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SYSTEMATIC REVIEW/META-ANALYSIS

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ABSTRACT

BACKGROUND: Neuroimaging in the acute phases after the onset of the stroke symptoms is necessary to determine large vessel occlusion presence as well as the extent of the ischemic insult before deeming eligibility for endovascular thrombectomy (EVT).

PURPOSE: To evaluate the clinical outcomes in acute ischemic stroke patients selected for EVT based on initial imaging; non-contrast computed tomography (NCCT) compared to those selected using magnetic resonance imaging (MRI).

DATA SOURCES: PubMed, Embase, Scopus, and Web of Science were searched from inception to August, 2024.

STUDY SELECTION: We included observational studies comparing functional independence (mRS 0-2), successful reperfusion (TICI 2b-3), symptomatic intracerebral hemorrhage (sICH) or mortality in patients selected for EVT using NCCT±CT angiography versus MRI ±MR angiography. We excluded studies that used perfusion imaging in their patient selection for EVT.

DATA ANALYSIS: Data were pooled using random-effects model, and heterogeneity was assessed using I^2 statistics. A subgroup analysis was performed to determine the effect of treatment window (<6h vs >6h from last known well). The quality of eligible studies was assessed by using Newcastle Ottawa Scale.

DATA SYNTHESIS: Seven studies (n=3,940 patients) met the inclusion criteria. Two studies had low risk of bias and others had some concerns. Patients with MRI selection showed better chances of functional independence (Odds ratio (OR), 1.85 [95% CI, 1.28-2.67]; p<0.01, I^2=45%), lower rates of sICH (OR 0.59, 95% CI 0.39–0.89; p=0.01, I2=0%), reduced 90 days mortality (OR 0.63, 95% CI 0.51–0.78; p<0.01, I^2=0%) and no difference in successful reperfusion (OR 0.99, 95% CI 0.62–1.58; p=0.95, I^2=0%) compared to NCCT in patients treated within 6 hours of stroke onset. There were no significant differences in any endpoints between MRI and NCCT for patients treated beyond 6 hours.

LIMITATIONS: Our meta-analysis comprised only observational studies, with different populations and imaging protocols limiting the strength of the conclusions.

CONCLUSIONS: Within the crucial <6-hour window, MRI's superior patient selection justifies its use despite longer acquisition times. Beyond 6 hours, the focus should shift to rapid EVT access rather than imaging modality choice, as the benefits of MRI diminish.

ABBREVIATIONS: EVT = Endovascular Thrombectomy; IVT =Intravenous Thrombolysis; AIS-LVO = Acute Ischemic Stroke-Large Vessel Occlusion

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INTRODUCTION

The two main imaging modalities used to evaluate candidates for Endovascular Thrombectomy (EVT) are noncontrast computed tomography (NCCT) and diffusion-weighted magnetic resonance imaging (MRI-DWI), and each of those two modalities has advantages and disadvantages. NCCT-based imaging in the acute stroke setting holds the advantage of faster acquisition time as compared to MRI-based imaging[1], and time is known to affect the outcomes of both EVT[2] and intravenous thrombolysis (IVT)[3]. Furthermore, NCCT is more readily available than MRI especially in emergencies such as acute ischemic stroke (AIS) [4]. However, NCCT alone has limitations in providing a comprehensive evaluation of stroke patients, particularly in identifying large-vessel occlusions (LVOs), which are critical for determining eligibility for EVT. This limitation underscores the necessity of combining NCCT with CT angiography (CTA). CTA enables the rapid detection of LVOs by visualizing stenosis or occlusion in extracranial and intracranial arteries, offering essential information about vascular patency and collateral status[5, 6]. On the other hand, MRI provides more accurate estimations of the location, volume and age of ischemic lesions [7]. In the hyperacute and acute settings, MRI is more sensitive for detecting early tissue changes associated with the ischemic injury in Acute Ischemic Stroke due to LVO patients [8]. Magnetic Resonance Angiography (MRA) can detect LVOs with high accuracy, offering a non-invasive alternative for patients in whom CTA or contrast-based imaging is contraindicated. Additionally, MRA excels in assessing collateral circulation and vessel wall abnormalities, which are critical in predicting patient outcomes and tailoring EVT strategies[9]. Nonetheless, MRI requires a longer acquisition time as compared with NCCT, particularly when perfusion sequences are obtained[10]. MRI is vulnerable to motion artefacts [11] which can be challenging in AIS patients who are unable to cooperate due to their neurological deficits. Moreover, the exquisite sensitivity of MRI to ischemic changes may lead to overestimation of the core, thereby excluding certain patients from potentially life-saving reperfusion therapies particularly in late-window settings. Perfusion scans, either CT perfusion (CTP) or MR perfusion (MRP) can be added to evaluate for the presence of ischemic penumbra and assessing tissue viability. CTP can also be used to gauge the size of the ischemic core itself although it may sometimes overestimate core size[12]. In anterior circulation strokes, perfusion imaging becomes particularly insightful when ischemic volume is analyzed using AI tools. Furthermore, in patients with favorable collateral circulation, CTP extends the eligibility for treatment, allowing for intervention even in extended time windows. However, perfusion imaging modalities are less broadly available, limiting their widespread use despite their significant clinical utility[13].

A few studies have compared the outcomes of utilizing NCCT versus MRI in AIS-LVO patients before making the decision on EVT. These studies assessed the impact of either neuroimaging modality on the in-hospital workflow as well as the clinical outcomes after EVT. However, these investigations are limited by small sample sizes and inconsistent findings. For instance, while some studies observed a clear benefit for patients evaluated with MRI[14, 15], others found no substantial difference in outcomes between the two imaging modalities[16, 17]. This conflicting evidence underscores the need for a comprehensive meta-analysis to clarify the relative advantages of NCCT and MRI in this context. Therefore, we conducted this systematic review and meta-analysis to pool the results of studies comparing NCCT versus MRI for selection of patients with AIS from LVO for EVT.

MATERIALS AND METHODS

This systematic review and meta-analysis followed the guidelines provided by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). PRISMA checklists for abstract18 and main document are included in the supplementary materials. No protocol was registered for this review.

Search Strategy

A comprehensive search of the literature was conducted without any restriction on language, geographical location or time. We searched PubMed, Embase, Scopus, and web of science spanning records published from inception to August 16th, 2024. For our PubMed search, we utilized a variety of Medical Subject Headings (MeSH) terms, complemented by relevant titles and text words. The search syntax was tailored to other databases to meet their specific requirements. The search strategy targeted studies on endovascular thrombectomy for acute ischemic stroke, using keywords related to imaging modalities, including “computed tomography”, “magnetic resonance imaging”, and terms like "initial," "baseline," "selection," and "triage" for patient assessment. Search syntax for all databases is provided in the supplementary materials (eTable 1). Hand searching of bibliographic data of included articles was also performed.

Eligibility criteria and selection process

Studies were included if they met the following criteria: (1) Design: Retrospective or prospective cohort or case control studies (2) Population: Adult patients (≥18 years) with acute ischemic stroke in anterior or posterior circulation (3) Investigation: EVT (4) Comparison: Imaging-based patient selection using MRI±MRA versus NCCT±CTA scans. Studies incorporating DWI with fluid-attenuated inversion recovery (FLAIR) imaging (FLAIR-mismatch), as well as those utilizing Apparent Diffusion Coefficient (ADC) maps for selection, were also included. (5) Outcome: Efficacy: favorable functional recovery and successful of recanalization; Safety: Symptomatic intracranial hemorrhage (ICH) in first 48-72 h from EVT and mortality at 90 days follow up. The following studies were excluded: (1) Studies that used IVT without EVT, (2) Studies without mentioning their imaging modality used for patient selection for EVT (3) No direct comparison between MRI and NCCT or studies with groups using combination of NCCT and MRI that could not be extracted separately (4) Studies that used perfusion imaging including CTP, perfusion weighted imaging (PWI), or MRP as part of their patient selection for EVT (5) Case series, conference abstracts, letters, editorials, book chapters, non-human studies, and reviews.
Two authors independently reviewed the titles and abstracts using eligibility criteria. If there was any disagreement, a third author was brought in to reach consensus. The same two authors independently evaluated the full texts of all abstracts that fulfilled the inclusion criteria and performed hand searching. The included studies were reviewed to ensure institutional review board approval was obtained.

Data extraction

A standardized data collection form was designed, including the first author's name and year of publication, country and period of observation, imaging modality used for patient selection, baseline patient characteristics (age, sex, occlusion site, comorbidities, severity of stroke, infarct size and treatment window), and patient outcomes. Afterward, two authors independently conducted data extraction. Any discrepancies or differences

in data extraction were resolved through discussion and consensus.

Risk of Bias Assessment

Two independent reviewers assessed the quality of studies using Newcastle Ottawa Scale (NOS). Eight criteria were considered, each receiving 1 or 2 stars if the criterion was met and otherwise receiving no stars for a maximum possible score of 9. Studies scoring 8-9 were considered low risk, 6-7 indicated some concern, and scores 5 and lower were deemed high risk of bias.

