648
CT	243/1,392 (17.5)	21/94 (22.3)	0.289
MRI	1,122/1,392 (80.6)	70/94 (74.5)	0.190
Acute treatment and time metrics			
IVT	506/1,392 (36.4)	32/94 (34.0)	0.734
EVT	362/1,392 (26.0)	22/94 (23.4)	0.663
Missed IVT	5/683 (0.7)	1/41 (2.4)	0.776
Onset known	905/1,392 (65.0)	57/94 (60.6)	0.454
Onset-to-door delay (min)	210 (82–642)	338 (110–793)	<0.001
Door-to-imaging delay (min)	27 (19–139)	27 (18–148)	>0.999
Door-to-IVT delay (min)	43 (33–59)	41 (32–52)	<0.001
Door-to-groin puncture delay (min)	101 (90–122)	108 (91–120)	>0.999

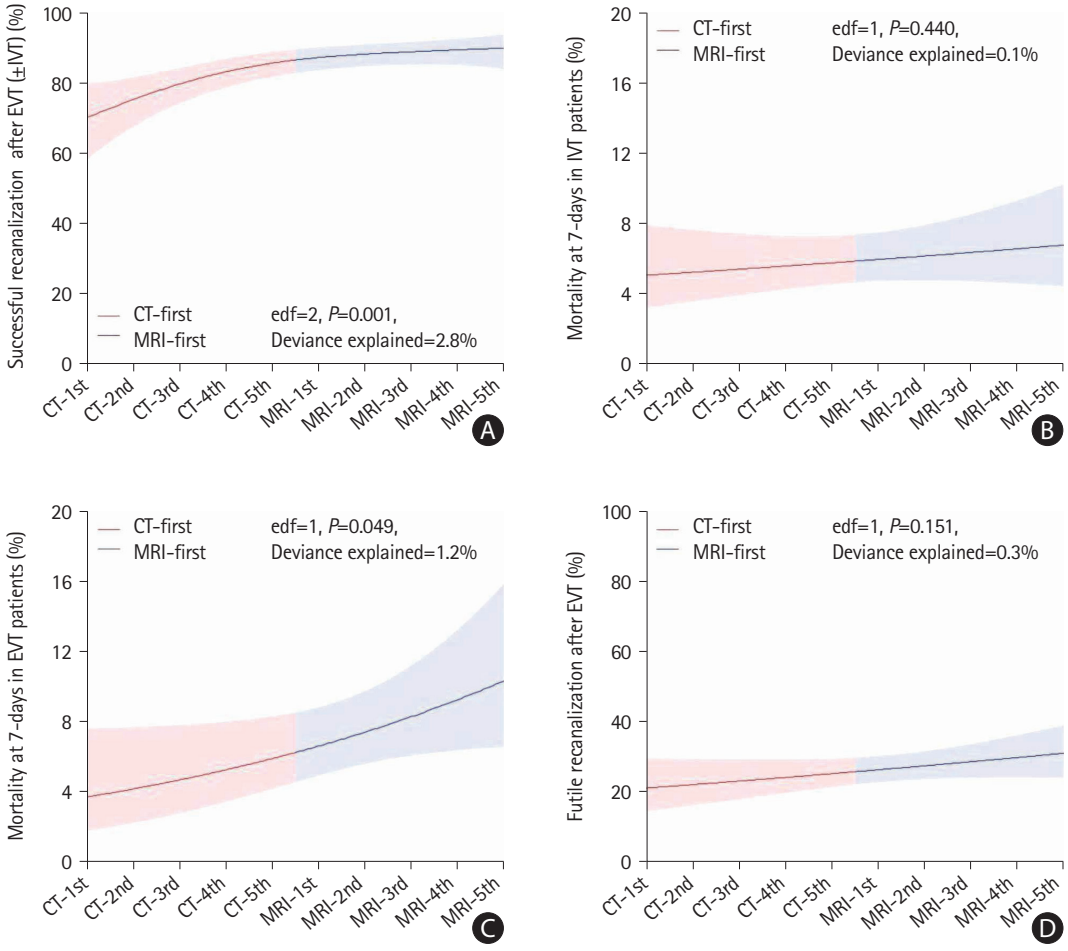
Continuous and ordinal variables were expressed as medians (interquartile range), and categorical variables as absolute counts (percentage), unless stated otherwise. Since proportions are calculated on the total number of patients with data available, some variables may display different denominators depending on the number of missing data.

mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; CT, computed tomography; MRI, magnetic resonance imaging; IVT, intravenous thrombolysis; EVT, endovascular treatment.



Supplementary Figure 1. Flowchart displaying the numbers and reasons for not performing MRI as first imaging modality during the MRI-paradigm. AIS, acute ischemic stroke; MRI, magnetic resonance imaging.

https://doi.org/10.5853/jos.2025.02229



Supplementary Figure 2. Time trend analyses. (A) Successful recanalization (eTICI ≥2b67) after EVT (±IVT); (B) mortality at 7 days in IVT patients; (C) mortality at 7 days in EVT patients; and (D) futile recanalization after EVT. Red lines and shaded areas represent the estimate and 95% CI for the CT-paradigm, while blue lines and shaded areas represent the estimate and 95% CI for the MRI-paradigm. The time variable was obtained by dividing the study period into ten consecutive groups, each containing an equal number of patients (approximately 300). CT 1st, 2nd, etc. = first, second, etc. groups in the CT-paradigm; MRI 1st, 2nd, etc. = first, second, etc. groups in the MRI-paradigm. CT, computed tomography; MRI, magnetic resonance imaging; IVT, intravenous thrombolysis; EVT, endovascular treatment; CI, confidence interval; edf, estimated degrees of freedom.