RESEARCH ARTICLE

Bridging or Direct Thrombectomy in Posterior Circulation Large-Vessel Occlusion Stroke

Analysis of Binational Registries and Meta-Analysis

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Abstract

Background and Objectives

The role of IV thrombolysis before endovascular thrombectomy (bridging thrombectomy, BT) in posterior circulation large-vessel occlusion stroke remains uncertain. This study evaluated the effectiveness and safety of BT compared with direct thrombectomy (DT) using data from 2 nationwide registries and an updated meta-analysis.

Methods

Patients from collaborative registries in Taiwan and South Korea who underwent thrombectomy for vertebral, basilar, and posterior cerebral artery occlusions were included. This observational study included hospital-based registry data with standardized collection of treatments and outcomes. Propensity score matching was applied to adjust for baseline differences between BT and DT groups. Outcomes included 90-day modified Rankin Scale (mRS) score, mortality, successful reperfusion, and symptomatic intracranial hemorrhage (sICH). We also performed a systematic review and meta-analysis of observational studies comparing BT vs DT in posterior circulation large-vessel occlusion stroke.

Results

Among the combined 9,942 patients, 873 (median age 71, 32% female) who underwent thrombectomy for posterior circulation stroke were analyzed. Of them, 281 received BT and 592 received DT. BT was associated with a lower 90-day mRS score (median 3 vs 4; adjusted odds ratio [OR] 1.44 per 1-point improvement, 95% CI 1.09–1.91) and lower mortality (17.4% vs 26.9%; adjusted OR 0.51, 95% CI 0.33–0.81). The proportions of successful reperfusion (79.3% vs 81.1%) and sICH (2.5% vs 2.9%) were comparable. In propensity score–matched cohorts (n = 205 each), BT remained associated with better functional outcomes (OR 1.44, 95% CI 1.00–2.07) and reduced mortality (matched OR 0.45, 95% CI 0.26–0.78). The meta-analysis, which included 39 studies and 7,288 patients, confirmed that BT was associated with higher odds of achieving 90-day mRS score 0–2 (OR 1.57, 95% CI 1.28–1.94), 90-day mRS score 0–3 (OR 1.33, 95% CI 1.05–1.68), and lower mortality (OR 0.77, 95% CI 0.61–0.97), without an increased risk of sICH (OR 1.01, 95% CI 0.71–1.44).

Discussion

BT was associated with better 90-day functional outcomes and lower mortality, without increasing hemorrhagic risk in posterior circulation large-vessel occlusion stroke. These findings support the use of BT in eligible patients, pending further validation from randomized trials.

Classification of Evidence

This study provides Class III evidence that in patients with posterior circulation stroke undergoing thrombectomy, previous IV thrombolysis is associated with better 90-day functional outcomes and lower mortality without increasing hemorrhagic risk.

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Glossary

BA = basilar artery; **BT** = bridging thrombectomy; **CRCS-K** = Comprehensive Registry of Stroke in Korea; **DT** = direct thrombectomy; **ETIS** = Endovascular Treatment in Ischemic Stroke; **EVT** = endovascular thrombectomy; **IVT** = IV thrombolysis; **LVO** = large-vessel occlusion; **mRS** = modified Rankin Scale; **MR CLEAN** = Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands; **NIHSS** = NIH Stroke Scale; **OR** = odds ratio; **PCA** = posterior cerebral artery; **pc-ASPECTS** = Posterior Circulation Alberta Stroke Program Early CT Score; **sICH** = symptomatic intracranial hemorrhage; **TREAT-AIS** = Taiwan Registry of Endovascular Thrombectomy for Acute Ischemic Stroke; **VA** = vertebral artery.

Introduction

In patients presenting with large-vessel occlusion (LVO) acute ischemic stroke within 4.5 hours of onset, 6 major randomized clinical trials and subsequent meta-analysis did not establish clear noninferiority or superiority between patients treated with IV thrombolysis (IVT) followed by endovascular thrombectomy (EVT) and EVT alone.[1] However, these trials included only patients with anterior circulation LVO. Therefore, current guidelines recommend IVT for patients with anterior circulation LVO stroke if they are eligible and within the time window for IVT.[2,3]

For patients with posterior circulation LVO, however, this question remains unsolved. Patients with posterior circulation LVO stroke may be more challenging to identify, often presenting later to the emergency department, which decreases the likelihood of receiving IVT.[4,5] Therefore, whether administering IVT followed by EVT provides benefits in this group of patients, and whether there is a time window beyond which these benefits are no longer observed, still requires further investigation.

