ACUTE ISCHAEMIC STROKE PUBLICATION ALERT NEWSLETTER (08/2021)

Please be aware that the purpose of this Newsletter is to make you familiar with the most recent scientific publications, and you must keep in mind that all aspects may not be covered by the label. Please always refer to the current prescribing information as in force in your country.

Intravenous thrombolysis (IVT) is the backbone of treatment for acute ischaemic stroke (AIS) and the only systemic reperfusion therapy approved in this indication. Current guidelines recommend that all eligible patients receive alteplase before mechanical thrombectomy (MT). For this reason, research efforts continue to refine the population of patients who benefit from IVT. At present, the use of MT is generally restricted to comprehensive stroke centres, while IVT is much more widely available. The question of whether direct MT is non-inferior to bridging IVT is addressed in a meta-analysis of the four randomized controlled trials (RCTs) that have been published thus far, which is summarized at the start of this month's Newsletter. The meta-analysis showed that the likelihood of good clinical outcome was similar with both treatment strategies. Oral communication of the results of two further RCTs on this topic, SWIFT DIRECT and DIRECT SAFE, is planned at ESOC 2021 (in September) and WSC 2021 (in October), respectively. In addition, an RCT comparing tenecteplase vs placebo before MT (the RESILIENT DIRECT TNK trial) is starting in Brazil.

This issue of the Acute Ischaemic Stroke Publication Alert Newsletter also reports the results of an RCT that compared endovascular therapy (EVT) with medical therapy in patients with basilar artery occlusion. This is followed by discussion of a subgroup analysis from the THRACE trial that identified the clinical and imaging factors associated with excellent outcome in patients with AIS due to large vessel occlusion (LVO) who were treated with IVT. The issue concludes with a summary of an analysis from the MR CLEAN registry that evaluated the sensitivity of commonly used prehospital stroke scales in identifying LVO locations in patients with AIS.

The list of presented publications is as follows:

1. Podlasek A *et al.* Direct mechanical thrombectomy without intravenous thrombolysis versus bridging therapy for acute ischemic stroke: A meta-analysis of randomized controlled trials. *Int J Stroke* 2021.
2. Langezaal LCM *et al.* Endovascular therapy for stroke due to basilar-artery occlusion. *N Engl J Med* 2021.
3. Fisher M. Endovascular therapy for basilar-artery occlusion - still waiting for answers. *N Engl J Med* 2021.
4. Riou-Comte N *et al.* Clinical imaging factors of excellent outcome after thrombolysis in large-vessel stroke: a THRACE subgroup analysis. *Stroke Vasc Neurol* 2021.
5. Duvekot MHC *et al.* Sensitivity of prehospital stroke scales for different intracranial large vessel occlusion locations. *Eur Stroke J* 2021.

1. DO PATIENTS WITH ACUTE ISCHAEMIC STROKE AND LARGE VESSEL OCCLUSION WHO UNDERGO BRIDGING IV THROMBOLYSIS HAVE BETTER OUTCOMES THAN THOSE WHO UNDERGO DIRECT MECHANICAL THROMBECTOMY?

SUMMARY

- A meta-analysis of four RCTs that compared direct MT with bridging IVT followed by MT (MT + IVT) in patients with AIS and LVO
- There was no difference between direct MT and MT + IVT with regard to the likelihood of achieving good clinical outcome
- Compared with MT + IVT, direct MT was associated with a significantly lower risk of any ICH, but it was also associated with a significantly lower likelihood of successful reperfusion

MT is the standard of care in patients with AIS and LVO. However, the benefit of bridging IVT in this indication is uncertain. While IVT may facilitate MT and lyse distal thrombi, it may also result in a time penalty, lead to clot fragmentation and distal embolization, and increase the risk of symptomatic ICH. Furthermore, the efficacy of IVT in patients with LVO is limited (10% achieve successful reperfusion).

