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# Efficacy and safety of mechanical thrombectomy alone for the treatment of acute ischemic stroke

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## Abstract

*Background:* Intravenous thrombolysis (IVT) and bridging therapy (BT) (IVT+mechanical thrombectomy [MT]) are the main treatments for acute ischemic stroke (AIS). Recent studies suggested that the curative effects of MT alone and BT are equivalent. However, there is no consensus regarding the curative effect and safety of MT alone. Therefore, a systematic review and meta-analysis are needed for further clarification. *Methods:* Seven databases, including PubMed, EMBASE, and Web of Science, were searched up to May 2021 for studies on MT alone and BT for the treatment of AIS. The modified Rankin scale (mRS) score and recanalization rate were the efficacy outcomes. Symptomatic and asymptomatic intracranial hemorrhage (SICH and aSICH) and mortality were the safety outcomes. RevMan 5.4 was used for analysis. *Results:* Thirty-five studies including 10,462 patients (MT alone: 4,612, BT: 5850) were selected. The improvement in the mRS score (mRS1: risk ratio [RR]=1.22, 95% confidence interval [CI] 1.09-1.35; P<.05; mRS2: RR=1.21, 95% CI 1.12-1.31; P<.05) was greater and the recanalization rate (RR=1.06, 95% CI 1.02-1.09; P<.05) was higher with BT than with MT alone. The rates of overall intracranial hemorrhage (RR=1.20, 95% CI 1.07-1.34; P <.05) and aSICH (RR=1.31, 95% CI 1.41-1.51; P<.05) were lower after MT alone than after BT. There was no significant difference in the rate of SICH (RR=1.05, 95% CI.87-1.26; P>.05). The mortality rate (RR=.76, 95% CI.70-.83; P<.05) was higher after MT alone than after BT.
*Conclusions:* MT alone is inferior to BT regarding improvements in neurological function and recanalization and is associated with a higher mortality rate, although the associated rate of aSICH is lower.

*Keywords:* Acute ischemic stroke (AIS), bridging treatment (BT), mechanical thrombectomy (MT), meta-analysis.

## INTRODUCTION

Stroke has high incidence, mortality, disability, and recurrence rates, imposing heavy burdens on patients, their families, and society. Ischemic stroke accounts for 70%-80% of all stroke cases.[1] Intravenous thrombolysis (IVT) and bridging treatment (BT) are the main protocols used for the treatment of acute ischemic stroke (AIS).[2] Three recent high-quality randomized controlled trials (RCTs) showed that the curative effects of mechanical thrombectomy (MT) alone are equivalent to those of BT, with no significant difference in the risk of bleeding or mortality.[3-5] Another high-quality RCT has shown that the curative effects of MT alone are equivalent to those of BT, with a lower mortality rate within 3 months and no significant difference in the risk of bleeding.[6] However, two other studies showed that although MT alone can improve the neural function of patients, the 3-month mortality rate was higher.[7,8] Because there is no consensus on the curative effects and safety of MT alone, this systematic review and meta-analysis were performed to clarify the curative effects and safety of MT alone for the treatment of AIS.

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## METHODS

*Search strategy*

Seven databases, including PubMed, EMBASE, and Web of Science, were searched for published cohort studies or randomized controlled trials (RCTs) that compared the curative effects and safety of MT alone and BT for the treatment of AIS. All studies were published in English before May 2021. The search terms were "cerebral infarction", "acute ischemic stroke" and "alteplase", "actilyse", "intravenous thrombolysis", "mechanical thrombectomy", and "bridging treatment". All references of the studies included in this analysis and previous meta-analyses were also searched for potentially eligible studies.

*Data extraction*

We created a data extraction form and downloaded and printed all the involved articles. Two trained evaluators independently evaluated all the articles using a uniform method, reading them one by one and extracting the relevant information on the year of publication, author, study type, drug name, treatment method, number of patients, patient age, patient sex, standard National Institutes of Health Stroke Scale/Score (NIHSS) score, time from attack to femoral artery puncture, medical history, modified Rankin Scale (mRS) score 3 months after treatment, 3-month rate of intracranial hemorrhage, 3-month rate of symptomatic intracranial hemorrhage, 3-month rate of asymptomatic intracranial hemorrhage, vessel recanalization rate, mortality rate and follow-up duration. The quality of the study was also recorded.

*Criteria for study selection and quality evaluation*

*Study selection criteria*

Studies were selected based on the following criteria: 1) a clinical study comparing the clinical curative effects and safety of BT and MT for the treatment of AIS; 2) an RCT or cohort study; 3) complete data, including the mRS score 3 months after treatment; the 3-month rates of intracranial hemorrhage, symptomatic intracranial hemorrhage, and asymptomatic intracranial hemorrhage; vessel recanalization rate; and mortality rate; and 4) internationally recognized criteria.

*Evaluation criteria for study quality*

The quality of the selected studies was independently assessed by two evaluators using the Newcastle-Ottawa Scale for cohort studies and the Jadad score for RCTs. Any discrepancies were resolved by discussion or with the assistance of a third researcher.

*Diagnostic criteria*

*Symptomatic intracranial hemorrhage*

The following criteria were used to diagnose symptomatic intracranial hemorrhage: 1) the European Cooperative Acute Stroke Study (ECASS), which defined it as blood at any site in the brain on a CT scan (as assessed by the panel of CT readers, independent of the assessment by the investigator) or documentation by the investigator of clinical deterioration or adverse events indicating clinical worsening (e.g., drowsiness, increase of hemiparesis) or causing a decrease in the NIHSS score of 4 or more points[9]; 2) the Safe Implementation of Thrombolysis in Stroke-Monitoring Study (SITS-MOST), which defined it as local or remote parenchymal hemorrhage type 2 on the 22–36 h posttreatment imaging scan, combined with a neurological deterioration of 4 points or more on the NIHSS from baseline or from the lowest NIHSS value between baseline and 24 h, or death[10]; 3) the NINDS, which defined a hemorrhage as symptomatic if it had not been seen on a previous CT scan and there had subsequently been either a suspicion of hemorrhage or any decline in neurologic status[11]; 4) the Heidelberg bleeding classification, which defined a symptomatic hemorrhage as any parenchymatous hematoma grade 1 (PH1) or grade 2 (PH2), remote intracerebral hemorrhage, subarachnoid hemorrhage (SAH), or intraventricular hemorrhage (IVH) associated with a decline in the NIHSS score ≥ 4 points within 24 h of the end of the revascularization procedure[12]; and 5) the PROACT II, which defined it as an increase in the NIHSS score ≥4 points compared with the preangiography score within 36 h of treatment initiation.[13]

*Revascularization*

The revascularization criteria were as follows: 1) an evaluation of the thrombolysis in myocardial infarction (TIMI) flow grade for which the rate of perfusion was divided into four categories (0 = no perfusion, 1 = penetration through occlusion

without distal branch refilling, 2 = partial perfusion, and 3 = complete perfusion) and successful recanalization (TIMI 2 or 3) and [14] 2) successful revascularization, defined as a thrombolysis in cerebral infarction (TICI) score 2b-3.[15]

*Curative effects*

A mRS score of 0 to 1 (mRS1) at 3 months was considered a good clinical outcome, a mRS score of 0 to 2 (mRS2) was considered functional independence, and a mRS score of 5 to 6 was considered a poor clinical outcome.[16]

*Statistical analyses*

RevMan 5.4 software (The Nordic Cochrane Centre, Copenhagen, Denmark) was used for the statistical analyses, and the P value and $I^2$ statistic were used to assess the heterogeneity among the studies, with $P < .05$ and $I^2 > 50\%$ indicating the presence of substantial heterogeneity. If there was no heterogeneity among the studies, the fixed-effect model was selected. Otherwise, the random-effect model was selected. For binary variables, the relative risk (RR) and its 95% confidence interval (CI) were calculated. For continuous variables, weighted mean difference (WMD) and its 95% CI were used. Publication bias was analyzed using a funnel plot. The level of statistical significance was set at $P < .05$.