In 4 randomized clinical trials evaluating the efficacy of EVT in patients with basilar artery occlusion, the proportion of patients receiving IVT ranged from 14% to 79%, depending on the inclusion time window of each trial.[6-9] A recent patient-level meta-analysis of EVT for basilar artery occlusion showed that the benefit of EVT was consistent across different subgroups, including patients with and without IVT use.[10] However, there were no direct comparisons between patients who received IVT plus EVT and EVT alone. Several multicenter cohort-based observational studies have not found consistent benefits of bridging (BT) over direct thrombectomy (DT) in patients with posterior circulation LVO stroke.[11-18] Besides, these studies were limited by modest sample sizes and often included patients presenting in later time window, particularly in the DT group, complicating the interpretation of IVT's effects.

Therefore, our study aims to address these gaps by examining the effectiveness of IVT plus EVT vs EVT alone in posterior circulation LVO stroke through the integration of 2 nationwide stroke registries from Taiwan and South Korea, creating a larger sample size. We will investigate whether specific patient subgroups respond more favorably to BT, and whether a defined time window exists beyond which BT's effectiveness diminishes. In addition, by pooling data from previous studies, we will conduct a meta-analysis to provide a more robust assessment of the comparative efficacy of BT vs DT in patients with posterior circulation LVO stroke. Accordingly, the primary research question is whether IVT before EVT confers additional benefit over EVT alone in posterior circulation LVO stroke, including potential differences by time window and patient subgroups.

Methods

Study Population

The study was based on a harmonized database from the collaborations of the Comprehensive Registry of Stroke in Korea (CRCS-K) and the Taiwan Registry of Endovascular Thrombectomy for Acute Ischemic Stroke (TREAT-AIS). The detailed establishment and harmonization of the 2 EVT registries and the baseline characteristics have been published before.[19] In brief, the CRCS-K is a multicenter stroke registry started in 2008 and expanded in 2011 to include over 100,000 patients with acute stroke, capturing comprehensive stroke-related data for outcome tracking and quality improvement. CRCS-K requires participating centers to register all consecutive patients with acute ischemic stroke hospitalized within 7 days of symptom onset, with data entry initiated within 24 hours of admission.[20] TREAT-AIS, launched in 2019, prospectively enrolled all patients aged 20 years or older who received EVT for acute ischemic stroke at 19 participating hospitals in Taiwan, based on indications aligned with national guidelines.[21] In 2023, researchers standardized data elements across both registries, resulting in a harmonized data set of 9,942 EVT patients with 200 common variables. Of them, 7,835 patients were from Korea and 2,099 were from Taiwan.

In this study, we focused on patients with posterior circulation LVO. Specifically, only those whose primary LVO target was located in the intracranial vertebral artery (VA), basilar artery (BA), or posterior cerebral artery (PCA) were included. Patients were classified into the BT group if they received both IVT and EVT or into the DT group if they received only

EVT. Furthermore, we included only patients who underwent EVT after 2015 because standard stent retrievers and aspiration catheters became widely adopted thereafter.

Standard Protocol Approvals, Registrations, and Patient Consents

Both CRCS-K and TREAT-AIS registries were built on informed consent obtained from individual patients. Ethics approval was granted by Seoul National University Bundang Hospital (B-2410-928-104) and National Taiwan University Hospital (201708026RINA).

Clinical Variables and Outcomes

The common data elements from 2 registries included baseline demographic characteristics, prestroke functional status, vascular risk factors, use of antithrombotic agents, ischemic stroke subtypes, baseline NIH Stroke Scale (NIHSS) scores, location of LVO, and treatment workflow time metrics. Relevant time metrics of treatment workflow included onset (or last known well)-to-door, onset-to-thrombolysis, and onset-to-puncture time. During the study period, both countries expanded the time window for EVT up to 24 hours after symptom onset or last known well.