Endpoints

Favorable functional recovery was defined as modified Rankin Scale (mRS) score 0-2 and a poor outcome was defined as mRS 3-6. Successful recanalization was defined as Thrombolysis In Cerebral Infarction (TICI) scale score ≥2b. Studies defined ICH based on follow-up NCCT or MRI imaging of patients and symptomatic ICH (sICH) was defined as the presence of any neurological deterioration in addition to signs of hemorrhage in imaging.

Statistical analysis

Meta-analyses were conducted using R software version 4.3.3 (R Project for Statistical Computing) meta package version 7.0-0. For binary outcomes, we calculated odds ratios (ORs) and their corresponding 95% confidence intervals (CI) using a random-effects model (Generalized linear mixed models). For continuous outcomes we calculated the mean difference (MD) between MRI-selected group and NCCT-selected group and their corresponding 95% CI. Heterogeneity was assessed using the Q statistic and I2 test, with I2 greater than 50% or $P < 0.05$ considered significant. In the case of significant heterogeneity, a sensitivity analysis was performed with the removal of outlier studies to bring the heterogeneity to an insignificant level. Outliers were detected using "dmetar" packages consistent with the method previously described in the literature[19]. If no outlier was found, we assessed the influence of studies using one-leave-out method[20]. Given that meta-regression requires at least 10 studies per examined covariate to avoid overfitting[21], we were unable to adjust for various confounders due to the limited number of included studies. To mitigate this limitation, we compared potential confounders between the NCCT and MRI groups to assess for any significant differences. In addition, a subgroup analysis is performed to determine the effect of treatment window (<6h from last known well (LKW) vs >6h from LKW) on the outcomes.

Data Availability

Data that support this study are available from the corresponding author on reasonable request.

RESULTS

Search and Screening Results

The initial search retrieved 2,323 records including 514 duplicates. After removing duplicates, the title and abstracts of 1,809 remaining records were screened, of which, 1,760 were excluded and 49 full texts underwent further checks. We excluded seven studies either because they incorporated perfusion imaging in their selection criteria[1, 22-26] or lacked data on advanced imaging[27]. Finally, seven studies were determined to satisfy the inclusion and exclusion criteria with the appropriate report of outcomes of interest[14-17, 28-30] (Figure 1).

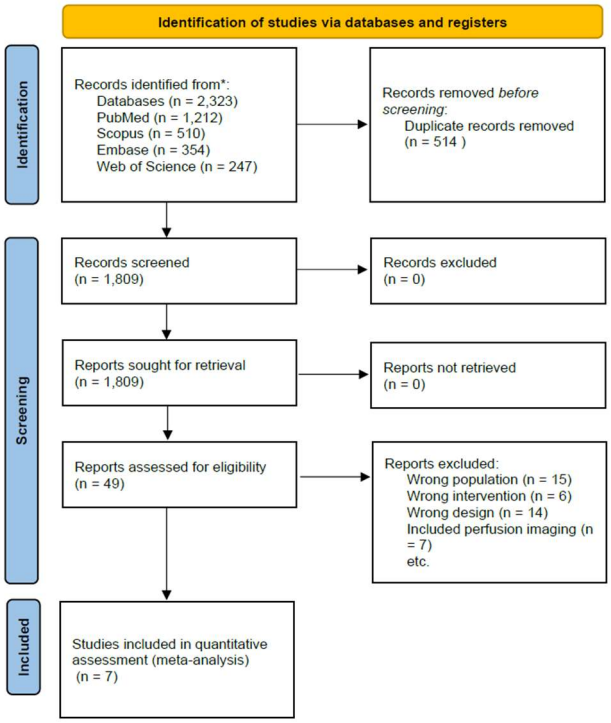

FIG 1. PRISMA 2020 flow diagram of data selection

Study characteristics and risk of bias

Of the seven included studies, only one study used a prospective design[14], and six studies were multicenter studies[15-17, 28-30]. Details of patient selection for EVT in each study are presented in eTable 2 and studies inclusion and exclusion criteria are detailed in eTable 3. In total studies included 3,940 patients with 52.6% male and mean age of patients was 71.5 years old. Patient characteristics, such as age, baseline NIHSS, baseline ASPECTS, use of intravenous thrombolytics (IVT), comorbidities, and workflow metrics are detailed in eTable 4. Two studies had low risk of bias[14, 28] and other studies had some concerns mainly in comparability domain and blinded reporting of outcomes. Details of quality scores is presented in eTable 5.

The details on baseline characteristics of MRI -selected and NCCT-selected patients are presented in supplemental materials. There was no difference in age, sex, rate of IVT use, atrial fibrillation, smoking, dyslipidemia and time flow metrics between groups. However, patients who were selected based on NCCT had higher baseline NIHSS (MD: 1.3 points 95%CI 0.4-2.3, P<0.01, I^2=71%), and higher ASPECTS (MD: 0.9 points, 95%CI 0.2-1.5; p=0.01, I^2=92%). In addition, patients with MRI selection protocol had significantly lower rates of hypertension (OR, 0.82; 95%CI, 0.69-0.98; p=0.3, I^2=1%).

Functional Independence (mRS 0-2)

Seven studies, with a total of 3,696 patients, compared functional independence rates between MRI-selected and NCCT-selected patients. The rate of mRS 0-2 was comparable among two groups (OR 1.39, 95% CI 0.98-1.96; p = 0.06), with significant heterogeneity among studies (I^2 = 72%, p < 0.01) (Figure 2). On sensitivity analysis excluding the outlier study (Vajpeyee, 2023), the heterogeneity of the remaining studies remained significant (I^2 = 63%; P = 0.02). The results of the sensitivity analysis confirmed the main analysis (OR, 1.22 [95% CI, 0.93-1.60]; p=0.15) (eFigure 14). Further subgroup analysis showed that MRI-selected patients had significantly more favorable functional recovery in a treatment window <6h (OR, 1.85 [95% CI, 1.28-2.67]; p<0.01, I^2=45%) while no difference was seen in patients beyond 6h treatment window (OR, 0.97 [95% CI, 0.74-1.26]; p=0.31, I^2=5%) (Figure 3).

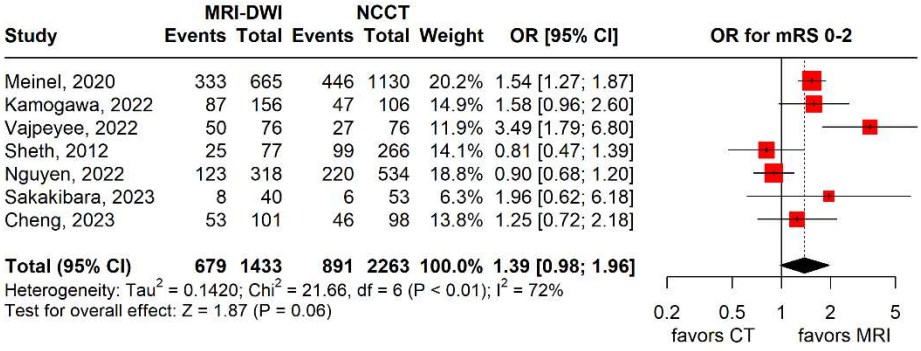

FIG 2. Forest plot of functional independence

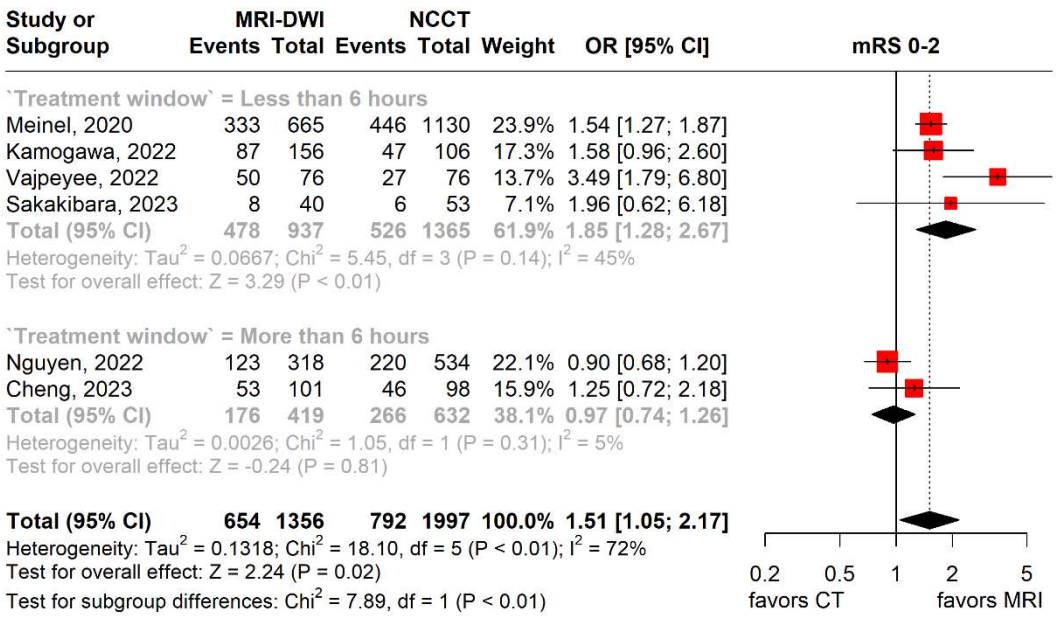

FIG 3. Subgroup analysis of functional independence based on treatment window

Successful reperfusion (TICI 2b-3)

Six studies, with a total of 1,929 patients, compared successful reperfusion rates between MRI-selected and NCCT-selected patients. There were comparable rates of TICI 2b-3 between the 2 groups (OR 0.81, 95% CI 0.53–1.23; p = 0.32), with moderate heterogeneity noted among these studies (I^2 = 58%, p = 0.04) (Figure 4). No outlier was detected, however the leave-one-out study showed Nguyen,2022 study as an influential study in explaining heterogeneity (eFigure 15). The results were again the same for MRI-selected and NCCT-selected patients after removing the influential study (OR 0.94, 95% CI 0.67–1.31; p = 0.7) with low heterogeneity among remaining studies (I^2=8%). The subgroup analysis showed no difference among subgroups based on treatment window (eFigure 16).