## RESULTS

*Selected studies*

The first search identified 518 studies for review. After reading their titles and abstracts, 468 irrelevant studies were removed. After intensive reading, an additional 15 studies were removed, 2 of which used IVT alone as the control group[17,18], 7 of which were reviews[19-25], 4 of which were meta-analyses on MT[26-29], and 2 of which were meta-analyses on IVT.[30,31] Finally, 35 studies were selected for this systematic review and meta-analysis.[3-8,32-60] All studies were published in English. The selection process is shown in Figure 1.

The selected studies included 10,462 patients (4,612 in the MT alone group and 5,850 in the BT group). Of the 35 studies, 6 were conducted in Asia (3 in China)[3-5,40,43,50], 1 was conducted in the Middle East[33], 4 were conducted in North America[5,6,45,53], and 24 were conducted in Europe.[7,8,32,34-39,41,42,44,46-49,51,52,54,55-59] Five were RCTs.[3-6,45] Among the 35 studies, 2 reported differences in age[34,60], 5 reported differences in sex[4,5,34,43,54], 1 reported differences in the standard NIHSS score[34], 2 reported differences in the medical history of hypertension[34,53], 3 reported differences in the medical history of diabetes[8,45,60], 8 reported differences in the medical history of atrial fibrillation[34-36,45,52,53,59,60], 3 reported differences in the medical history of coronary atherosclerotic heart disease, 1 reported

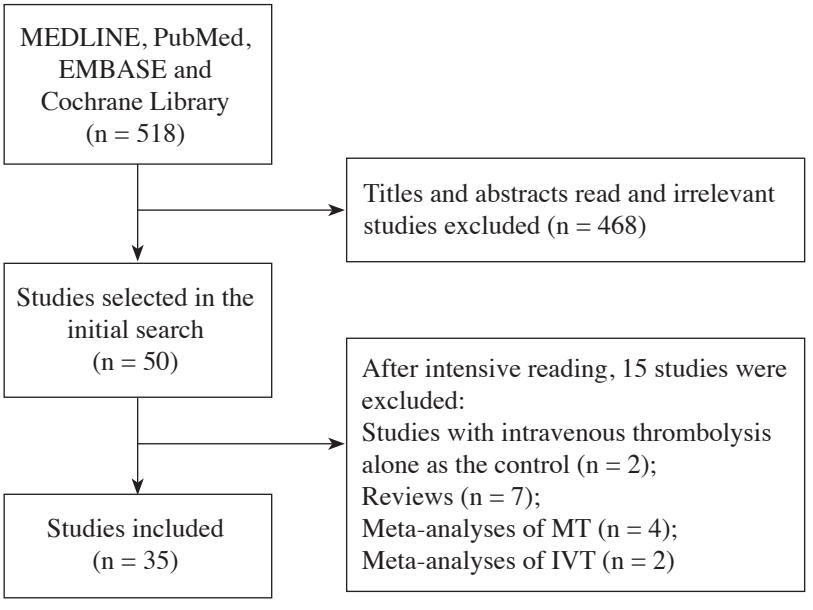


Figure 1. Study selection process.

differences in the history of smoking[35], and 6 reported differences in the time from the attack to femoral artery puncture.[7,35,38,44,50,54] Among the 24 studies that provided data on symptomatic intracranial hemorrhage, 6 used the ECASS criteria[39,41,55,58-60], 1 used the NINDS criteria[32], 9 used the SITS-MOST criteria[7,8,35,37,42-45], 1 used both the ECASS and SITS-MOST criteria[52], and 7 used other criteria.[7,85,37,42-45,56,57] Overall, the quality of the selected studies was high. The specific features of the selected studies are shown in Table 1.

*Good clinical outcome*

Among the 35 selected studies, 10 reported mRS1 (0–1). The heterogeneity test showed $\chi 2 = 8$ (P>0.05) and $I^2$=0, indicating that there was no heterogeneity among the selected studies. Thus, the fixed-effect model was used for analysis: 3.63 (P < .05); RR = 1.22, 95% CI (1.09, 1.35) (Figure 2).

*Functional independence*

Among the 35 studies, 28 reported mRS2 (0–2), and the heterogeneity test showed $\chi^2$ =60.08 (P<0.05) and $I^2$=53%, indicating that there was heterogeneity among the selected studies. Thus, the random-effect model was used: Z=4.61 (P<.05); RR =1.21, 95% CI (1.12, 1.31). The following were the results of the subgroup analyses: prospective group, Z=3.37 (P < .05), RR=1.25, 95% CI (1.10, 1.42); retrospective group, Z= 3.93 (P < .05), RR=1.24, 95% CI (1.11, 1.38); and RCT group, Z = 0.98 (P=0.33), RR=1.12, 95% CI (0.89, 1.40) (Figure 3).

*Recanalization rate*

Among the 35 selected studies, 31 compared the recanalization rate after treatment. The heterogeneity test showed $\chi^2 = 85.44$ (P < 0.05) and $I^2$=64%, indicating that there was heterogeneity among the selected studies. Thus, the random-effect model was used for analysis, yielding the following results: Z=2.95 (P<.05), RR=1.06, 95% CI (1.02, 1.09). The results of the subgroup analyses were as follows: prospective group, Z=1.77 (P > .05), RR=1.03; retrospective group, Z=2.33 (P <.05), RR=1.1, 95% CI (1.02, 1.2); and RCT group, Z= 1.16 (P > 0.05), RR=1.03, 95% CI (0.99, 1.08) (Figure 4).

*Symptomatic intracranial hemorrhage*

Among the 35 selected studies, 24 calculated the rate of symptomatic intracranial hemorrhage 3 months after treatment. The heterogeneity test showed $\chi 2 = 23.54$ (P>0.05) and $I^2$=0%, indicating that there was no heterogeneity among the selected studies. Thus, the fixed-effect model was used for analysis: Z=0.52 (P > .05), RR=1.05, 95% CI (0.87, 1.26). The results of the subgroup analyses were as follows: prospective group, Z ==0.50 (P > .05), RR=0.92 and 95% CI (0.66, 1.29); retrospective group, Z=0.80 (P > .05), RR=1.11 and 95% CI (0.86, 1.42); and RCT group, Z =0.56 (P > .05), RR=1.14 and 95% CI (0.72, 1.80) (Figure 5).

*Asymptomatic intracranial hemorrhage*

Among the 35 selected studies, 11 calculated the rate of asymptomatic intracranial hemorrhage 3 months after treatment. The heterogeneity test showed $\chi 2 = 9.44$ (P > 0.05) and $I^2$=0%, indicating that there was no heterogeneity among the selected studies. Thus, the fixed-effect model was used for analysis: Z = 3.84 (P < 0.05), RR=1.31 and 95% CI (1.14, 1.51). The results of the subgroup analyses were as follows: prospective group, Z=3.18 (P < 0.05), RR=1.56 and 95% CI (1.19, 2.06) and retrospective group, Z = 2.73 (P < 0.05), RR=1.42, 95% CI (1.10, 1.82) (Figure 6).