Clinical outcomes included 90-day modified Rankin Scale (mRS) scores, 90-day independent function outcome (defined as mRS scores 0, 1, or 2), and 90-day mortality rates. The 90-day mRS was assessed by trained case managers at each participating institute, who had received standardized mRS training and were independent of treatment decisions, thereby minimizing potential bias. Radiologic outcomes included symptomatic intracranial hemorrhage (sICH) and successful reperfusion (defined as a modified Thrombolysis in Cerebral Infarction score of 2b–3 on post-EVT angiography). sICH was defined as a type 2 parenchymal hematoma observed on post-EVT neuroimaging (CT or MRI) within 24–36 hours after the procedure, along with an increase of 4 or more points in the total NIHSS score from baseline.

Statistical Analyses

Baseline characteristics were summarized and compared between the BT and DT groups using chi-squared tests for categorical variables, independent *t* tests for parametric variables, and median tests for nonparametric data. Owing to an inherent imbalance in time metrics—specifically, the BT group received treatment earlier than the DT group—we applied propensity score matching based on age, sex, country, prestroke mRS score, and onset-to-door time. Each participant was assigned a propensity score, and a matched cohort was formed. Standardized mean differences of baseline variables were calculated, with a threshold of <0.2 indicating a balanced distribution between the 2 groups, and will be further adjusted in the models.

To evaluate the effects of BT vs DT on the clinical and radiologic outcomes, we used hierarchical logistic regression models that accounted for country-specific effects, presenting results as odds ratios (ORs) with 95% CIs. For the 90-day mRS score, ordinal logistic regression was used, with an OR >1 indicating higher odds of achieving a better functional outcome (lower mRS score) and an OR <1 indicating lower odds. We calculated 3 types of ORs: crude OR, adjusted OR, and matched OR. For adjusted ORs, we controlled for relevant covariates, including age, sex, prestroke independence (mRS score 0–1), diabetes mellitus, previous stroke, direct anticoagulant use, stroke classification, and onset-to-puncture time. These variables were either clinically relevant or statistically different between the BT and DT groups. The matched OR was derived from the propensity score–matched cohort and was adjusted for postmatching imbalanced covariates including previous stroke, direct anticoagulant use, and onset-to-puncture time.

We further analyzed the effects of BT vs DT on 90-day mRS scores in predefined subgroups, which include (1) basilar artery occlusion vs other vessel occlusions, (2) NIHSS scores (<10 vs ≥10), and (3) onset-to-puncture time (<6 hours, ≥6 hours). For subgroup analyses, multivariable logistic regression models were applied and *p* for interaction tested effect modification across subgroups.

Statistical significance was defined as a 2-tailed *p* value of <0.05. Because this was an explorative analysis, *p* values were not adjusted for multiple comparisons. All statistical analyses were performed using SAS version 9.4.

Meta-Analysis

To evaluate how our data on functional independence compare with previously published findings and to contribute to the broader understanding of this topic, we conducted a meta-analysis following a preregistered protocol (PROSPERO: CRD42024614626).[22] A comprehensive literature search was performed across MEDLINE, Embase, Web of Science, and Google Scholar. Detailed search strategies for each database are provided in eMethods.

Studies were included if they (1) involved patients with acute ischemic stroke due to posterior circulation large-vessel occlusion (intracranial VA, BA, or PCA) treated with EVT; (2) compared EVT preceded by IVT with EVT alone; (3) reported at least 1 outcome of interest—functional independence (defined as mRS score 0–2 or 0–3), mortality, and sICH; and (4) were conducted in tertiary stroke centers or high-volume EVT institutions. Exclusion criteria included studies limited to anterior circulation stroke, those lacking comparative data between BT and DT, or those not involving primary research (e.g., reviews and editorials). No language restrictions were applied. Data extraction was independently performed by C.-H. Chen and C.L. Chai, with any discrepancies resolved through consensus discussions involving S.-C. Tang.