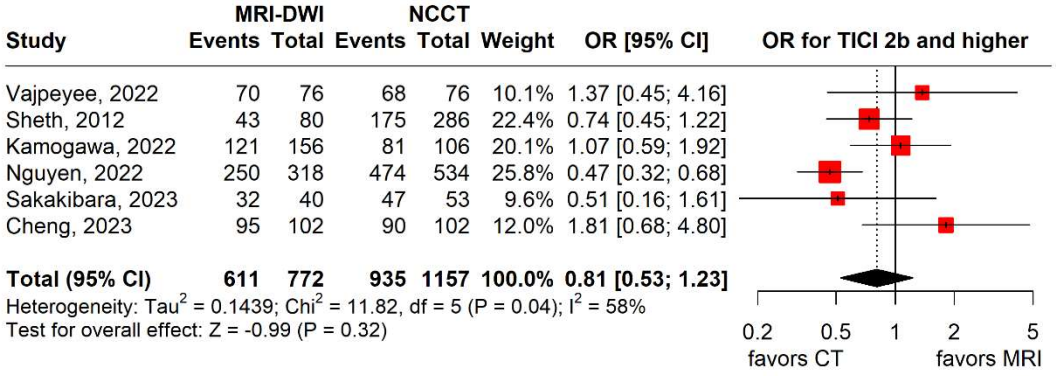

FIG 4. Forest plot of successful reperfusion (TICI 2b-3)

Symptomatic ICH

Five studies, with a total of 3,503 patients, compared sICH rates between MRI-selected and NCCT-selected patients. The rate of sICH was significantly lower among MRI-selected group (OR 0.60, 95% CI 0.44–0.82; p < 0.01), with no heterogeneity among studies (I^2 = 0%, p = 0.99) (Figure 5). The subgroup analysis based on treatment window showed lower sICH rate in MRI-selected group in <6h treatment window (OR 0.59, 95% CI 0.39–0.89; p=0.01, I^2=0%). However, the studies in >6h treatment window showed insignificant results (OR 0.6, 95% CI 0.35–1.03; p=0.06, I^2=0%) (eFigure 17).

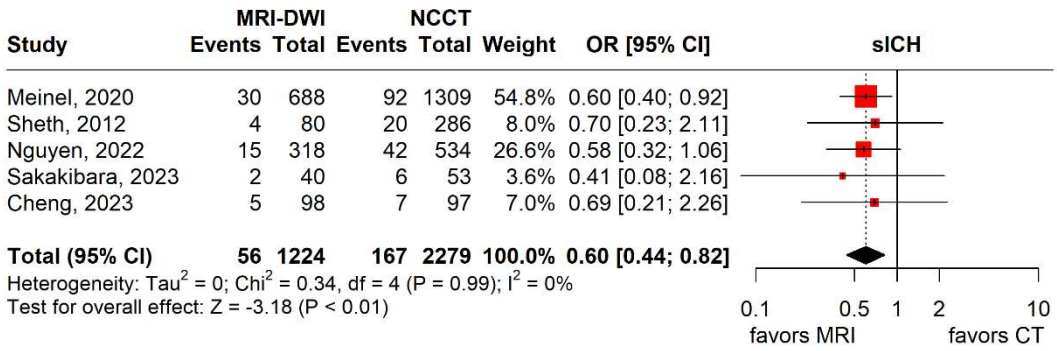

FIG 5. Forest plot of symptomatic intracranial hemorrhage

Mortality

Six studies, with a total of 3,544 patients, compared mortality rates between MRI-selected and NCCT-selected patients. The rate of mortality was significantly lower in the MRI-selected group as compared to the CT-selected group (OR 0.71, 95% CI 0.59–0.85; p < 0.01), with low heterogeneity among studies (I^2 = 18%, p = 0.29) (Figure 6). The subgroup analysis based on treatment window showed lower mortality rate in MRI-selected group in <6h treatment window (OR 0.63, 95% CI 0.51–0.78; p<0.01, I^2=0%). However, the studies in >6h treatment window showed insignificant results (OR 0.76, 95% CI 0.55–1.05; p=0.09, I^2=0%) (eFigure 18**).**

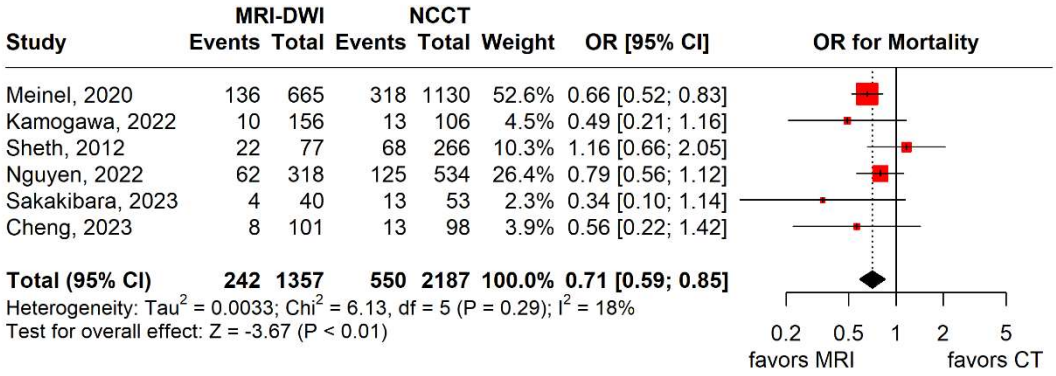

FIG 6. Forest plot of mortality

DISCUSSION

Our systematic review and meta-analysis included seven studies with a total of 3,940 patients. Overall, patients selected by MRI tended to have better functional outcomes and had lower rates of sICH and mortality as compared to patients selected with NCCT±CTA. We also found significant differences among patients based on initial imaging selection in subgroups of patients based on treatment window. Better functional recovery and lower rates of sICH and mortality were noted among patients selected by MRI in treatment window <6h. However, there was no differences between MRI and NCCT-selected patients across any of the endpoints beyond 6h.

Despite the proven feasibility and efficacy of EVT in AIS-LVO patients, futile recanalization (i.e. achieving successful recanalization without impacting clinical outcomes) remains a significant challenge. Thus, it is very important to study and understand treatment-, hospital-, and patient-related factors that might influence such outcomes. The imaging modality used to select patients for EVT may affect rates of functional recovery after recanalization by optimizing identification of patients with chances to recover. Studies comparing MRI- vs CT-based selection have limitations, but their pooled analysis may inform best practice[1, 17, 29, 31, 32].

Interestingly, while MRI has a longer acquisition time, our pooled analysis indicated that it did not result in extended workflow metrics such as onset to imaging, onset to puncture, and onset to reperfusion compared to NCCT. This could be due to streamlined workflows in centers that employ MRI, compensating for the longer imaging time with more efficient patient handling and processing.

We found better chances of functional independence, lower sICH and lower mortality among patients selected with MRI as compared with NCCT-based imaging in patients with AIS-LVO treated with EVT within the treatment window<6h. In fact, all studies that showed an advantage for MRI were conducted in the <6h window[14, 15, 29]. Meinel et al. found lower rate of futile recanalization among MRI-selected patients from BEYOND-SWIFT registry, despite the fact that MRI-selected patients had a 30 minute delay in workflow metrics[29]. In a sub-analysis of RESCUE-Japan LIMIT trial among patients with a large ischemic core (ASPECTS of 3–5), better functional recovery, lower mortality and higher improvement in the NIHSS score at 48 was observed for patients selected by DWI-MRI compared to NCCT[15]. The only prospective study found in our series used a fast MR protocol in which the sagittal T2, coronal FLAIR and axial T1 and axial T2 sequences were removed to reduce MRI acquisition time. The results showed a similar rate of successful recanalization. However, lower rates of hemorrhagic transformation and mortality was observed for MRI-selected group. These advantages of MRI over NCCT can be explained by more precise estimation of the ischemic core with MRI, which would allow for better candidates for EVT[14, 33, 34]. In contrast, the analysis of data from RESCUE (Recovery by Endovascular Salvage for Cerebral Ultra-acute Embolism)-Japan Registry 2 showed no difference in safety and efficacy outcomes for patients based on imaging modality[30].