Previous meta-analyses that compared direct MT with MT + IVT have produced conflicting findings, and the optimal reperfusion strategy in patients with AIS and LVO remains unclear. Therefore, the authors sought to conduct a meta-analysis of RCTs that compared direct MT and MT + IVT in patients with AIS and LVO.[1]

Study details

- Electronic databases, as well as the International Stroke Conference (ISC) 2021, were searched up to January 2021 for RCTs that compared direct MT and MT + IVT in patients with AIS and LVO
- The primary outcome was good functional outcome (defined as mRS score ≤2) at 90 days
- The secondary clinical outcomes were excellent functional outcome (defined as mRS score ≤1), mortality, symptomatic ICH, and any ICH
- The secondary procedural outcomes were successful reperfusion (defined as modified Thrombolysis in Cerebral Infarction [TICI] score ≥2b) and procedure-related complications
- The meta-analysis was conducted using a random effects model and the Mantel–Haenszel method; non-inferiority for the primary outcome was assessed on the basis of risk difference and OR; publication bias for the primary outcome was assessed based on the funnel plot and Egger's test
- Four RCTs (N=1633; n=817 in the direct MT group and n=816 in the MT + IVT group) were included (DEVT, DIRECT-MT, MR-CLEAN NO-IV, SKIP)
- The mean age (SD) was 70.2 years (12.1) in the direct MT group and 69.5 years (11.8) in the MT + IVT group, 57.6% and 56.7% of patients were male in the direct MT and the MT+ IVT group, respectively
- The mean NIHSS score (SD) was 16.3 (7.0) in the direct MT group and 16.6 (6.7) in the MT + IVT group

Study results

- There were no significant differences between the direct MT and the MT + IVT groups with regard to good functional outcome, excellent functional outcome, mortality, symptomatic ICH, or procedure-related complications (**Table 1**)
- Any ICH occurred in 27.8% of patients in the direct MT group and in 36.3% of patients in the MT + IVT group
  - Direct MT was associated with significantly lower risk of any ICH than MT + IVT (p=0.003)
- Successful reperfusion was achieved in 76.5% of patients in the direct MT group and in 80.9% of patients in the MT + IVT group
  - Direct MT was associated with significantly lower likelihood of successful reperfusion than MT + IVT (p=0.03)

Table 1. Primary and secondary outcomes

Outcome	Direct MT		MT + IVT		OR (95% CI)	*p* value (overall effect)	I^2, %
	Events	Total	Events	Total			
Primary outcome							
Good functional outcome at 90 days	376	817	371	816	1.02 (0.84–1.25)	0.83	0
Secondary clinical outcomes							
Excellent functional outcome at 90 days	209	817	198	816	1.08 (0.86–1.36)	0.49	0
Mortality at 90 days	142	817	135	816	1.06 (0.82–1.37)	0.67	0
Symptomatic ICH	48	816	58	813	0.82 (0.55–1.21)	0.31	0
Any ICH	227	816	296	815	0.65 (0.49–0.86)	0.003	38
Secondary procedural outcomes							
Successful reperfusion	625	817	661	816	0.76 (0.60–0.97)	0.03	0
Procedure-related complications	83	440	95	446	0.83 (0.49–1.40)	0.49	56

Study limitations

- The paucity of data on the outcomes according to clot location, stroke aetiology and clot composition, and first-line MT techniques precluded the possibility of conducting subanalyses
- Three of the four included studies were conducted in Asian populations, limiting generalizability
- Inclusion of the MR CLEAN NO-IV study, which was presented during ISC 2021 and, therefore, was not peer-reviewed, could have introduced bias
- All analyses were performed in the intention-to-treat populations and, therefore, the actual treatment administered may have differed from the group allocation, which could have influenced the results
- Only patients with anterior circulation strokes were included in the studies analysed, and, therefore, the findings cannot be extrapolated to all patients with ischaemic stroke
- Alteplase was the only therapy used in IVT and, therefore, the findings cannot be extended to other therapies
- Analysis of the ordinal shift in mRS based on individual patient data would have provided a more complete understanding of the effect of direct MT and MT + IVT on clinical outcomes

Study conclusions

- In patients with AIS and LVO, there was no difference between direct MT and MT + IVT with regard to the likelihood of achieving good clinical outcome
- Compared with MT + IVT, direct MT was associated with a significantly lower risk of any ICH, but it was also associated with a significantly lower likelihood of successful reperfusion

"The application of these findings is limited to patients presenting directly to MT-capable centers and real-world workflow times may differ against those achieved in a trial setting."[1]

2. WHAT IS THE EFFICACY OF ENDOVASCULAR THERAPY COMPARED WITH MEDICAL THERAPY IN PATIENTS WITH STROKE DUE TO BASILAR ARTERY OCCLUSION?