*Mortality*

Among the 35 selected studies, 26 compared the mortality rate 3 months after treatment. The heterogeneity test showed $\chi 2 = 30.15$ (P > .05) and $I^2$=14%, indicating that there was no heterogeneity among the selected studies. Thus, the fixed-effect model was used for analysis: Z = 5.96 (P < .05), RR=0.76 and 95% CI (0.70, 0.83). The results of the subgroup analyses were as follows: prospective group, Z = 5 (P < 0.05), RR=0.72, 95% CI (0.63, 0.82); retrospective group, Z=4.05 (P < 0.05), RR=0.75, 95% CI (0.65, 0.86); and RCT group, Z=0.06 (P > 0.05), RR=0.99, 95% CI (0.77, 1.27) (Figure 7).

*Publication bias*

We assessed publication bias with funnel plots. There was no indication of publication bias because the standard inverted funnel was observed, except for mRS1 (Figure 8).

*Sensitivity analyses*

The present study performed sensitivity analyses by removing the studies one by one. After

## Table 1: Characteristics of the studies included in the meta-analysis

| Studies | Study type | QA† | Location | Patients | | Female | | Age | | S-ICH | | AS-ICH | | Mortality | | Successful | | Admission NIHSS | | mRS 1 | | mRS2 | | Onset-to-groin puncture | | Hypertension | | Diabetes | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | BT group | MT group | BT group £ %£ © | MT group £ %£ © | BT group | MT group | BT group £ %£ © | MT group £ %£ © | BT group £ %£ © | MT group £ %£ © | BT group £ %£ © | MT group £ %£ © | BT group £ %£ © | MT group £ %£ © | BT group | MT group | BT group £ %£ © | MT group% | BT group £ %£ © | MT group £ %£ © | BT group | MT group | BT group £ %£ © | MT group £ %£ © | BT group £ %£ © | MT group £ %£ © |
| ©Yang et al 2020[3] | RCT | 6‡ | China | 329 | 327 | 148(45) | 138£ 42.2£ © | 69±11.17 | 69±11.17 | 20 (6.1) | 14 (4.3) | 119 (36.2) | 109 (33.3) | 62(18.8) | 58 (17.7) | 267/316 (84.5) | 243/306 (79.4) | / | / | 74 (22.5) | 80 (24.5) | 121(36.8) | 119 (36.4) | 36±21.22 | 32±18.62 | 201 (61.1) | 193 (59.0) | 65 (19.8) | 59 (18.0) |
| Wenjie et al 2021[4] | RCT | 5‡ | China | 118 | 116 | 52 (44.1) | 50 (43.1) | 69.9±3.52 | 69.85±3.33 | 10/117 (8.5) | 9/115 (7.8) | / | / | 21 (17.8) | 20 (17.2) | 102 (87.2) | 100 (88.5) | 16.05±1.37 | 16±1.57 | / | / | 55 (46.6) | 63 (54.3) | 210.7±14.87 | 200.1±18.03 | 74 (62.7) | 69 (59.5) | 20 (17.0) | 25 (21.6) |
| Suzuki et al 2021[5] | RCT | 3‡ | Japan | 103 | 101 | 31 (30) | 45 (45) | 75.72±2.59 | 73.94±2.6 | / | / | / | / | 9 (8.7) | 8 (7.9) | 96 (93.2) | 91 (90.1) | 17±1.99 | 18.89±2 | / | / | 59 (57.3) | 60 (59.4) | / | / | 61 (59) | 61 (60) | 17 (17) | 16 (16) |
| Goyal et al 2015[6] | RCT | 6‡ | Canada | 165 | 150 | 86 (52.1) | 79 (52.7) | 71±15.71 | 70±15.71 | 6 (3.6) | 4 (2.7) | / | / | / | / | / | / | / | / | / | / | 87/164 (53.0) | 43/147 (29.3) | / | / | 105 (63.6) | 108 (72.0) | 33 (20.0) | 39 (26.0) |
| Julian et al 2018[7] | Retrospective | 7† | Ireland | 210 | 145 | 94 £ 44.8£ © | 64£ 44.1£ © | 66± 45 | 68± 14 | 15 (7) | 14 (10) | / | / | 33 (16) | 45 (31) | 179 (85) | 105 (72) | 17±5 | 17±6 | / | / | 113 (54) | 49 (34) | 257±104 | 342±223 | / | / | / | / |
| Fabrizio et al 2018[8] | Retrospective | 7† | Italy | 193 | 132 | 111 £ 57.5£ © | 74£ 56.1£ © | 71.8±14.2 | 70.3±12.9 | 24 (12.5) | 23 (17) | / | / | 49 (25.4) | 48 (36.4) | 146 (75.5) | 90 (68) | 15±17.92 | 15±16.49 | / | / | 78 (40.4) | 45 (34.1) | 227±226.32 | 376±565.93 | / | / | / | / |
| Fabrizio et al 2013[32] | Prospective | 7† | Italy | 16 | 30 | 6£ 37.5£ © | 13£ 43.3£ © | 64.5±12.1 | 63.4±12.7 | 2 (12.5) | 3 (10) | 8 (50) | 12 (40) | 2 (12.5) | 10 (33) | 16 (100) | 27 (90) | 19±5 | 18±4 | / | / | 7(43) | 12 (40) | / | / | / | / | / | / |
| Ronen et al 2015[33] | Prospective | 8† | Israel | 24 | 33 | 16 £ 66.7£ © | 18£ 54.5£ © | 66.8 ± 13.7 | 64.4±14.7 | 2£ 8£ © | 0 | 7 (29) | 5 (15) | / | / | 21 (87.5) | 28 (85) | 19.2±5.1 | 19.1±5.8 | / | / | 6 (18) | 17 (59) | / | / | 16 (67) | 22 (67) | 8 (33) | 22 (67) |
| Jens et al 2016[34] | Prospective | 9† | Germany | 603 | 504 | 299 (49.6) | 262 (52.0) | 68.3±13.7 | 68.7±14.7 | / | / | / | / | 102 (17.8) | 130 (27.8) | / | / | 15.1 ±6.4 | 14.3±6.7 | 140 (32.4) | 84 (23.5) | 205 (47.5) | 136 (38.1) | / | / | 461 (76.5) | 382 (75.8) | 118 (19.6) | 93 (18.5) |
| María et al 2016[35] | Prospective | 8† | Spain | 53 | 21 | 29 £ 54.7£ © | 12£ 57.1£ © | 64±16.76 | 73±9.54 | 3 (6) | 0 | 13 (25) | 2 (10) | 2 (4) | 3 (14) | / | / | 18±6.1 | 18±7.15 | / | / | 36 (68) | 9 (43) | 282±91.44 | 212±70.76 | 28 (53) | 11 (52) | 8 (15) | 4 (19) |
| Sònia et al 2017[36] | Prospective | 7† | Spain | 567 | 599 | 261 (46) | 290 (48.4%) | 68.6 ±12.8 | 68.1 ±13.5 | | | / | / | / | / | 449 (79.2) | 455 (76.0) | 17±5.2 | 16±5.94 | / | / | / | / | / | / | 352 (62.1) | 382 (63.8) | 127 (21.2) | 96 (16.9) |
| Gaspard et al 2017[37] | Prospective | 6† | France | 100 | 59 | 43£ 43£ © | 30£ 50.8£ © | 71±15.8 | 70±18.24 | 2 (2.0) | 2 (3.4) | / | / | / | / | 84 (84.0) | 47 (79.7) | 17±4.51 | 19±6.84 | / | / | 61 (61) | 30 (50.8) | 253±53.41 | 188±37.24 | 48 (48.0) | 31 (52.5) | 16 (16.0) | 12 (20.3) |
| Giovanni et al 2017[38] | Prospective | 5† | Italy | 33 | 33 | 15 £ 45.5£ © | 19£ 57.6£ © | 69.6±12.7 | 70.8±12.2 | / | / | / | / | 6 (18.2) | 10 (30.3) | / | / | / | / | / | / | 17 (51.5) | 6 (18.2) | / | / | 26 (78.8) | 21 (63.6) | 7 (21.2) | 3 (9.1) |
| Sebastian et al 2017[39] | Prospective | 6† | Switzerland and Germa | 249 | 111 | 122/249 (49) | 49/110 (44.5) | 73±14 | 75±15 | 13/246 (5.3) | 3/110 (2.7) | 49/246 (19.9) | 13/110 (11.8) | 68 (27.3) | 30 (27) | 193/247 (78.1) | 90(81.1) | 18±26.1 | 18±28.54 | 72 (28.9) | 31 (27.9) | 102 (41) | 49 (44.1) | / | / | 171/246 (69.5) | 85(76.6) | 42/246 (17.1) | 17/108 (15.7) |
| Hong et al 2017[40] | Prospective | 7† | Korea | 458 | 181 | 198 £ 43.2£ © | 78£ 43.1£ © | 68±12 | 69±12 | / | / | / | / | 68 (15) | 44 (24) | 336 (73) | 118 (65) | 15±5.95 | 14±6.35 | / | / | 180 (39) | 58 (32) | / | / | 302 (66) | 116 (64) | 118 (26) | 50 (28) |
| Mohamed et al 2018[41] | Prospective | 7† | Germany | 144 | 92 | 82 (57) | 46 (46) | 69±13 | 68.7±14 | 3 (2) | 7 (8.7) | / | / | / | / | 33(22.9) | 28(30.4) | 13±5.24 | 13±5.27 | / | / | 73 (52) | 21 (23) | / | / | 101 (72) | 71 (78) | 31 (22) | 18 (20) |
| Arturs et al 2018[42] | Prospective | 7† | UK | 84 | 62 | 46 £ 54.8£ © | 34£ 54.8£ © | 72 ± 12.5 | 72±9.9 | 10 (12) | 6 (10) | 17 (20) | 6 (10) | 14 (17) | 13 (21) | 79 | 55 | 15±4.53 | 17±4.55 | / | / | / | / | / | / | / | / | / | / |
| Jai et al 2018[43] | Prospective | 6† | Korea | 43 | 38 | 14(32.6) | 21(55.3) | 68.9±12.8 | 72.6±14.1 | 2 (4.6) | 2 (5.3) | / | / | 4 £ 9.3 £ © | 7 (18.4) | 25 (58.1) | 23(60.5) | 13±4.6 | 14±4.62 | / | / | 22 £ 51.2£ © | 14 (36.8) | 204.7±63.7 | 221.6±110.5 | / | / | / | / |
| Nitin et al 2018[44] | Prospective | 6† | Greece | 292 | 277 | 153 £ 52.4£ © | 131£ 47.3£ © | 62.5 ± 17.0 | 61.0 ± 19.8 | 21£ 7.3£ © | 29 £ 10.5£ © | / | / | 62 £ 21.4 £ © | 73 £ ¨ 26.5 | 229(78.) | 217(78.4) | 17±5.96 | 16±6.71 | 73 £ 25£ © | 58 £ 20.9 £ © | 121(41.4) | 95(34.3) | 225±102.06 | 318±193.76 | / | / | / | / |