Interestingly, for patients treated beyond the 6-hour window, our findings revealed no significant differences in any endpoints between MRI and NCCT imaging. Although at first glance this result appears counterintuitive, they can be reasonably explained. Patients who do not develop early changes on head CT over several hours are more likely to have better collaterals and, in these cases, precise identification of the ischemic core may be less critical for patient selection. The results indicate that, for patients presenting beyond six hours, NCCT and CTA may suffice in selecting candidates for EVT without necessitating advanced imaging modalities such as MRI. This conclusion is reinforced by evidence from the CT for Late Endovascular Reperfusion (CLEAR) trial, which reported no significant differences in clinical outcomes between patients selected with NCCT and those evaluated with CTP or MRI[17]. Furthermore, a propensity matched analysis from the Endovascular Treatment Key Technique and Emergency Workflow Improvement of Acute Ischemic Stroke (ANGEL-ACT) study indicated that patients presenting with anterior large vessel occlusion in the extended time window may derive meaningful benefit from EVT, even in the absence of MRI-based selection criteria[28]. These findings underscore the potential to broaden the indications for EVT in the extended time window through a streamlined, widely available NCCT-only based paradigm.

Strengths and Limitations

We conducted extensive baseline feature analyses to explore potential factors influencing the observed associations. Additionally, subgroup analyses were performed based on the treatment window to gain deeper insights. A notable strength of this study was the inclusion of workflow metrics, particularly those related to timing. It is important to note that this meta-analysis deliberately excluded studies utilizing CT perfusion as an adjunct to NCCT to maintain a focused evaluation of non-advanced imaging modalities. This approach minimizes variability introduced by differing imaging protocols, ensuring that the analysis specifically reflects the utility of NCCT±CTA in isolation for patient selection. Nonetheless, our study has several limitations. All the studies included in this meta-analysis were observational in nature, which inherently limits the robustness of the conclusions drawn from our analysis. The retrospective design of these studies subjects them to a risk of selection bias. For example, patients with more severe conditions or communication challenges are more likely to undergo CT instead of MRI, a factor that could not be controlled for in our analysis. Additionally, baseline characteristics of the MRI-selected group, such as lower NIHSS scores and lower prevalence of hypertension, and differences in imaging protocols might have contributed in high heterogeneity and might have affected observed differences among patients. Furthermore, the methods employed to detect LVO and the specific criteria used to guide decisions regarding EVT were not explicitly reported in all included studies. The results are specifically applicable to patients with anterior circulation stroke who underwent EVT and should not be generalized to other stroke populations or treatment modalities.

CONCLUSIONS

Although EVT was safer and tended to be more effective in patients selected by MRI, the differential outcomes based on the treatment window deserve attention and highlight the importance of timely intervention. More advanced imagings are typically used in practice to refine patient selection in the extended time window. Yet, our results suggest that beyond 6 hours the choice of imaging modality may actually become less impactful on overall outcomes. This suggests that in extended time windows, the focus should perhaps shift more towards ensuring rapid access to EVT rather than the choice of imaging modality. It is also important to interpret our findings with caution. Access to treatment and avoiding exclusion of patients with LVO who may benefit from EVT should be prioritized. In that sense, NCCT remains a valid option because of its rapid acquisition and widespread availability. While MRI may refine patient selection and reduce the chances of futile recanalization, it can overestimate the size of the ischemic core and lead to inappropriate exclusion from treatment of patients who can benefit from reperfusion. Future research should further investigate the merits of these two imaging modalities, balancing precision with accessibility and the competing interests of

reducing rates of futile recanalization while maximizing identification of good candidates for EVT.

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None

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SUPPLEMENTAL FILES

eTable 1. Search strategy

Scopus: 510
ALL (thrombectomy OR endovascular) AND (((TITLE (computed AND tomograph*) OR TITLE (ct) OR TITLE (cta) OR TITLE (ctp)) AND (TITLE (diffusion AND weight*) OR TITLE (dwi) OR TITLE (magnetic AND resonance) OR TITLE (mri) OR TITLE (mra))) OR ((TITLE (initial) OR TITLE (baseline) OR TITLE (selection) OR TITLE (triage)) AND TITLE (imaging)))
embase: 354
(thrombectomy OR endovascular) AND (('computed tomograph*':ti OR ct:ti OR cta:ti OR ctp:ti) AND ('diffusion weighted':ti OR dwi:ti OR 'magnetic resonance':ti OR 'mri':ti OR 'mra':ti) OR (('initial':ti OR 'baseline':ti OR 'triage':ti OR 'selection':ti) AND 'imaging':ti))
PubMed: 1212
(((thrombectomy) OR (endovascular)) AND ((((computed tomograph*[Title]) OR (ct[Title]) OR (cta[Title]) OR (ctp[Title])) AND ((diffusion weighted[Title]) OR (DWI[Title]) OR (magnetic resonance[Title]) OR (MRI[Title]) OR (mra[Title]))) OR (((initial[Title]) OR (baseline[Title]) OR (selection[Title]) OR (triage[Title])) AND (imaging[Title])))) OR ((("Thrombectomy"[Mesh] OR "Endovascular Procedures"[Mesh]) AND ("Tomography, X-Ray Computed"[Mesh] OR "Tomography, Spiral Computed"[Mesh]) AND ("Magnetic Resonance Imaging"[Mesh] OR "Diffusion Magnetic Resonance Imaging"[Mesh])))
Web of Science: 247
ALL=(thrombectomy OR endovascular) AND ((TI=(computed tomograph* OR CT OR CTA OR CTP) AND TI=(diffusion weighted OR dwi OR magnetic resonance OR mri OR MRA)) OR (TI=(initial OR baseline OR selection OR triage) AND TI=(imaging)))

eTable 2. Details of patient selection for each study.		
Study	How was LVO detected?	How was EVT decided?
Kamagowa, 2022	- MRA, CTA, or DSA on admission.	- Indication of EVT were determined by the physician in charge, based on initial imaging. - Although the reasons for not performing EVT were not available from the data set of this study, low ASPECTS could be a possible reason for exclusion.
Sheth, 2012	- Infarct volume was obtained on MRI or delayed CT through manually measuring each region of interest on each slice of the infarct. The measurements were then summated to obtain the final infarct volume accounting for slice thickness.	- Patients who underwent NCCT only were chosen for endovascular treatment based on standard criteria used for assessing NCCT for intravenous thrombolysis (eg, no evidence of hemorrhage, absence of hypodensity that occupies greater than one-third of the area of the middle cerebral artery territory). - Patients who underwent multimodality imaging were selected based on each institution's protocol for evaluating core and penumbral tissue regions.
Vajpeyee,2022	- MRA, CTA, or DSA on admission.	- The decision was based on a MRI brain-based protocol or CT-based protocol consecutively. - The MRI protocol included: diffusion-weighted imaging (DWI), EPI fluid attenuation inversion recovery imaging (FLAIR), EPI-gradient recalled echo (GRE), MRA brain & neck (TOF). - All the CT scan head and CT angiography were performed on the 128 slice dual source CT scanner of Somatom definition by Siemens.
Nguyen, 2022	- CTA or MRI - CT or DWI–adjudicated ASPECTS scores were used to measure core volumes. - Collateral score was not measured;	- In the CT group, triage was mainly based on CT-ASPECTS. - In the MRI group was based on core volume, Tmax, ADC, mismatch volume or NIHSS
Sakakibara, 2023	- CTA or MRA was simultaneously performed to determine the occlusion site when acute LVO was suspected on NCCT or DWI-MRI.	- CT-ASPECTS vs DWI-ASPECTS
Cheng, 2023	- (1) NCCT ± CTA. - (2) brain MRI (T1 + T2 + fluid-attenuated inversion recovery [FLAIR] + diffusion-weighted imaging [DWI] ± magnetic resonance angiography [MRA]).	- CT-ASPECTS - In the MRI group, the ischemic core volume was defined as lesions on DWI or an apparent diffusion coefficient [ADC] threshold of <620 × 10−3 mm/s
Meinel, 2020	- Indications for MRI as opposed to CT included both favorable prognostic features (low	- Choice of EVT after imaging was a tissue-based approach in all participating centers putting slightly

	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). - 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, …).	different emphasis on NIHSS, time elapsed, infarct core/ASPECTS, collaterals and overall prognosis. - A clear-cut intracranial hemorrhage excluded both IVT and EVT in all centers. - Cerebral microbleeds were no absolute contraindication for intravenous thrombolysis or endovascular treatment in the centers that used MRI as initial imaging modality

eTable 3. Studies' inclusion and exclusion criteria		
Study	Inclusion criteria	Exclusion criteria
Kamagowa, 2022	Patients with acute LVO who were aged ≥20 years and were hospitalized within 24 hours after last known well (LKW) were enrolled. (1) prestroke modified Rankin Scale (mRS) score of 0 to 1, (2) LKW-to-hospital-arrival time <6 hours, (3) occlusion of the internal carotid artery (ICA) or M1 segment of the middle cerebral artery.	Patients who had ASPECTS data both on NCCT and DWI.
Sheth, 2012	Patients who presented within 8 h of symptom onset with an anterior circulation large vessel occlusion involving the internal carotid artery or middle cerebral artery (MCA) were considered in the study.	-
Vajpeyee,2022	Patients aged 18–80 years with acute ischemic stroke and symptomatic anterior proximal large vessel occlusion on CTA/MRA/DSA with NIHSS of at least 2 points within 6 h of stroke onset with informed consent was included in the study.	Specific exclusion criterion for intended EVT is concurrent myocardial infarction or severe infection (endocarditis or sepsis), uncontrollable hypertension defined as systolic blood pressure > 185 mmHg or diastolic pressure > 110 mmHg, Life expectancy of less than 90 days before stroke onset, pregnant or lactating women, known severe allergy to radiographic contrast medium and improvement of NIHSS score > 4 in less than 1 h. CT or MRI evidence of significant mass effect with midline shift, CT or MRI showing more than 1/3 of MCA territory infarct, CT or MRI evidence of intracranial hemorrhage (ICH), Subarachnoid Hemorrhage (SAH), Aneurysm or Cerebral arteriovenous malformations (CAVMs).