SUMMARY

- An RCT comparing EVT with standard medical therapy in patients with stroke due to basilar artery occlusion
- The proportion of patients who had a favourable functional outcome at 90 days was similar with EVT and standard medical therapy
- However, the benefit of EVT could not be excluded and data from larger trials are needed

Basilar artery occlusion accounts for approximately 10% of all ischaemic strokes due to proximal LVO and is associated with high morbidity and mortality.[2] However, recruitment into dedicated RCTs on basilar artery occlusion has been difficult because of case reports of favourable outcomes with EVT. Therefore, the BASICS Study Group conducted a multicentre, open-label, international RCT based on information obtained from the BASICS registry, which failed to show the benefit of EVT versus medical therapy.[2]

In the accompanying editorial, Marc Fisher notes that, while the benefit of EVT in patients with AIS due to LVO in the proximal anterior circulation is established, the present study and the previously available evidence (registry data and the BEST trial) failed to demonstrate a similar benefit in patients with basilar artery occlusion.[3] Analysis of the present study is hampered by the lack of data on 124 eligible patients who were not enrolled and, of whom, 98 received EVT. Dr Fisher suggests that the benefit of EVT in patients with basilar artery occlusion has not been established because the extent of ischaemic injury, extent of collateral circulation, and thrombus on computed tomography (CT) or magnetic resonance angiography (MRA) were not used as selection criteria in the present study or in BEST, in contrast to RCTs of patients with anterior circulation LVO. In addition, the modified Rankin Scale (mRS) is inappropriate for assessing outcomes in patients with basilar artery occlusion, and therefore more sensitive outcome measures are needed.[3]

Study details

- Patients with a proven basilar artery occlusion on CT angiography (CTA) or MRA were enrolled between October 2011 and December 2019
  - Initially, patients aged <85 years with a National Institutes of Health Stroke Scale (NIHSS) score of ≥10 were included
  - Due to slow enrolment, after 4 years the inclusion criteria were expanded to patients aged ≥85 years, with an NIHSS score of <10, and contraindicated for IVT

- Patients were randomized to EVT within 6 h after estimated onset of basilar artery occlusion or medical therapy (conventional care according to local practice) at a 1:1 ratio
    - Patients in both groups could receive IVT, if eligible
- The primary outcome was favourable functional outcome (defined as mRS score of 0–3) at 90 days
- The primary safety outcomes were symptomatic intracranial haemorrhage (ICH) within 3 days after treatment initiation and mortality at 90 days
- Secondary clinical outcomes were excellent outcome (defined as mRS score of 0–2), NIHSS score at 24 h, distribution of mRS scores, and health-related quality of life (measured using the European Quality of Life–5 Dimensions [EQ-5D] questionnaire) at 90 days
- Secondary imaging outcomes were extent of cerebral infarction (measured using the posterior circulation Acute Stroke Prognosis Early CT Score [PC-ASPECTS]) on non-contrast CT and CTA, and basilar artery patency (assessed on CTA or MRA) at 24 h (±6 h)
- Original sample size calculation assumed 40% rate of favourable outcome in the EVT group and 30% in the medical therapy group (odds ratio [OR]: 1.56; risk ratio [RR]: 1.33); it was later revised to 46% in the EVT group, but remained the same in the medical therapy group (OR: 2.0; RR: 1.53)
- For the primary outcome, treatment groups were compared using RRs for dichotomous outcome (mRS 0–3 vs 4–6); linear regression and mean difference were used to compare treatment groups for secondary outcomes
- A total of 154 patients were included in the EVT group and 146 in the medical therapy group
    - The mean age (standard deviation [SD]) was 66.8 (13.1) and 67.2 (11.9) years, respectively, and 35.1% and 34.2% of patients, respectively, were female
    - The proportion of patients with atrial fibrillation was higher in the EVT (28.6%) than in the medical therapy group (15.1%)
    - 78.6% and 79.5% of patients in the EVT and medical therapy groups, respectively, received IVT

Study results

- The difference between the EVT group and the medical therapy group in the proportion of patients with favourable functional outcome at 90 days was not statistically significant (p=0.19) (**Table 2**)
- The baseline-adjusted common OR across mRS score for EVT compared with medical care was 1.35 (95% confidence interval [CI]: 0.88–2.88)
- For secondary outcomes, there was no prespecified plan for the adjustment of CIs for multiple comparisons; therefore, no definite conclusions can be drawn from the results
- The difference between the EVT group and the medical therapy group in mortality at 90 days was not statistically significant (p=0.29) (**Table 2**)
- The risk of symptomatic ICH was significantly higher in the EVT group than the medical therapy group (p=0.06)