| Studies | Study type | QA† | Location | Patients | | Female | | Age | | S-ICH | | AS-ICH | | Mortality | | Successful | | Admission NIHSS | | mRS 1 | | mRS2 | | Onset-to-groin puncture | | Hypertension | | Diabetes | | Coronary | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | BT group | MT group | BT group £ %£ © | MT group £ %£ © | BT group | MT group | BT group £ %£ © | MT group £ %£ © | BT group £ %£ © | MT group £ %£ © | BT group £ %£ © | MT group £ %£ © | BT group £ %£ © | MT group £ %£ © | BT group | MT group | BT group £ %£ © | MT group% | BT group £ %£ © | MT group £ %£ © | BT group | MT group | BT group £ %£ © | MT group £ %£ © | BT group £ %£ © | MT group £ %£ © | BT group £ %£ © | MT group £ %£ © |
| Jonathan et al 2012[45] | RCT | 3‡ | Canada | 160 | 131 | 97 (60.6) | 73 (55.7) | 67 ±13 | 69 ±12 | 2 (1.1) | 5 (3.8) | / | / | 13 (8.1) | 16 (12.2) | 127/151 £ 84.1 £ © | 105/124 £ 84.7£ © | 17±5.24 | 17±5.25 | 65/156 (41.7) | 46/128 (35.9) | 90/156 (57.7) | 61/128 (47.7) | 251±82.29 | 280±130.43 | 99 (61.9) | 87 (66.4) | 22 (13.8) | 32 (24.4) | / | / |
| Antoni et al 2012[46] | Retrospective | 6† | Spain | 74 | 67 | 29 (39) | 33 (49) | 66.2 ±12.7 | 66.4 ±13.6 | / | / | / | / | 11 (14) | 15 (24) | 64/73 (87.7) | 56/69(81.2) | 16±7.56 | 18±3.79 | / | / | 49(66) | 28 (42) | / | / | / | / | / | / | / | / |
| Johannes et al 2016[47] | Retrospective | 7† | Germany | 160 | 79 | 87 £ 54.4£ © | 43£ 54.4£ © | 69.8 ± 15.5 | 73.3 ± 12.4 | / | / | / | / | / | / | 139 £ 86.9 £ © | 59 £ 74.7£ © | 14±4.49 | 15±5.29 | / | / | / | / | 200±67.33 | 195±91.37 | / | / | / | / | / | / |
| Daniel et al 2016[48] | Retrospective | 7† | Germany | 66 | 27 | 32 £ 48.5£ © | 18£ 66.7£ © | 65± 44.72 | 71± 33.66 | / | / | / | / | / | / | 59 (89) | 18 (66) | 16±6 | 17±8 | / | / | / | / | 226±277.22 | 198±201.15 | / | / | / | / | / | / |
| ¡ Anne et al 2016[49] | Retrospective | 5† | Switzerland | 156 | 40 | 74 (47.4) | 15 (37.5) | 73± 14 | 77±14 | 7 (4.5) | 1 (2.5) | 38 (24.4) | 5 (12.5) | 41 (26.3) | 8 (20.0) | 126 (80.8) | 35 (87.5) | 18±25.44 | 19±26.14 | 50 (32.1) | 11 (27.5) | 71(45.5) | 17 (42.5) | / | / | 100 (64.5) | 30 (75) | 28 (18.1) | 5 (12.5) | 24 (15.7) | 12 (30.8) |
| ©Wang et al 2017[50] | Retrospective | 7† | China | 138 | 138 | 60 £ 43.5£ © | 62£ 44.9£ © | 66± 10.68 | 67± 12.17 | 18 (13.0) | 19 (13.8) | 62 (44.9) | 39 (28.3) | 33 (23.9) | 35 (25.4) | 113 (81.9) | 127 (92.0) | 17±6.18 | 17±5.99 | 36 (26.1) | 30 (21.7) | 62 (44.9) | 56 (40.6) | 154±64.43 | 100±53.44 | / | / | / | / | / | / |
| Chee et al 2017[51] | Retrospective | 6† | Singapore | 21 | 29 | 13 £ 61.9£ © | 13£ 44.8£ © | 73±16 | 71±14 | / | / | / | / | / | / | 19 (90.5) | 27 (93.1) | 15 ±5 | 15±7 | / | / | / | / | / | / | / | / | / | / | / | / |
| Ralph et al 2017[52] | Retrospective | 6† | Germany | 105 | 145 | 53(50.5) | 67(46.2) | 70.2 ±12.6 | 69.3 ±14.9 | 6 (5.9) | 5 (3.5) | 18 (17.6) | 22 (15.6) | 28 (26.7) | 46 (31.7) | 76 (73.8) | 106 (73.1) | 16±6.01 | 14±7.49 | / | / | 37 (35.2) | 58 (40.0) | 243±72.91 | 232±133.29 | 82 (79.6) | 104 (71.7) | 16 (16.7) | 28 (19.9) | / | / |
| Ansaar et al 2017[53] | Retrospective | 6† | USA | 38 | 52 | 18£ 47£ © | 32£ 61£ © | 63± 19 | 69±18 | / | / | / | / | 4 (10.5) | 13 (25) | 31 £ 81.6 £ © | 35£ 67£ © | 18±7.7 | 16±9.15 | / | / | / | / | / | / | 21 (55) | 38 (73) | 7 (18) | 15 (29) | / | / |
| Romain et al 2017[54] | Retrospective | 5† | France | 85 | 56 | 30 (35) | 32 (57) | 68±15 | 73±15 | 15 (18) | 7 (13) | / | / | 18 (21) | 21 (38) | 68 (80) | 42 (75) | 18±6.03 | 19±5.33 | / | / | 37 (44) | 19 (34) | 247±75.17 | 207±106.52 | 48 (56) | 27 (48) | 18 (21) | 10 (18) | / | / |
| Mariana et al 2018[55] | Retrospective | 8† | Portugal | 152 | 82 | 82 (53.9) | 43 (52.4) | 70.90 ±12.60 | 71.93 ±13.67 | 5 (3.3) | 4 (4.9) | 21 (13.8) | 11 (13.4) | 15 (9.9) | 14 (17.5) | 143 (94.1) | 71(86.6) | 16.28±4.98 | 15.67 ±4.48 | 61 (40.4) | 27 (33.8) | 98 (64.9) | 42 (52.5) | / | / | 104 (68.4) | 54 (65.9) | 30 (19.7) | 24 (29.3) | / | / |
| Pierre et al 2015[56] | Retrospective | 0† | France | 28 | 40 | 17 £ 60.7£ © | 25£ 62.5£ © | 69.2 ±13.5 | 64.6 ± 15.3 | 2 (7.1) | 2 (5.0) | / | / | 3 (10.7) | 7 (17.5) | 27 (96.4) | 29 (72.5) | 17±4.69 | 15±7.69 | / | / | 19(67.9) | 21 (52.5) | 234±68.74 | 224±88.43 | 11 (39.3) | 17 (42.5) | 2 (7.1) | 2 (5.0) | / | / |
| Ettelt et al 2020[57] | Prospective | 5' | German | 103 | 63 | 48 (46.6) | 24 (38.1) | 67(±14.28 | 69 ±11.18 | / | / | / | / | / | / | 98 (95) | 60 (95) | 12±1.79 | 10.2.15 | / | / | / | / | / | / | 69 (67) | 45 (71.4) | 17 (16.5) | 14 (22.2) | / | / |
| Cappellari et al 2021[58] | Prospective | 5† | Italia | 248 | 101 | 128 £ 51.6£ © | 51£ 50.5£ © | 70±14 | 72±14 | 6 (2.5) | 1 (1.1) | / | / | 36 (15.1) | 18 (19.1) | 185 (74.9) | 67 (67) | 17±1.42 | 16±1.60 | 103 (43.1) | 25 (26.6) | 131 (54.8) | 37 (39.4) | 240±15.33 | 241±23.38 | 138 (63.6) | 49 (65.3) | 24 (11.1) | 17 (22.7) | | / |
| | | | | 123 | 111 | 75 £ 12.2£ © | 61£ 54.5£ © | 71±12 | 69±13 | 2 (1.8) | 2 (2) | / | / | 16 (13.7) | 11 (10.7) | 97 (78.9) | 86 (79.6) | 18±1.36 | 19±1.58 | 44 (37.6) | 35 (34) | 63 (53.8) | 55 (53.4) | 240±17.50 | 233±25.83 | 80 (71.4) | 67 (67.7) | 14 (12.5) | 14 (14.1) | | / |
| Cabrera-Maqueda et al 2021 | Retrospective | 4† | Spain | 247 | 376 | 119 (48.2) | 195 (51.9) | 68.36±12.24 | 67.53±14.12 | 31 (12.6) | 25 (6.6) | / | / | 49 (25.5) | 91 (28.8) | 222 (91.7) | 348 (93) | 17.21±5.84 | 18.1±7.54 | / | / | 93 (48.4) | 117 (37) | 294.18±90.99 | 306.48±152.76 | Hypertension | 254 (67.6) | 68 (27.5) | 95 (25.3) | / | / |
| Sarraj et al 2021[60] | Prospective | 6† | USA | 162 | 64 | 75 £ 46.3£ © | 34£ 46.9£ © | 64.96 ±3.94 | 73.3 ± 3.53 | 10 (6.2) | 4 (6.3) | 61 (37.7) | 19 (29.7) | 17 (10.5) | 14 (21.9) | 133 (83.1) | 53 (82.8) | 16.96±1.69 | 15.15±2.57 | 69 (42.6) | 21 (32.8) | 92 (56.8% | 28 (43.8) | / | / | 117 (72.7) | 53 (82.8) | 38 (23.5) | 24 (37.5) | 24 (15.1) | 24 (38.1) |