Outcome estimates were summarized as OR, and heterogeneity variance was assessed using the Hartung-Knapp-Sidik-Jonkman method under a random-effects model.[23] The meta-analysis was conducted using the R package *meta*.[24] Detailed definitions and outcome measurement methodologies are available in the preregistered protocol.[22]

Data Availability

The data that support the findings of this study are available from the corresponding author on reasonable request.

Results

Patient Characteristics

There were 9,942 patients in the collaborative CRCS-K and TREAT-AIS registries. After excluding patients before 2015 (n = 184), those with occlusion in the anterior circulation (n = 8,603), those without occlusion vessel information (n = 194), those without 90-day mRS scores (n = 86), and those with unclear onset-to-needle time (n = 2), 873 patients were included in this analysis (eFigure 1). The main occluded vessels were BA (n = 679), VAs (n = 103), and PCA (n = 91). The median age was 71 years, and 32% were female.

Of them, 281 received BT and 592 received DT, and the clinical characteristics and profiles are summarized in Table 1. During the study period, alteplase was the only available IVT agent, and approximately 43% of patients received low-dose alteplase (0.6 mg/kg). Compared with the DT group, patients in the BT group were younger (median, 70 vs 72 years), more likely to have prestroke independency (94.8% vs 84.7%), less likely to have previous stroke (10.3% vs 26.5%), and less likely to take direct oral anticoagulants (1.1% vs 5.9%). The initial stroke severities, blood pressure at arrival, and main occluded vessels were comparable between the 2 groups. It is important to note that the BT group had a significantly shorter onset-to-door time (78 vs 299 minutes) and onset-to-puncture time (220 vs 507 minutes) than the DT group. The BT group has comparable procedural characteristics to the DT group, including number of passes (median 2 vs 1), rates of permanent stenting (9.8% vs 13.0%), balloon angioplasty (5.4% vs 9.4%), and EVT-related complications (2.3% vs 6%).

After propensity score matching, 205 patients were included in each group (Table 1). eFigure 2 shows the propensity score density plot, suggesting that there is a considerable overlap of propensity scores between the 2 groups. The onset-to-door time was more comparable in the matched cohorts (84 vs 120 minutes, $p = 0.16$), although the onset-to-puncture time was still longer in the DT group (231 vs 288 minutes, $p = 0.002$).

Clinical and Radiologic Outcomes

The median 90-day mRS scores were 3 (interquartile range 1–5) in the BT group and 4 (2–6) in the DT group. At 90 days, 40.9% of the BT group and 28.6% of the DT group achieved mRS score 0–2; 52.7% and 41.1% achieved mRS score 0–3, and the mortality rate was 17.4% and 29.6%, respectively. The overall distribution of 90-day mRS scores between the BT and DT groups in both the full and matched cohorts is shown in Figure 1. In the adjusted models, BT was significantly associated with a better 90-day mRS score (adjusted OR 1.44, 95% CI 1.09–1.91). A consistent finding was observed in the matched cohort (matched OR 1.44, 95% CI 1.00–2.07). Mortality was also reduced in the BT group (adjusted OR 0.51, 95% CI 0.33–0.81; matched OR 0.45, 95% CI 0.26–0.78; Table 2). Furthermore, the BT group was associated with higher odds of achieving 90-day mRS score 0–2 and mRS score 0–3 in the adjusted models, but not in the matched cohorts (Table 2).

Successful reperfusion was achieved in 79.3% of the BT group and 81.1% of the DT group while sICH occurred in 2.5% and 2.9% of patients, respectively. The reperfusion rate and risk of sICH did not differ significantly between the 2 groups when analyzed using adjusted or matched ORs (Table 2).

We then assessed the effects of onset-to-puncture time on achieving functional independence associated with BT vs DT. The specific distribution of onset-to-puncture time in the BT and DT group is shown in Figure 2A. As shown in Figure 2B, an onset-to-puncture time of 6 hours 40 minutes (or 400 minutes) marks the threshold where the lower boundary of the 95% CI for the estimated effectiveness of BT first crosses the line of no association (1.0). Beyond this threshold, BT was no longer associated with improved functional independence compared with DT.