Nguyen, 2022	Baseline National Institutes of Health Stroke Scale (NIHSS) scores of 6 or more, occlusion of the internal carotid artery or proximal middle cerebral artery (M1/M2 segments), prestroke modified Rankin Scale (mRS) scores of 0 to 2, and TLSW to treatment of 6 to 24 hours	Patients presenting with large-vessel occlusion stroke presenting in an early time window (0 to <6 hours fromTLSW), prestroke baseline mRS scores of 3 to 5, or large-vessel occlusion of the posterior circulation
Sakakibara, 2023	This trial exclusively enrolled patients with CT-ASPECTS of 3–5 or DWI-ASPECTS of 3–5. Additional eligibility criteria were: (1) acute ischemic stroke; (2) age≥18 years; (3) National Institutes of Health Stroke Scale (NIHSS) score of 6 or higher on admission; (4) modified Rankin Scale (mRS) score of 0–1 before onset;15 (5) occlusion site at the internal carotid artery (ICA) or M1 segment of the middle cerebral artery (M1) on computed tomography angiography (CTA) or magnetic resonance angiography (MRA); (6) randomization could be completed within 6 hours from the time the patient was last known to be well, or 6–24 hours from the time the patient was last known to be well if there were no ischemic changes on fluid attenuated inversion recovery imaging; and EVT could be initiated within 60 minutes from randomization	(1) a significant mass effect with a midline shift on NCCT or MRI, (2) evidence of acute intracranial hemorrhage (ICH) on NCCT or MRI, and (3) a high risk of hemorrhage or other conditions
Cheng, 2023	Acute large vessel occlusion involving the intracranial carotid artery (ICA), or either the M1 or M2 segments of the middle cerebral artery, premorbid modified Rankin Score (mRS) of 0 to 2, LKW to arterial puncture time of 6 to 24 h.	Patients with missing baseline mRS, NIHSS, core infarct volume in the MRI group and occlusion sites other than ICA, M1 or M2 segments of the middle cerebral artery were excluded
Meinel, 2020	Inclusion criteria of the registry were treatment with a Medtronic market-released thrombectomy device for an intracranial large vessel occlusion with attributable neurological symptoms. For this analysis, authors included all patients from the registry with available information on initial imaging modality.	Current participation in another clinical trial was the only exclusion criterion.

eTable 4. Summary of study and patient characteristics

Study	Meinel, 2020		Kamogawa, 2022		Sheth, 2012		Vajpeyee, 2022		Nguyen, 2022		Sakakibara, 2023		Cheng, 2023	
Design	Retrospective, multicenter		Retrospective, multicenter		Retrospective, multicenter		Prospective, single center		Retrospective, multicenter		Retrospective, multicenter		Retrospective, multicenter	
Country	Multinational		Japan		United States		India		Multinational		Japan		China	
Quality score	6		6		8		7		7		7		9	
Treatment window	<6h		<6h		<8h		<6h		>6h		<6h		>6h	
Group, n	CT (n=1321)	MRI (n=690)	CT (n=106)	MRI (n=156)	CT (n=286)	MRI (n=80)	CT (n=76)	MRI (n=76)	CT (n=534)	MRI (n=318)	CT (n=53)	MRI (n=40)	CT (n=102)	MRI (n=102)
Age, median (IQR) or mean ±SD	74 (62-82)	72 (60-80)	75 (67-83)	72 (64.5-79.5)	65±15	67±15	Mean (range) 51.4 (22-76)	Mean (range) 57.8 (23-80)	71 (58-81)	71.5 (61-80)	76.5±10.2	77.3±10.0	66 (54-73)	63 (55-70)
Gender, male (%)	50.9	49.1	67	67.9	51	47	65.7	68.4	47.1	46.9	52.8	57.5	67.6	68.6
NIHSS at baseline, median (IQR)	17 (12-21)	15 (9-19)	20 (16-24)	16 (13-21)	19 (15-22)	18 (15-20)	17 (4-30)	16 (4-30)	17 (13-21)	16 (12-21)	22 (17-26)	22 (18-26)	14 (12-19)	15 (11-18)
ASPECTS at baseline, median (IQR)	9 (7-10)	8 (5-9)	10 (7-10)	7 (6-8)	ASPECTS>7: 87/133 (65%)	ASPECTS>7: 19/27 (70)	-	-	8 (7-9)	8 (6-9)	4 (4-5)	3 (3-5)	8 (6-10)	8 (7-9)
Premorbid mRS 0-2, %	91.9	95.1	-	-	-	-	-	-	100	100	-	-	100	100
LKW to door, minute Median (IQR)	150 (75-245)	133 (73-274)	70 (40-150)	90 (50-180)	-	-	Mean:227 (range: 45-360)	Mean: 229 (range: 47-360)	-	-	197 (83-413)	166 (85-360)	-	-
LKW to picture Median (IQR)	-	-	-	-	202 (165-231)	239 (181-276)	-	-	9.4 (6.6-13.3) h	10.9 (8.0-14.3) h	198 (88-431)	175 (85-379)	-	-
LKW to groin puncture, minute Median (IQR)	228 (165 - 314)	240 (174 - 359)	-	-	Image to puncture: 61 (40-117)	Image to puncture: 124 (87-165)	Mean: 342 (range 120-600)	Mean: 350 (range 126-610)	10.4 (7.8-14.4) h	12.4 (9.4-15.4) h	260 (175-508)	219 (135-446)	540 (425-698)	485 (410-734)
LKW to recanalization, minute Median (IQR)	282 (215-375)	300 (225-409)	225 (150-285)	235 (160-310)	-	-	-	-	-	-	325 (229-536)	248 (164-466)	-	-
Time from admission to groin puncture Median (IQR)	76 (46-107)	100 (82-123)	55 (35-80)	55 (40-77.5)	-	-	-	-	-	-	-	-	-	-
HTN, %	66.4	65.3	57.6	53.2	72	60	44	43.4	72.1	64.5	71.7	75	-	-
DM, %	17.8	17.3	20.8	17.3	24	23	27.6	38.1	23.9	20.8	26.4	20	-	-
Afib, %	-	-	54.7	48.1	34	30	-	-	35.8	36.8	50.9	70	-	-
Smoking, %	28.3	29.6	-	-	-	-	30.2	34.2	-	-	15.1	25	-	-
Dyslipidemia, %	48.8	52.8	27.4	20.5	-	-	55.2	50	-	-	26.4	27.5	-	-
Location	88.2	92.5	100	100	100	100	100	100	100	100	100	100	100	100

anterior, %														
IVT, %	-	-	61.3	69.9	49	41	29	27.6	23.6	42.8	30.2	22.5	20.6	22.6
CT: Computed Tomography; MRI: Magnetic Resonance Imaging; NIHSS: National Institutes of Health Stroke Scale; ASPECTS: Alberta stroke programme early CT score; LKW: Last Known Well; HTN: Hypertension; DM: Diabetes Mellitus; Afib: Atrial fibrillation; IVT: Intravenous Thrombolysis;														

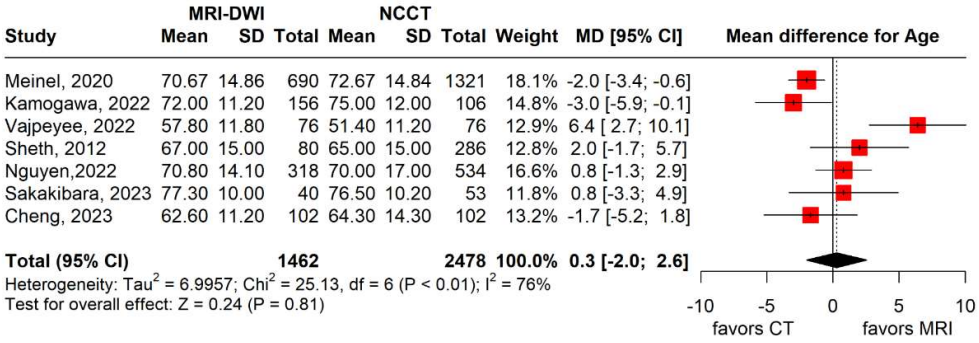
eTable 5. The Newcastle-Ottawa Scale for assessing the quality of the included studies