Abbreviations: mRS, modified Rankin Scale; mRS1, mRS score = 0–1; mRS2, mRS score = 0–2. QA, quality assessment; SICH, symptomatic intracranial hemorrhage; aSICH, asymptomatic intracranial hemorrhage; NIHSS, National Institutes of Health stroke scale; BT, bridging treatment; MT, mechanical thrombectomy; RCT, randomized controlled trial.

Data are expressed as the means ±standard deviations.

†Assessed by the Newcastle-Ottawa Scale for cohort studies.

‡Assessed by the modified Jadad Scale.

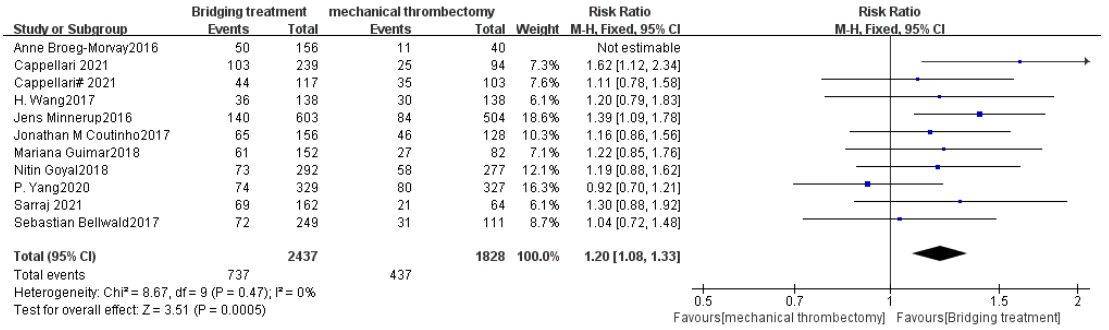


Figure 2. Forest plot of included studies reporting mRS1

removing 2 studies[6,41], the heterogeneity among the studies in the comparison of mRS2 disappeared. After removing 1 study[57], the heterogeneity among the studies in the comparison of recanalization disappeared. The removal of studies did not affect the heterogeneity among the studies in the comparisons of the 3-month mortality rate, symptomatic intracranial hemorrhage, symptomatic intracranial hemorrhage and mRS1.