Table 2. Outcome according to assigned treatment

Outcome	EVT (n=154)	Medical therapy (n=146)	RR/mean difference (95% CI)
Primary outcome			
Favourable functional outcome at 90 days, n (%)	68 (44.2)	55 (37.7)	1.18 (0.92 to 1.50)*
Secondary clinical outcomes			
Excellent functional outcome at 90 days, n (%)	54 (35.1)	44 (30.1)	1.17 (0.87 to 1.57)*
NIHSS score at 24 h, median (IQR)	11.0 (3.0–37.5)	15.0 (5.0–36.5)	−0.79 (−3.90 to 2.31)†
EQ-5D questionnaire score at 90 days, mean (SD)‡			
Visual analogue scale	67.6 (21.3)	61.9 (24.8)	6.0 (−1.9 to 13.8)†
Index value	0.65 (0.32)	0.61 (0.32)	0.05 (−0.05 to 0.16)†
Primary safety outcomes			
Overall mortality at 90 days, n (%)	59 (38.3)	63 (43.2)	0.87 (0.68 to 1.12)*
Symptomatic ICH ≤3 days after treatment initiation, n (%)	7 (4.5)	1 (0.7)	6.9 (0.9 to 53.0)*

*Risk ratio; †Mean difference; ‡On the visual analogue scale (range: 0–100) higher scores indicate better health perception; data were available for 72 patients in the EVT group and 59 patients in the medical therapy group. On the descriptive system yielding an index value (range: −0.33 to 1.00), higher values indicate better health status; data were available for 78 patients in the EVT group and 65 patients in the medical therapy group
IQR, interquartile range

Study limitations

- According to the screening logs, 29.2% of eligible patients were treated outside the trial, of which 79.0% received EVT; this could have introduced bias in the enrolled population and affected the outcome of the study
- 5% of the patients in the medical treatment group crossed over to the EVT group
- Advanced imaging, such as CT perfusion, was not used for patient selection
- There was an imbalance of patients with atrial fibrillation in the two treatment groups; adjustment for this imbalance did not substantially alter the effect size between the groups
- The NIHSS score, which was used for stratification in randomization, is less sensitive to symptoms of posterior than anterior circulation stroke
- The trial was underpowered for some analyses because of lower than anticipated recruitment

Study conclusions

- In patients with basilar artery occlusion, EVT and medical therapy were not significantly different with respect to favourable functional outcome
- However, based on the originally assumed 10% difference in the rate of primary outcome, the benefit of EVT cannot be excluded
- Data from larger trials are needed to determine the efficacy and safety of EVT in patients with basilar artery occlusion

"The trial therefore did not show an advantage of endovascular therapy over medical therapy, but these findings may be inconclusive."[2]

"The conclusion remains that endovascular therapy in patients with basilar-artery occlusion is of unproven value."[3]

3. WHICH FACTORS PREDICT THE EFFECTIVENESS OF IVT IN PATIENTS WITH AIS?

SUMMARY

- A subanalysis of patients who underwent IVT alone during the THRACE RCT
- Excellent outcome at 3 months was associated with no history of hypertension, not being a current smoker, shorter onset-to-treatment time (OTT), small diffusion-weighted imaging (DWI) volume, presence of susceptibility vessel signs (SVS), and shorter SVS length
- Excellent outcome at 3 months was also associated with strong neurological improvement (SNI), major neurological improvement (MNI), and improvement of ≥50% in the NIHSS score at 24 hours

IVT is a widely available treatment for patients with AIS caused by anterior circulation LVO, while MT is mostly performed in comprehensive stroke centres. However, there is debate about the indications and contraindications for IVT.

THRACE was an RCT conducted in 26 French centres that compared IVT alone with IVT plus MT in patients with AIS and proximal cerebral artery occlusion. The authors of this study performed a subgroup analysis of 247 patients who underwent IVT alone to identify the clinical and imaging predictors of excellent outcome (defined as mRS score of 0–1) at 3 months.[4] Predictors of excellent outcome were assessed by stepwise multivariable logistic regression analysis. Imaging method (magnetic resonance imaging [MRI] or CT) was considered to be a nesting covariate.

The mean age (SD) was 63.8 (13.9) years; the male/female ratio was 1.04. At 3 months, 31.2% (n=77) had excellent outcome.

Multivariate analysis showed that the following factors were independently associated with excellent outcome at 3 months: absence of hypertension (OR: 2.43; 95% CI: 1.74–3.38; p=0.007), not being a current smoker (OR: 2.76; 95% CI: 1.79–4.26; p=0.02), shorter OTT (OR per hour increase: 0.47; 95% CI: 0.23–0.78; p=0.003), smaller DWI (OR per 10 mL increase: 0.78; 95% CI: 0.68–0.89; p=0.0004), presence of SVS on MRI (OR: 7.89; 95% CI: 1.65–37.78; p=0.01), and shorter SVS length (OR per mm increase: 0.87; 95% CI: 0.80–0.94; p=0.001). The model allowed for good discrimination (C statistic: 0.79; 95% CI: 0.79–0.80) and was well calibrated (Brier score: 0.16; adjusted R^2: 0.31).