Study	Selection 1	Selection 2	Selection 3	Selection 4	Comparability	Outcome 1	Outcome 2	Outcome 3	Total Score
Meinel	*	*	*	*	-	-	*	*	6
Kamogawa	*	*	*	*	-	-	*	*	6
Vajpeyee	*	*	*	*	**	-	*	*	8
Sheth	*	*	*	*	*	-	*	*	7
Nguyen	*	*	*	*	*	-	*	*	7
Sakakibara	*	*	*	*	-	*	*	*	7
Cheng	*	*	*	*	**	*	*	*	9

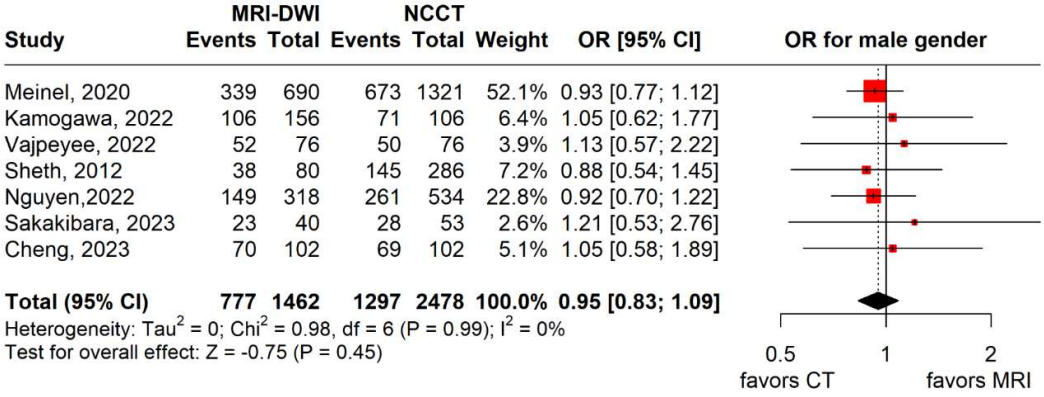
Selection 1: Representativeness of the exposed cohort
Selection 2: Selection of the non exposed cohort
Selection 3: Ascertainment of exposure
Selection 4: Demonstration that outcome of interest was not present at start of study
Comparability: Comparability of cohorts on the basis of the design or analysis
Outcome 1: Assessment of outcome
Outcome 2: Was follow-up long enough for outcomes to occur
Outcome 3: Adequacy of follow up of cohorts

Patients selected with MRI-DWI and NCCT had similar age (MD: 0.3 years, 95%CI -2.0–2.6, p=0.81); however, there was significant heterogeneity among included studies (I^2 = 76%; p<0.01) (eFigure 1). Proportion of male patients was not different among included studies (OR 0.95, 95% CI 0.83–1.09; p=0.45) with no heterogeneity among studies (I^2 = 0%; p=0.9) (eFigure 2). Rate of intravenous thrombolysis use was similar among groups (OR 1.2, 95% CI 0.8–1.8; p = 0.49); however, there was significant heterogeneity among included studies (I^2 = 79%; p<0.01) (eFigure 3). Baseline NIHSS was higher among NCCT-selected patients (MD: 1.3 points 95%CI 0.4-2.3, P<0.01) with high heterogeneity among studies (I^2=71%; p<0.01) (eFigure 4). Baseline ASPECTS was also higher among NCCT-selected patients (MD: 0.9 points, 95%CI 0.2–1.5; p=0.01) with high heterogeneity among studies (I^2=92%; p<0.01) (eFigure 5). Patients with MRI-DWI selection protocol had significantly lower rates of hypertension (OR, 0.82; 95%CI, 0.69-0.98; p=0.3), with no significant heterogeneity between studies (I^2 = 1%; p=0.41) (eFigure 6). There was no difference in other comorbidities between groups (data in eFigure 7-9). The time from LKW to admission was not different between groups (MD: 8.6 minutes, 95%CI -4.7–21.8; p=0.21) with no heterogeneity among studies (I^2=0%; p=0.37) (eFigure 10). Time from LKW to imaging was also comparable between groups (MD: 40.9 minutes, 95%CI -1.3–83.1; p=0.06) with moderate heterogeneity among studies (I^2=68%; p=0.06) (eFigure 11). The difference in time from LKW to groin puncture was also not significant between groups (MD: 23.7 minutes, 95%CI -29.3–76.5; p=0.38); however, the heterogeneity was high (I^2=79%; p<0.01) (eFigure 12). Finally, the time since LKW and reperfusion was comparable between included studies (MD: 9.0 minutes, 95%CI -0.7–18.6; p=0.07); with low heterogeneity among studies (I^2=30%; p=0.24) (eFigure 13)

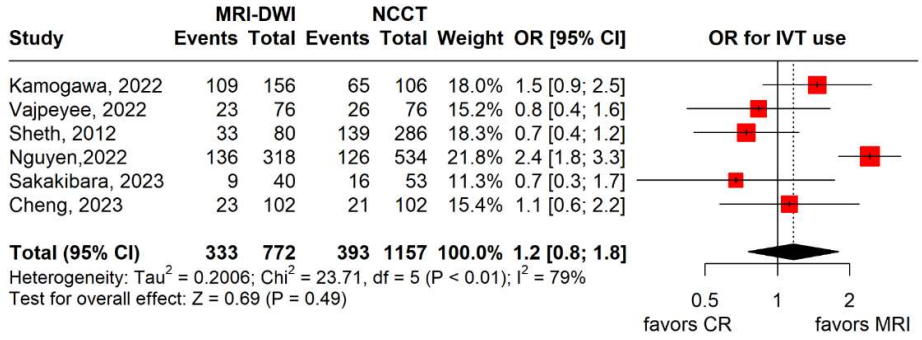
eFigure 1. Comparison of age among MRI-DWI and NCCT-selected cohorts



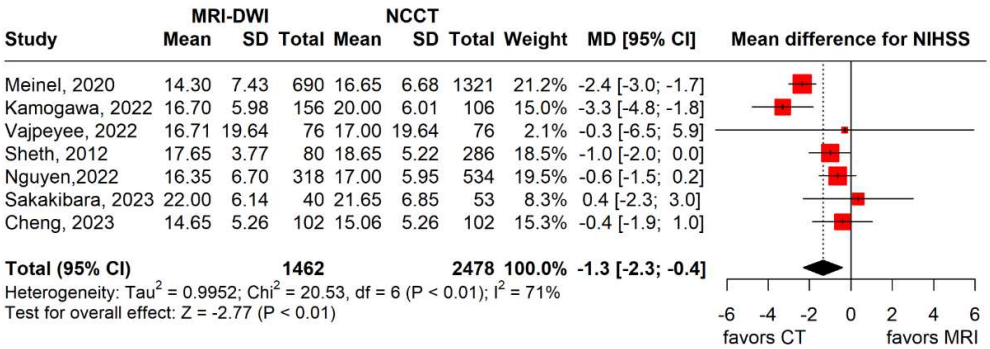
eFigure 2. Comparison of male gender among MRI-DWI and NCCT-selected cohorts



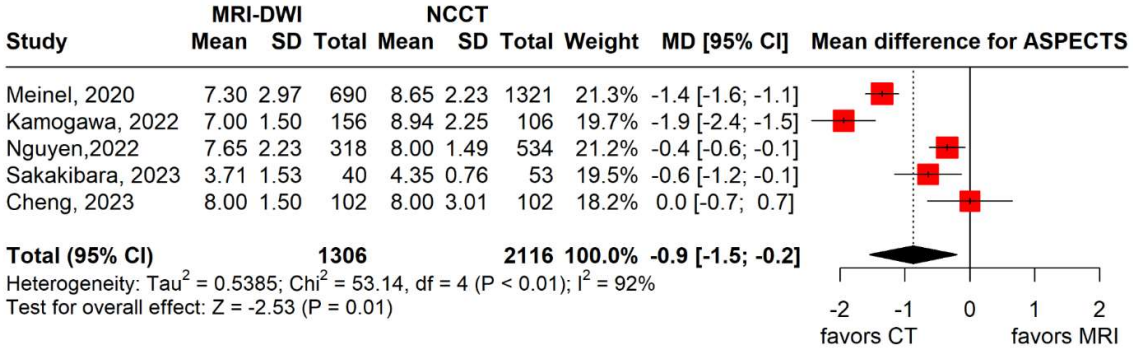
eFigure 3. Comparison of intravenous thrombolysis use among MRI-DWI and NCCT-selected cohorts



eFigure 4. Comparison of baseline NIHSS among MRI-DWI and NCCT-selected cohorts



eFigure 5. Comparison of baseline ASPECTS among MRI-DWI and NCCT-selected cohorts