## DISCUSSION

AIS involves ischemia, anoxia, and disordered cerebral blood circulation.[61,62] Studies have shown that the incidence, disability, mortality, and recurrence rates of AIS are high.[63] AIS is currently one of the most common cerebrovascular diseases worldwide. AIS has caused approximately 6.2 million deaths worldwide every year.[64] There is

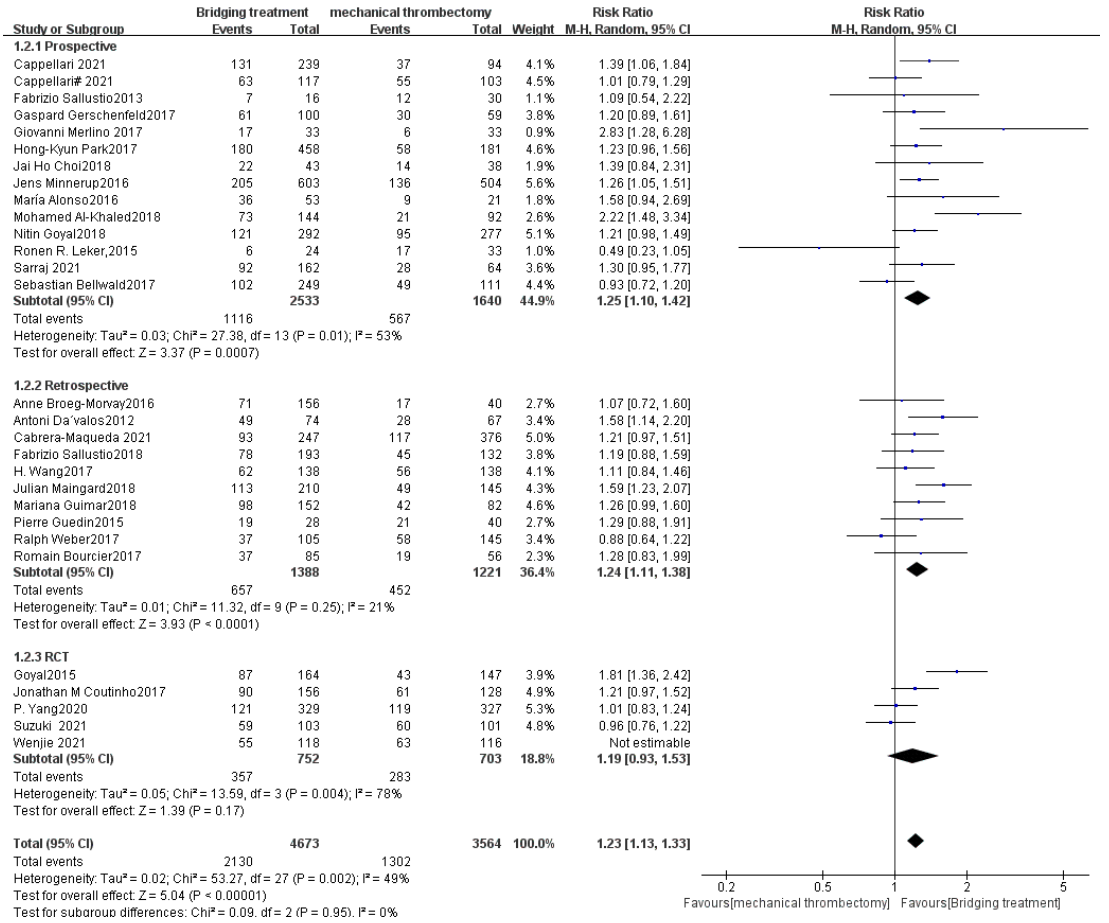


Figure 3. Forest plot of included studies reporting mRS2

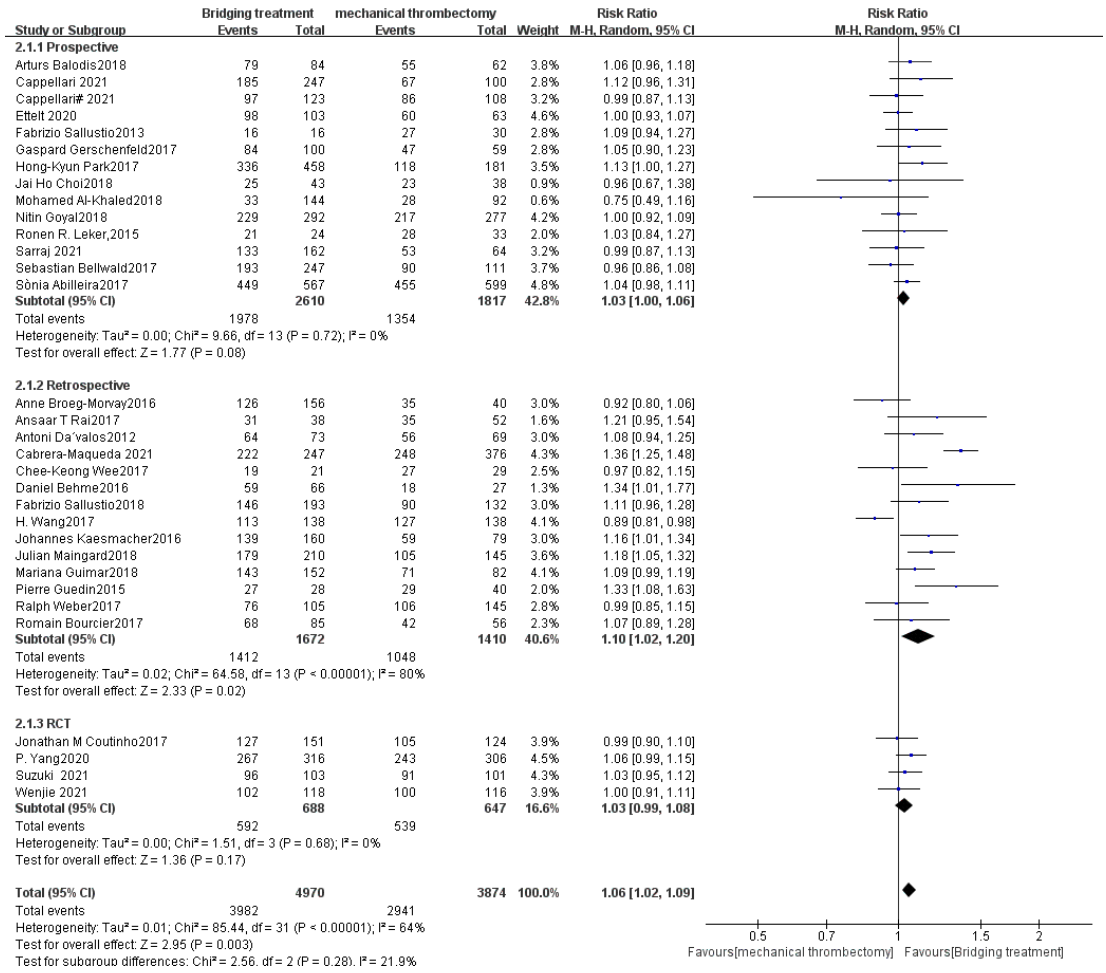


Figure 4. Forest plot of included studies reporting the recanalization rate

no optimal treatment for AIS, and most patients have sequelae of varying levels of severity, imposing heavy burdens on the patients, their families, and society. IVT and BT are the main methods of recanalization[2]; however, a recent study has shown that for patients with serious AIS, the use of MT after IVT may prolong the time to recanalization and increase the risk of hemorrhage.[50]

A meta-analysis showed that BT was more likely to improve functional activity, facilitate recanalization and reduce mortality than MT alone. In addition, the incidence of symptomatic intracranial hemorrhage in the BT group was not significantly different from that in the IVT group.[2] However, other studies have shown that there were no significant differences in survival rate and function between the BT group and IVT group.[4,5,59] Two recent high-quality RCTs showed that MT alone has curative effects that are equivalent to those of BT for patients with AIS, with no difference in the risks of hemorrhage and mortality between the two groups.[3,4] However, two other studies showed that MT could improve the neurological function of patients and reduce the risk of hemorrhage but resulted in a higher rate of mortality 3 months after treatment.[7,8] Given these conflicting results, there has been no consensus on the curative effects and safety of MT alone for the treatment of AIS. A meta-analysis is a method of increasing the credibility of the conclusions by enlarging the sample size to resolve the inconsistencies in the results; therefore, we conducted this meta-analysis to further clarify the curative effects and safety of MT alone for the treatment of AIS.