In the subgroup analysis, there were no treatment modifications between predefined subgroups and treatment methods (BT vs DT) on 90-day mRS score (all $p_{interaction} > 0.05$; Table 3). However, patients with NIHSS score ≥10 (OR 1.87, 95% CI 1.30–2.70) and those with onset-to-puncture time <6 hours (OR 1.55, 95% CI 1.08–2.22) showed numerically higher odds of favorable outcome with BT, compared with their counterparts.

As a sensitivity analysis, we retrospectively assessed Posterior Circulation Alberta Stroke Program Early CT Score (pc-ASPECTS) in 197 patients from Taiwan. The median pc-ASPECTS was 8 (interquartile range 7–10). When the pc-ASPECTS was further included in the models, BT remained associated with better functional outcomes than DT, although the difference did not reach statistical significance, likely because of the limited sample size and reduced power (eTable 1).

Meta-Analysis

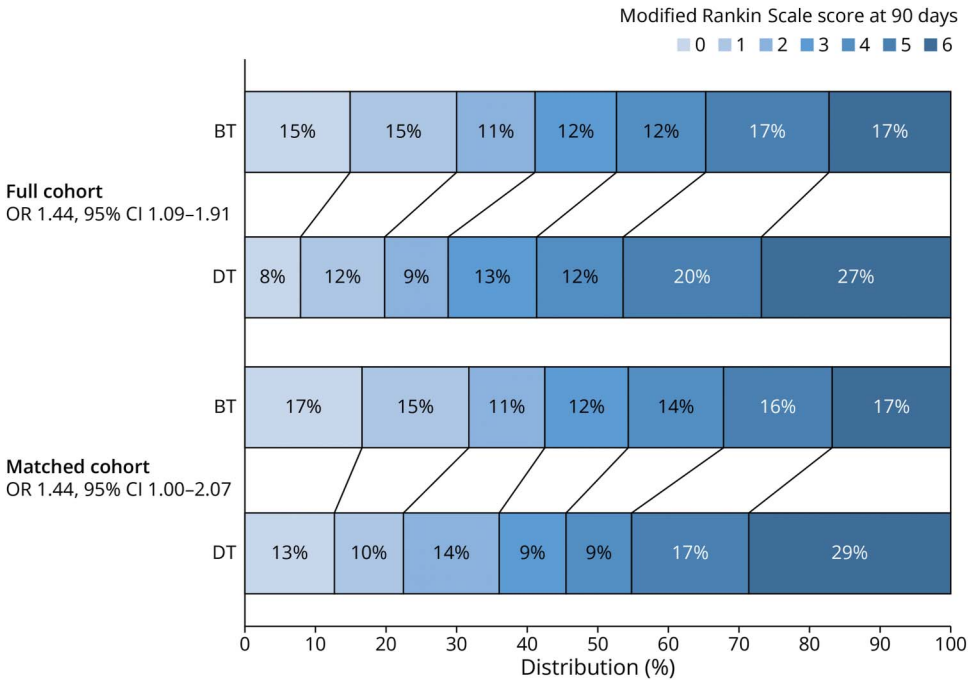
The search process followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 flowchart format, as shown in eFigure 3. A total of 39 studies involving 7,288 patients, including 873 from our cohort, were included

Table 1 Baseline Characteristics of Patients From the CRCS-K/TREAT-AIS Registries, Shown for the Full Cohort and the Propensity-Matched Cohort