Excellent outcome at 3 months was also independently associated with normalized NIHSS score change at 24 hours (adjusted OR for 10% increase: 1.79; 95% CI: 1.65–1.93; p<0.0001). In addition, SNI (defined as NIHSS score ≤3 at 24 hours) had a specificity of 0.96 and a positive predictive value of 0.88, while for MNI (defined as NIHSS score ≤1 or an improvement ≥8 points at 24 hours) and improvement of ≥50% in the NIHSS score at 24 hours, these were 0.86 and 0.73, and 0.85 and 0.74, respectively.

Limitations of the study included the fact that some inflammatory and clotting parameters, as well as previous antiplatelet therapy, were not recorded. In addition, the earliest NIHSS score assessment was performed at 24 hours after treatment. Lastly, data on patients examined using MRI and CT were merged for this analysis.

Conclusions

In patients with AIS due to LVO who were treated with IVT only, excellent outcome at 3 months was associated with no history of hypertension, not being a current smoker, short OTT, small DWI volume, presence of SVS, and short SVS length, as well as SNI, MNI, and improvement of ≥50% in the NIHSS score at 24 hours. These predictors may help identify patients likely to achieve optimal reperfusion after IVT, and thus aid clinical decision-making.

"For patients with LVO admitted in a centre without MT capability, IVT represents the first-line treatment in reperfusion strategy."[4]

4. WHAT IS THE SENSITIVITY OF COMMONLY USED PREHOSPITAL STROKE SCALES IN IDENTIFYING OCCLUSION LOCATIONS IN PATIENTS WITH ACUTE ISCHAEMIC STROKE?

SUMMARY

- An analysis of data from the national MR CLEAN Registry conducted in the Netherlands evaluated the sensitivity of 14 commonly used prehospital stroke scales in identifying occlusion locations in patients with AIS
- The Emergency Medical Stroke Assessment (EMSA) and Gaze-Face-Arm-Speech-Time (G-FAST) had the highest sensitivities for all occlusion locations evaluated
- Prehospital stroke scales were generally more sensitive in detecting proximal LVOs and less sensitive in detecting more distal occlusions

The effectiveness of EVT for ischaemic stroke is strongly time dependent. Prehospital stroke scales aim to reduce time to EVT by identifying patients with likely LVO, allowing them to bypass the primary stroke centre and to be transported directly to EVT-capable centres. Most prehospital stroke scales are derived from the NIHSS. The authors of the present study evaluated the sensitivity of 14 prehospital stroke scales in detecting various occlusion locations using the data from the Netherlands' national, prospective MR CLEAN Registry.[5]

The MR CLEAN Registry was conducted at EVT centres and included all patients with AIS caused by LVO (confirmed by CTA) who had at least a groin puncture as the start of EVT. This analysis included data on 3021 patients aged ≥18 years who were registered between 16 March 2014 and 1 November 2017, had EVT within 6.5 hours of stroke onset and had proximal intracranial occlusion of the internal carotid artery (ICA), ICA terminus (ICA-T) or middle cerebral artery (M1/M2). The scales were assessed as positive or negative based on the cut points proposed in the original publication. The sensitivities of prehospital scales for detecting LVO in various locations and for all locations were calculated and compared using the χ^2 test.

The median age of the patients was 72 years (IQR: 61–81) and 52% were male. The baseline NIHSS score was ≥17 in 44% of patients. IVT was administered in 76% of patients. The most common occlusion location was distal M1 (34%), followed by proximal M1 (24%), ICA-T (21%), M2 (15%) and intracranial ICA (5%).

All scales had the highest sensitivity in identifying ICA-T occlusions (sensitivity range: 0.21–0.97). Sensitivity was lower for more distal segments and for intracranial ICA, while M2 occlusions were least likely to be detected (sensitivity range: 0.08–0.84). The difference in sensitivity between occlusion locations was statistically significant for all scales (p<0.001).