The results of this meta-analysis show that both mRS1 ($P < .05$) and mRS2 were lower in the BT group than in the MT alone group. Subgroup analyses were also conducted for mRS2 by study type, which showed that mRS2 was lower in the BT group than in the MT alone group in both

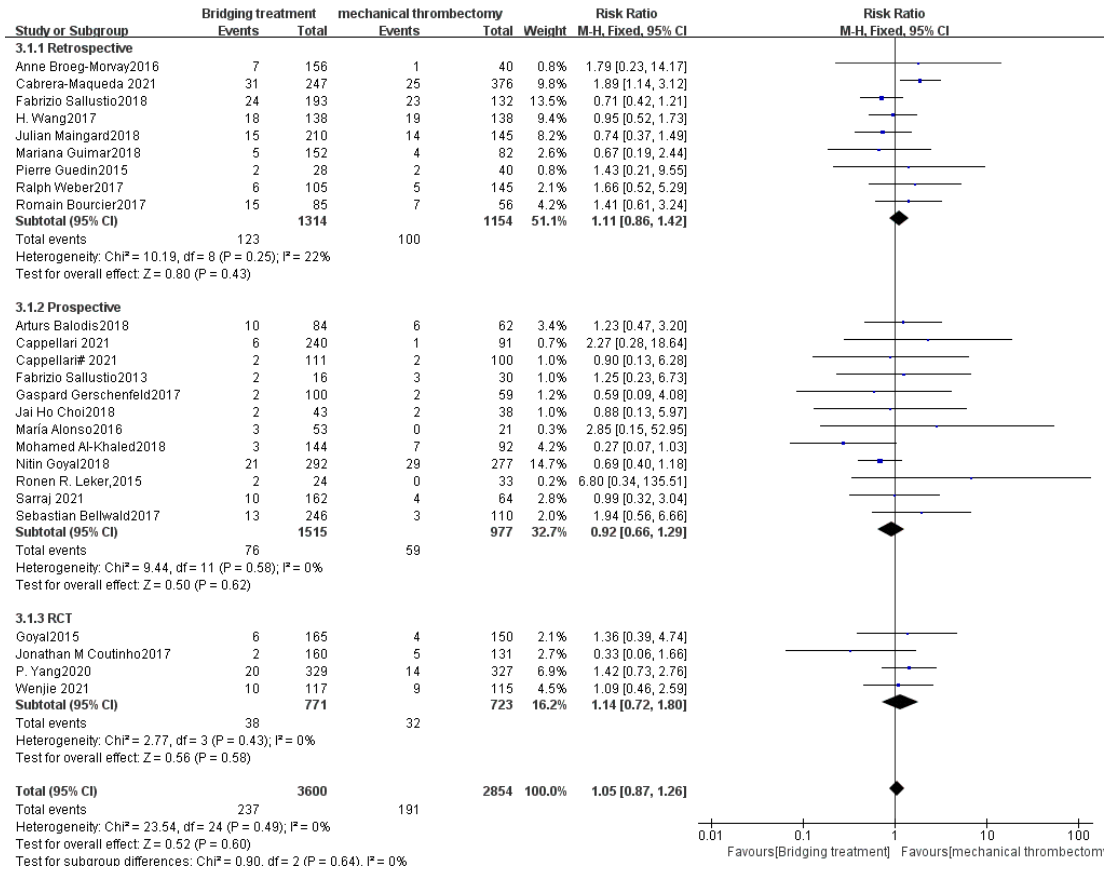


Figure 5. Forest plot of included studies reporting symptomatic intracranial hemorrhage

prospective and retrospective cohort studies (P <.05). These results indicate that BT results in better neurological function than MT alone. In addition, the present study showed that the mortality rate 3 months after treatment was lower in the BT group than in the MT alone group (P <.05), which was related to the higher rate of recanalization, younger age of the patients (both P <.05) and shorter duration from attack to femoral artery puncture (P <.05) in the BT group. The incidence rate of asymptomatic intracranial hemorrhage in the MT alone group was lower than that in the BT group (P <.05), which was mainly due to the use of IVT with alteplase before MT in the BT group; however, there was no significant difference between the two groups in the incidence rate of symptomatic intracranial hemorrhage (P >.05), which indicated that although BT increased the risk of intracranial hemorrhage, most of the bleeding symptoms were mild, and the risk of severe intracranial hemorrhage was not increased.

To test the stability of the conclusions, a sensitivity analysis was also conducted. The results showed good stability of the results. With the exception of 2 studies[6,41], which strongly influenced the heterogeneity among the studies reporting mRS2, the exclusion of the remaining studies did not change the results. With the exclusion of 1 study[57], the heterogeneity among the studies in the comparison of the recanalization rate disappeared.

Overall, all the selected studies for the present study were of high quality. The sample size with large, with a low degree of publication bias and good reliability.

### *Strengths and weaknesses of the study*

Although the present study is highly credible, this meta-analysis also had some weaknesses: 1) inconsistent benchmark data in some references (i.e., differences in patient age[34,60], sex[4,5,34,43,54], NIHSS score at admission[34], medical history of hypertension[34,53], medical history of diabetes[6,45,60], medical history of atherosclerotic heart disease[39,49,60], medical history of atrial fibrillation[34-36,45,52,53,59,60],

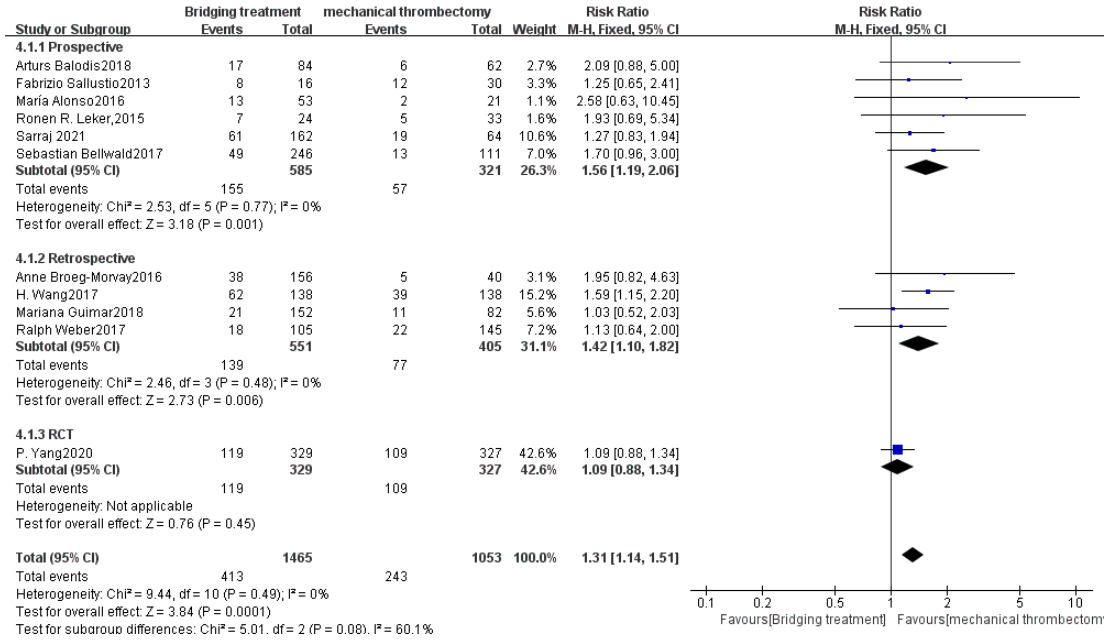


Figure 6. Forest plot of included studies reporting asymptomatic intracranial hemorrhage.