	Full cohort			Matched cohort			
	Bridging thrombectomy (n = 281)	Direct thrombectomy (n = 592)	*p* Value	Bridging thrombectomy (n = 205)	Direct thrombectomy (n = 205)	*p* Value	SMD
Age, y, median (IQR)	70 (60–78)	72 (62–80)	0.016	72 (61–79)	72 (61–80)	0.570	0.056
Female, n (%)	80 (28.5)	199 (33.6)	0.128	59 (28.8)	71 (34.6)	0.203	0.126
Country: Korea	238 (84.7)	425 (71.8)	<0.001	174 (84.9)	170 (82.9)	0.294	0.053
Medical history, n (%)							
Prestroke independency (mRS score 0–1)	257 (94.8)	475 (84.7)	<0.001	192 (93.7)	188 (91.7)	0.448	0.075
Hypertension	190 (67.6)	407 (68.8)	0.736	137 (66.8)	139 (67.8)	0.833	0.021
Diabetes mellitus	70 (24.9)	194 (32.8)	0.018	46 (22.4)	63 (30.7)	0.057	0.189
Hyperlipidemia	94 (33.5)	209 (35.3)	0.591	75 (36.6)	60 (29.3)	0.115	0.156
Atrial fibrillation	114 (40.6)	230 (38.9)	0.627	89 (43.4)	77 (37.6)	0.227	0.119
Old stroke	29 (10.3)	157 (26.5)	<0.001	18 (8.8)	61 (29.8)	<0.001	0.552
Ever smoking	97 (34.5)	186 (31.4)	0.361	67 (32.7)	61 (29.8)	0.523	0.063
Previous medication							
Antiplatelets	66 (23.5)	121 (20.4)	0.305	46 (22.4)	40 (19.5)	0.467	0.072
Anticoagulants, VKA	8 (2.9)	26 (4.4)	0.270	7 (3.4)	13 (6.3)	0.169	0.136
Anticoagulants, DOAC	3 (1.1)	35 (5.9)	0.001	3 (1.5)	16 (7.8)	0.002	0.305
Stroke etiology, n (%)			0.008			0.270	
Large-artery atherosclerosis	80 (28.5)	232 (39.2)		56 (27.3)	69 (33.7)		
Cardioembolism	116 (41.3)	212 (35.8)		86 (42.0)	85 (41.5)		0.010
Others	85 (30.3)	148 (25.0)		63 (30.7)	51 (24.9)		0.131
NIHSS score, median (IQR)	15 (9–23)	16 (8–24)	0.892	15 (9–22)	16 (6–24)	0.624	0.048
Systolic blood pressure, median (IQR)	151 (134–170)	150 (130–171)	0.346	151 (134–170)	150 (130–170)	0.271	0.109
Diastolic blood pressure, median (IQR)	84 (75–100)	83 (73–96)	0.138	84 (75–100)	85 (73–96)	0.302	0.102
Main occluded vessels, n (%)							
Basilar artery	215 (76.5)	464 (78.4)	0.536	154 (75.1)	155 (75.6)	0.909	0.011
Vertebral artery	60 (21.4)	140 (23.7)	0.451	44 (21.5)	47 (22.9)	0.721	0.035
Posterior cerebral artery	61 (21.7)	109 (18.4)	0.251	45 (22.0)	41 (20.0)	0.628	0.048
Time metrics, min, median (IQR)							
Onset to door	78 (43–165)	299 (132–596)	<0.001	84 (43–176)	120 (58–220)	0.157	0.140
Onset to needle	115 (88–193)	—	—	123 (89–210)	—	—	—
Onset to puncture	220 (155–306)	507 (304–880)	<0.001	231 (160–313)	288 (200–448)	0.002	0.303
Needle to puncture	71 (41–118)	—	—	72 (41–123)	—	—	—

Abbreviations: CRCS-K = Comprehensive Registry of Stroke in Korea; DOAC = direct oral anticoagulant; ICH = intracranial hemorrhage; IQR = interquartile range; mRS = modified Rankin Scale; NIHSS = NIH Stroke Scale; SMD = standardized mean difference; TREAT-AIS = Taiwan Registry of Endovascular Thrombectomy for Acute Ischemic Stroke; VKA = vitamin K antagonist.

Figure 1 Distribution of 90-Day mRS Scores Between the Bridging and Direct Thrombectomy Groups in the CRCS-K/TREAT-AIS Registries



This figure presents the distribution of mRS scores at 90 days in the full cohort (top panel) and the matched cohort (bottom panel), comparing patients treated with BT (blue, top rows) and DT (blue, bottom rows). BT = bridging thrombectomy; CRCS-K = Comprehensive Registry of Stroke in Korea; DT = direct thrombectomy; mRS = modified Rankin Scale; OR = odds ratio; TREAT-AIS = Taiwan Registry of Endovascular Thrombectomy for Acute Ischemic Stroke.

in the analysis. The characteristics of the included studies are listed in eTable 2. Of these, 9 studies, including our own, directly compared BT and DT, whereas the remaining 30 studies focused on posterior circulation EVT with BT and DT data indirectly retrieved from published materials. Twelve studies included PCA occlusion. Among 9 studies directly comparing BT and DT, the NIHSS scores were similar between groups and the BT group had faster onset-to-puncture time (median 240 vs 470 minutes).