eFigure 6. Comparison of hypertension among MRI-DWI and NCCT-selected cohorts

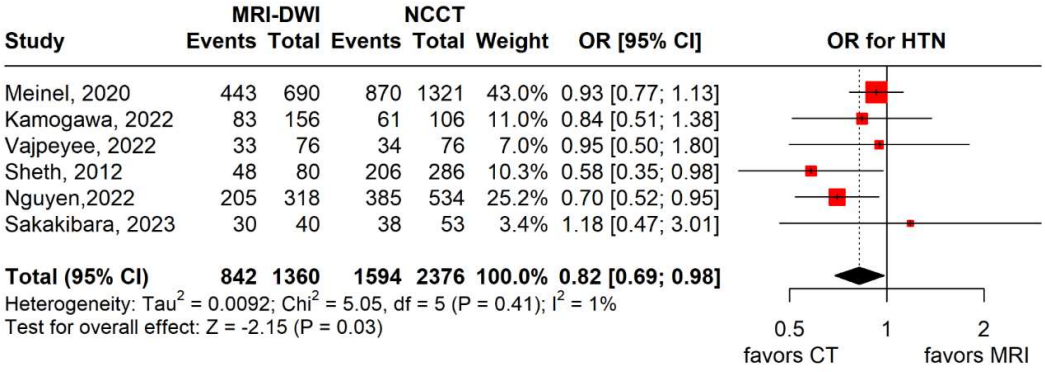
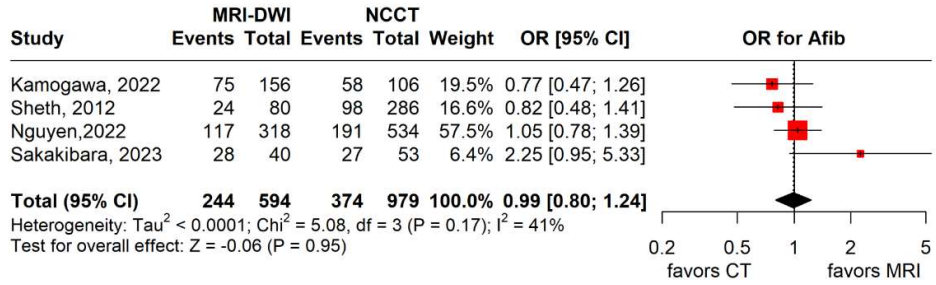
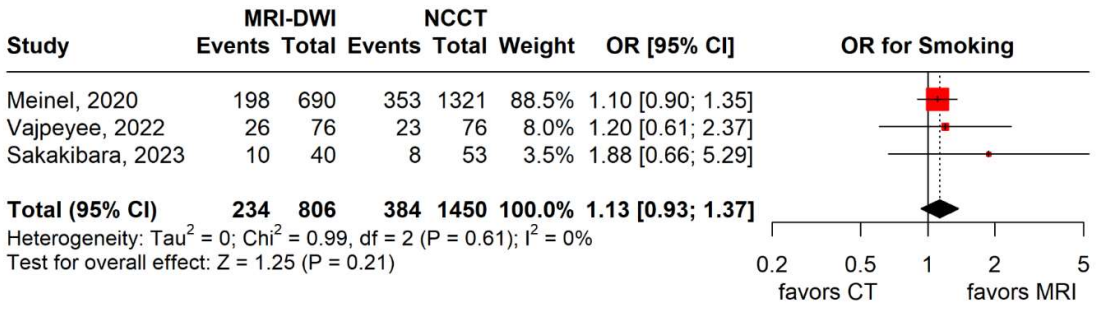


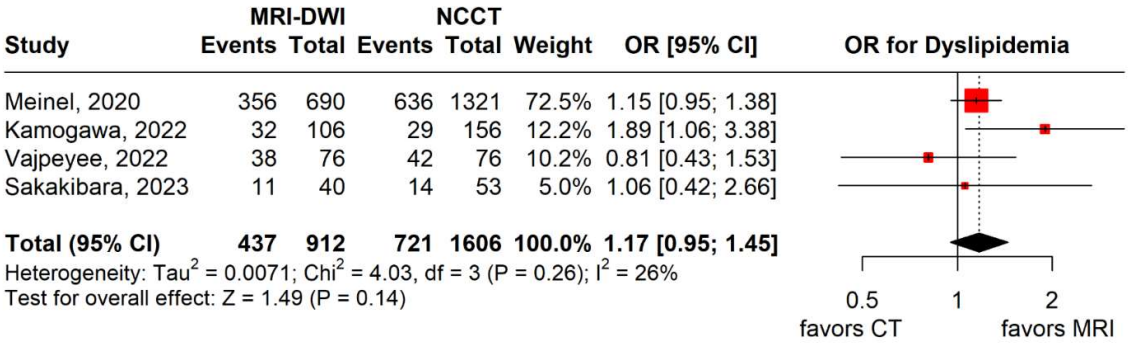
Figure 7. Comparison of atrial fibrillation among MRI-DWI and NCCT-selected cohorts



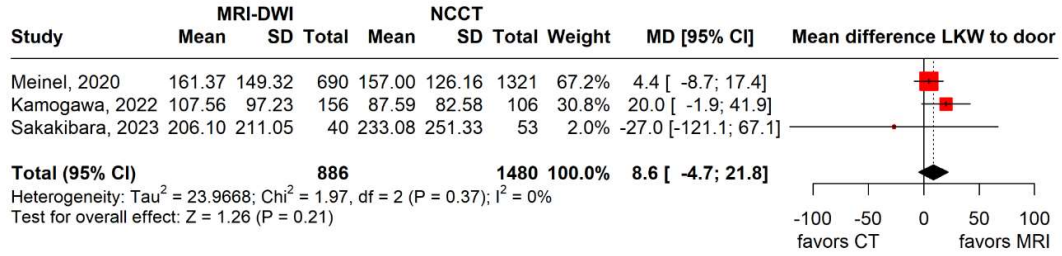
eFigure 8. Comparison of smoking history among MRI-DWI and NCCT-selected cohorts



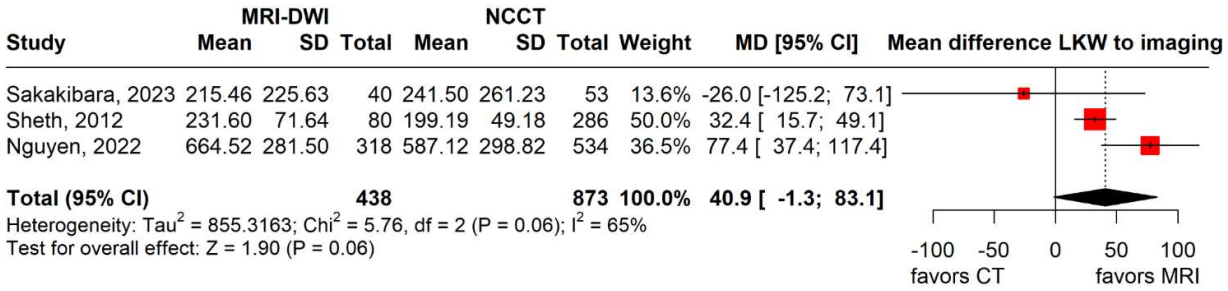
eFigure 9. Forest plot of dyslipidemia differences among studies.



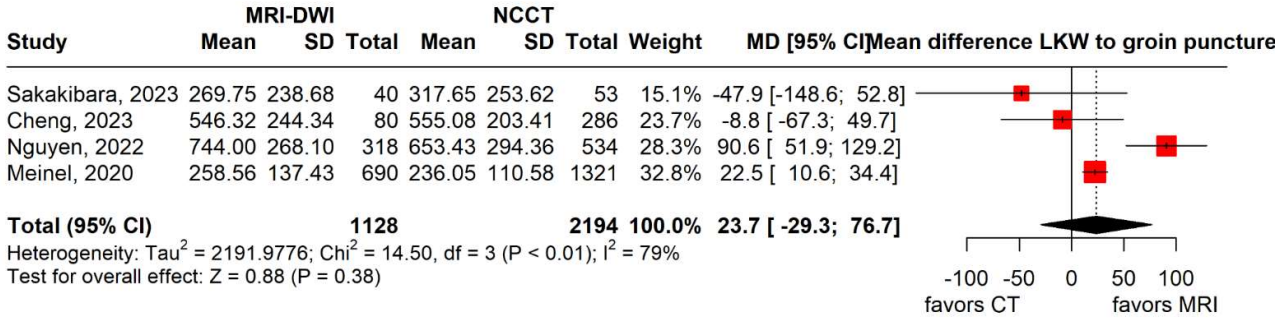
eFigure 10. Comparison of time from last known well to admission among MRI-DWI and NCCT-selected cohorts



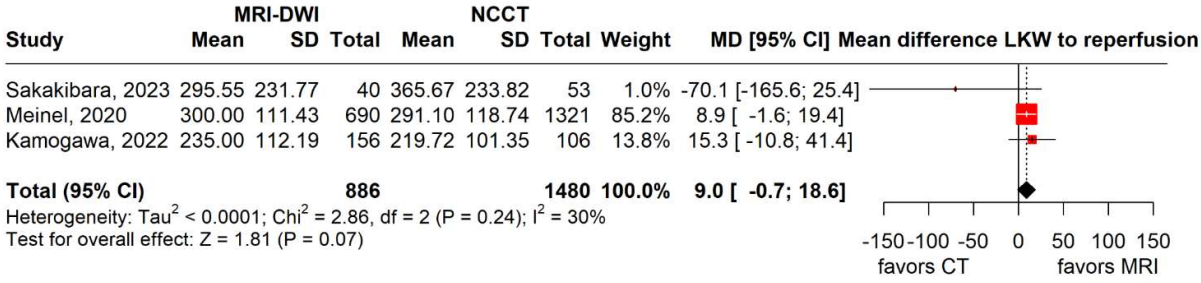
eFigure 11. Comparison of time from last known well to imaging among MRI-DWI and NCCT-selected cohorts