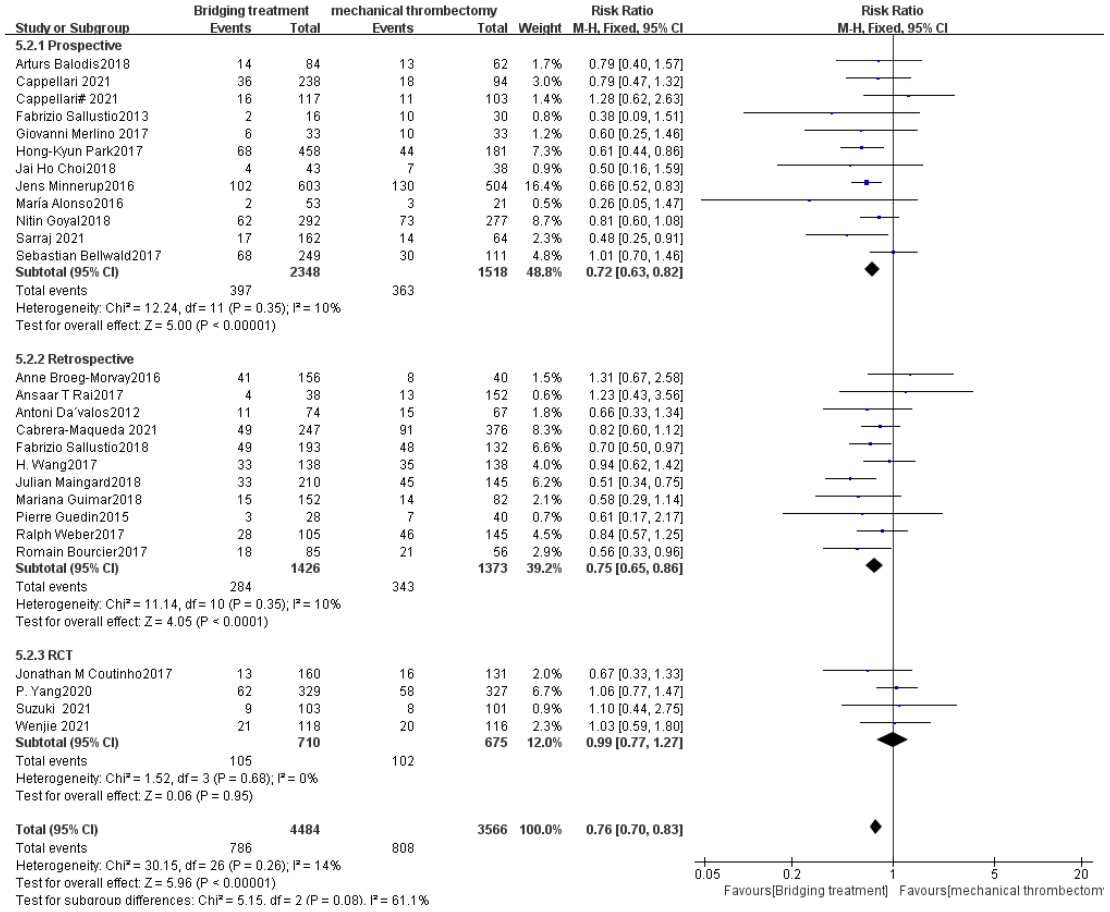


Figure 7. Forest plot of included studies reporting mortality

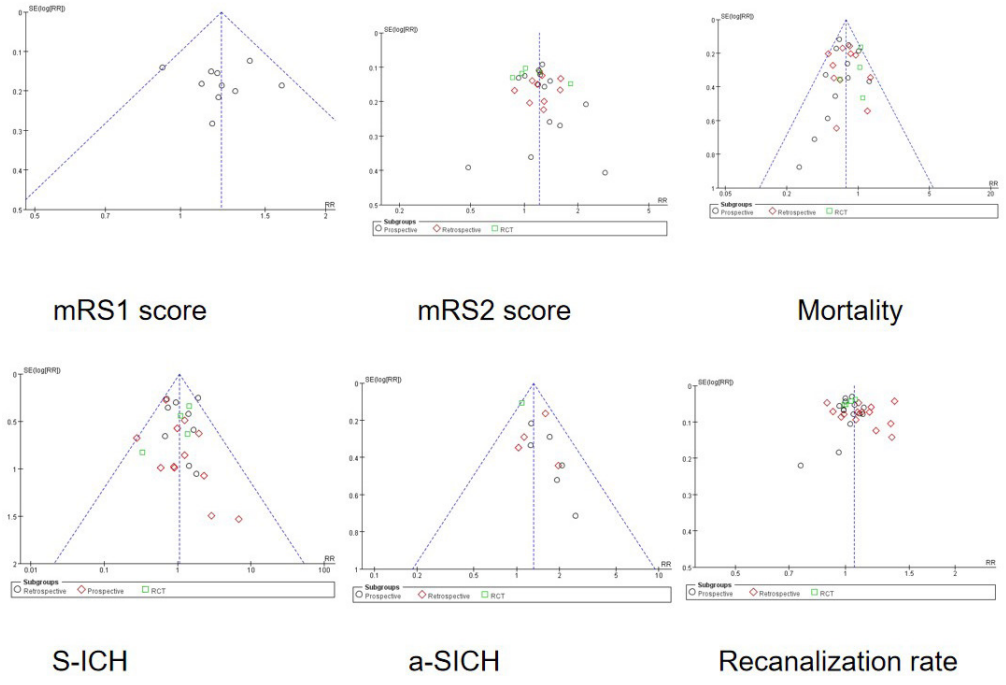


Figure 8. Funnel plots of the included studies for mRS1, mRS2, mortality rate, overall intracranial hemorrhage, symptomatic intracranial hemorrhage, asymptomatic intracranial hemorrhage and recanalization.

history of smoking[35], and time from attack to femoral artery puncture;[7,35,38,44,50,54] 2) low representativeness resulting from a high benchmark NIHSS score and the exclusion of patients with low NIHSS scores, who need to be assessed in a future study; and 3) the fact that most of the studies included in this meta-analysis were from Europe, while only four were from Asia. The results may not be generalizable to all populations in Asia, and additional studies need to be performed in these populations.

In conclusion, BT is better than MT alone with regard to improving neural function, facilitating recanalization and reducing mortality without increasing the risk of symptomatic intracranial hemorrhage. However, BT is associated with a higher incidence rate of asymptomatic intracranial hemorrhage. Thus, BT is still the best protocol for the treatment of AIS. However, the conclusions are more applicable to patients with severe AIS, given that the NIHSS scores in the selected studies were high. In addition, most studies in this analysis were conducted in Europe; therefore, similar studies should be conducted elsewhere.

## DISCLOSURE

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