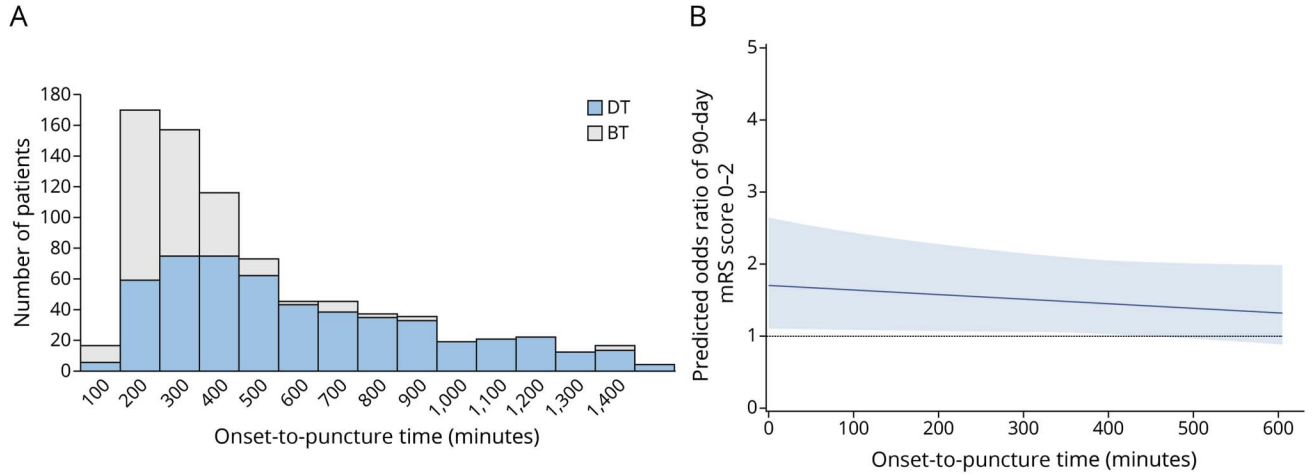
The outcomes for functional independence at 90 days were comparable when defined by mRS score 0–2 and mRS score 0–3. For mRS score 0–2, a meta-analysis of 31 studies (Figure 3A) demonstrated that patients treated with BT were

Table 2 Outcomes in the Bridging and Direct Thrombectomy Groups in the CRCS-K/TREAT-AIS Registries

Outcomes	Bridging thrombectomy (n = 281)	Direct thrombectomy (n = 592)	Crude OR (95% CI)	Adjusted OR (95% CI)[a]	Matched OR (95% CI)[b]
Clinical					
90-d mRS score	3 (1–5)	4 (2–6)	1.62 (1.26–2.09)[c]	1.44 (1.09–1.91)[c]	1.44 (1.00–2.07)[c]
90-d mRS score 0–2	115 (40.9%)	169 (28.6%)	1.73 (1.24–2.42)[c]	1.53 (1.01–2.30)[c]	1.19 (0.59–2.40)
90-d mRS score 0–3	148 (52.7%)	243 (41.1%)	1.59 (1.20–2.11)[c]	1.40 (1.01–1.92)[c]	1.31 (0.77–2.25)
90-d mortality	49 (17.4%)	159 (26.9%)	0.55 (0.38–0.82)[c]	0.51 (0.33–0.81)[c]	0.45 (0.26–0.78)[c]
Radiologic					
Successful reperfusion	199 (79.3%)	429 (81.1%)	0.93 (0.63–1.37)	0.82 (0.52–1.32)	0.74 (0.42–1.31)
Symptomatic ICH	7 (2.5%)	17 (2.9%)	0.84 (0.39–1.78)	0.99 (0.44–2.20)	0.83 (0.25–2.70)