EMSA and G-FAST had the highest sensitivities for all occlusion locations (0.94, 95% CI: 0.93–0.94 and 0.86, 95% CI: 0.85–0.87, respectively), while the Speech Arm Vision Eyes scale (SAVE; 0.42, 95% CI: 0.40–0.43), 3-Item Stroke Scale (3I SS; 0.42, 95% CI: 0.39–0.43), and three-item NIHSS (0.15, 95% CI: 0.14–0.17) had the lowest sensitivities.

The most commonly affected NIHSS items were motor arm, aphasia and dysarthria (combined), and facial paresis. The cut points/total scores were 3/6 for EMSA, 3/4 for G-FAST, 4/4 for SAVE, 4/6 for 3I SS, and 5/8 for three-item NIHSS.

This study had a number of limitations. First, NIHSS assessment was performed by experienced physicians at the emergency department and not by paramedics, as it would in real-world practice. Second, the number of patients with some of the occlusion locations was relatively low. Third, no patients with LVO of the anterior cerebral artery were included. Fourth, some of the commonly used scales that rely on items not included in NIHSS, such as the Los Angeles Motor Scale (LAMS) and the ambulance clinical triage for acute stroke treatment (ACT-FAST) algorithm, were not evaluated.

Conclusions

Prehospital stroke scales were generally more sensitive in detecting proximal LVOs and less sensitive in detecting more distal occlusions. The scales that mainly consisted of these items and had low cut points had the highest sensitivity.

"Prehospital stroke scales are least sensitive in detecting M2 occlusions. Since the treatment of isolated M2 occlusions is considered effective and safe, it is important to realise that a considerable proportion of treatable LVO patients will be missed."[5]

3I SS, 3-Item Stroke Scale; ACT-FAST, ambulance clinical triage for acute stroke treatment; AIS, acute ischaemic stroke; BASICS, Basilar Artery International Cooperation Study; BEST, Endovascular Treatment versus Standard Medical Treatment for Vertebrobasilar Artery Occlusion; CI, confidence interval; CT, computed tomography; CTA, computed tomography angiography; DEVT, Direct Endovascular Thrombectomy vs Combined IVT and Endovascular Thrombectomy for Patients With Acute Large Vessel Occlusion in the Anterior Circulation; DIRECT-MT, Direct Intraarterial Thrombectomy in Order to Revascularize Acute Ischemic Stroke Patients with Large Vessel Occlusion Efficiently in Chinese Tertiary Hospitals: a Multicenter Randomized Clinical Trial; DIRECT-SAFE, Randomized Controlled Trial of DIRECT Endovascular Clot Retrieval Versus Standard Bridging Thrombolysis With Endovascular Clot Retrieval; DWI, diffusion-weighted imaging; EMSA, Emergency Medical Stroke Assessment; EVT, endovascular therapy; EQ-5D, European Quality of Life–5 Dimensions questionnaire; G-FAST, Gaze-Face-Arm-Speech-Time; ICH, intracranial haemorrhage; ICA, internal carotid artery; ICA-T, internal carotid artery terminus; IQR, interquartile range; ISC, International Stroke Conference; IVT, intravenous thrombolysis; LAMS, Los Angeles Motor Scale; LVO, large vessel occlusion; MNI, major neurological improvement; MRA, magnetic resonance angiography; MR CLEAN, Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands; mRS, modified Rankin Scale; MRI, magnetic resonance imaging; MT, mechanical thrombectomy; NIHSS, National Institutes of Health Stroke Scale; OTT, onset-to-treatment time; OR, odds ratio; PC-ASPECTS, posterior circulation Acute Stroke Prognosis Early CT Score; RCT, randomized controlled trial; RESILIENT, Randomization of Endovascular Treatment With Stent-retriever and/or Thromboaspiration vs. Best Medical Therapy in Acute Ischemic Stroke Due to Large VEssel OcclusioN Trial; RR, risk ratio; SAVE, Speech Arm Vision Eyes scale; SD, standard deviation; SKIP, Direct Mechanical Thrombectomy in Acute LVO Stroke; SNI, strong neurological improvement; SVS, susceptibility vessel sign; SWIFT DIRECT, Bridging Thrombolysis Versus Direct Mechanical Thrombectomy in Acute Ischemic Stroke; THRACE, Mechanical Thrombectomy After Intravenous Alteplase vs Alteplase Alone After Stroke; TICI, Thrombolysis in Cerebral Infarction.

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1. Podlasek A *et al.* Direct mechanical thrombectomy without intravenous thrombolysis versus bridging therapy for acute ischemic stroke: A meta-analysis of randomized controlled trials. *Int J Stroke* 2021; doi: 10.1177/17474930211021353.
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