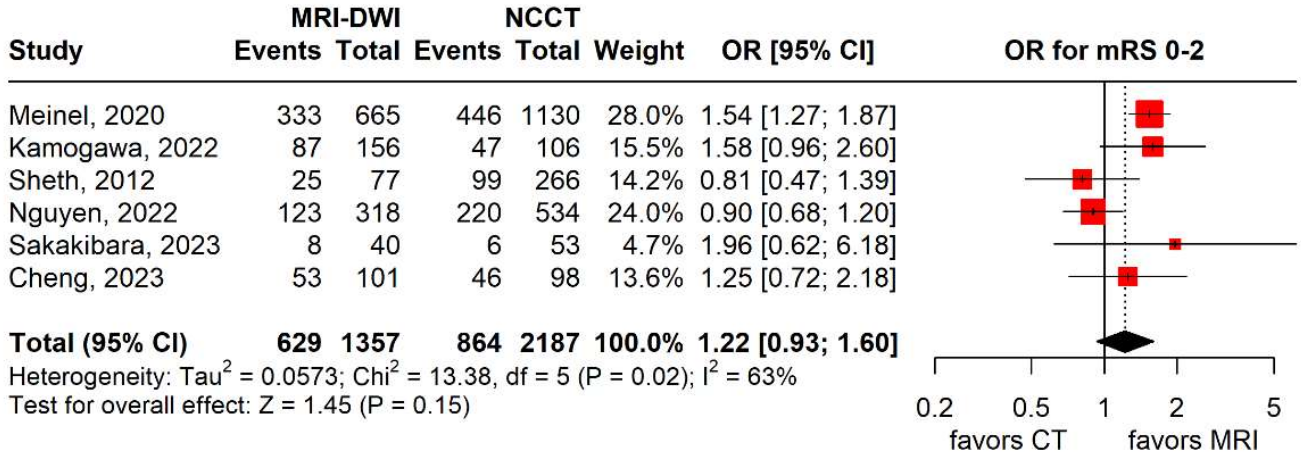
eFigure 12. Comparison of time from last known well to groin puncture among MRI-DWI and NCCT-selected cohorts



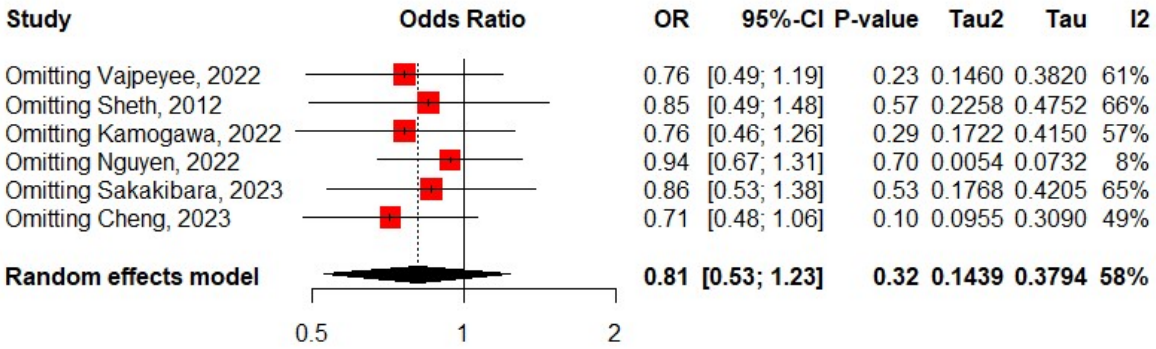
eFigure 13. Comparison of time from last known well to reperfusion among MRI-DWI and NCCT-selected cohorts



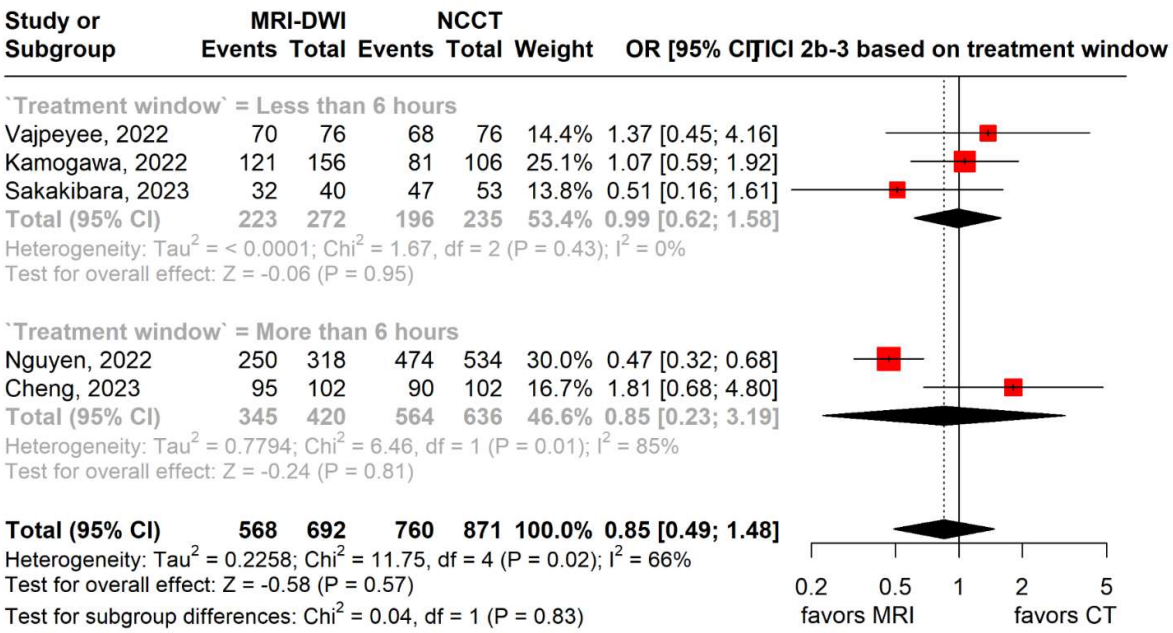
eFigure 14. Forest plot of sensitivity analysis for functional independence



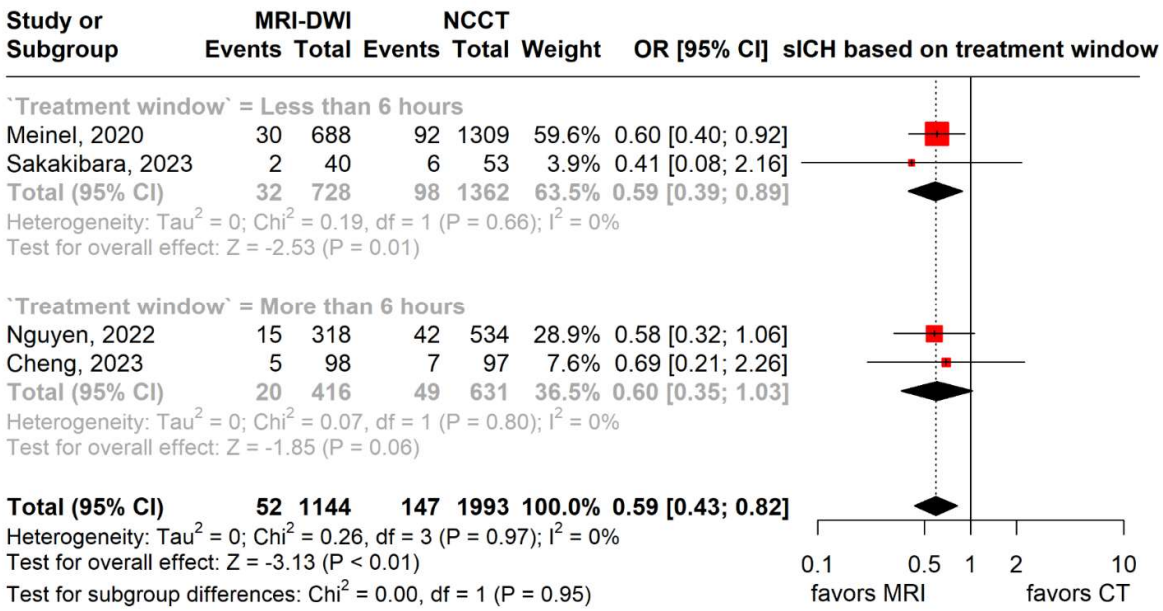
eFigure 15. Leave-one-out analysis shows influence of Nguyen, 2022 study on heterogeneity (I2)



eFigure 16. Subgroup analysis of successful reperfusion



eFigure 17. Subgroup analysis of symptomatic ICH



eFigure 18. Subgroup analysis of Mortality