Abbreviations: CRCS-K = Comprehensive Registry of Stroke in Korea; ICH = intracranial hemorrhage; mRS = modified Rankin Scale; OR = odds ratio; TREAT-AIS = Taiwan Registry of Endovascular Thrombectomy for Acute Ischemic Stroke.
[a] Adjusted covariates include age, sex, country, prestroke mRS score, diabetes mellitus, old-stroke, direct oral anticoagulant use, stroke etiology, and onset-to-puncture time.
[b] Propensity score–matched cohort-based analysis with adjusted covariates including old stroke, direct oral anticoagulants use, and onset-to-puncture time.
[c] Indicates statistical significance ($p < 0.05$).

Figure 2 Effect of Onset-to-Puncture Time on Functional Independence Associated With BT vs DT in the CRCS-K/TREAT-AIS Registries



(A) Distribution of onset-to-puncture time in patients receiving DT and BT. The light blue bars indicate patients in the DT group while the overlaid gray bars represent patients in the BT group. Most of the patients underwent the procedure within the first 400 minutes, with a notable proportion receiving BT compared with DT. (B) The predicted odds ratio represents the likelihood of achieving functional independence (modified Rankin Scale scores of 0, 1, or 2) at 90 days in the BT compared with the DT group. The shaded area indicates the 95% CIs of the odds ratio. When the onset-to-puncture time exceeds 400 minutes, the lower bound of CIs crosses the null point. BT = bridging thrombectomy; CRCS-K = Comprehensive Registry of Stroke in Korea; DT = direct thrombectomy; TREAT-AIS = Taiwan Registry of Endovascular Thrombectomy for Acute Ischemic Stroke.

more likely to achieve functional independence compared with those treated with DT (OR 1.57, 95% CI 1.28–1.94; 5,926 participants; 31 studies; I^2 = 42%). Similarly, for mRS score 0–3, a meta-analysis of 13 studies (Figure 3B) showed consistent findings (OR 1.33, 95% CI 1.05–1.68; 3,681 participants; 13 studies; I^2 = 14.9%). Lower mortality rates were observed in the BT group compared with the DT group in our meta-analysis of 11 studies (OR 0.77, 95% CI 0.61–0.97; 3,781 participants; 11 studies; I^2 = 24.8%; Figure 3C). For sICH, our meta-analysis indicated that the choice between BT and DT did not influence the rates of sICH. A meta-analysis of 10 studies (Figure 3D) found no significant difference between the 2 approaches (OR 1.01, 95% CI 0.71–1.44; 3,699 participants; 10 studies; I^2 = 0%).

Table 3 Subgroup Analyses of Bridging vs Direct Thrombectomy on 90-Day mRS Scores in the CRCS-K/TREAT-AIS Registries

Subgroups	Adjusted OR (95% CI)[a]	$p_{interaction}$
Location of occlusion		0.871
Basilar artery (n = 679)	1.29 (0.92–1.79)	
Nonbasilar artery (n = 194)	1.70 (0.94–3.09)	
NIHSS score		0.224
<10 (n = 599)	1.10 (0.66–1.84)	
≥10 (n = 274)	1.87 (1.30–2.70)[b]	
Onset-to-puncture time		0.641
<6 h (n = 463)	1.55 (1.08–2.22)[b]	
≥6 h (n = 410)	1.13 (0.62–2.08)	

Abbreviations: CRCS-K = Comprehensive Registry of Stroke in Korea; mRS = modified Rankin Scale; NIHSS = NIH Stroke Scale; OR = odds ratio; TREAT-AIS = Taiwan Registry of Endovascular Thrombectomy for Acute Ischemic Stroke.
[a] Effect estimates indicate the effect of bridging vs direct thrombectomy on a 1-point improvement in the 90-day mRS. Covariates adjusted for include age, sex, country, prestroke independency, diabetes mellitus, previous stroke, direct oral anticoagulant use, stroke etiology, and onset-to-puncture time (except for onset-to-puncture time subgroup).
[b] Indicates statistical significance ($p < 0.05$).

Classification of Evidence

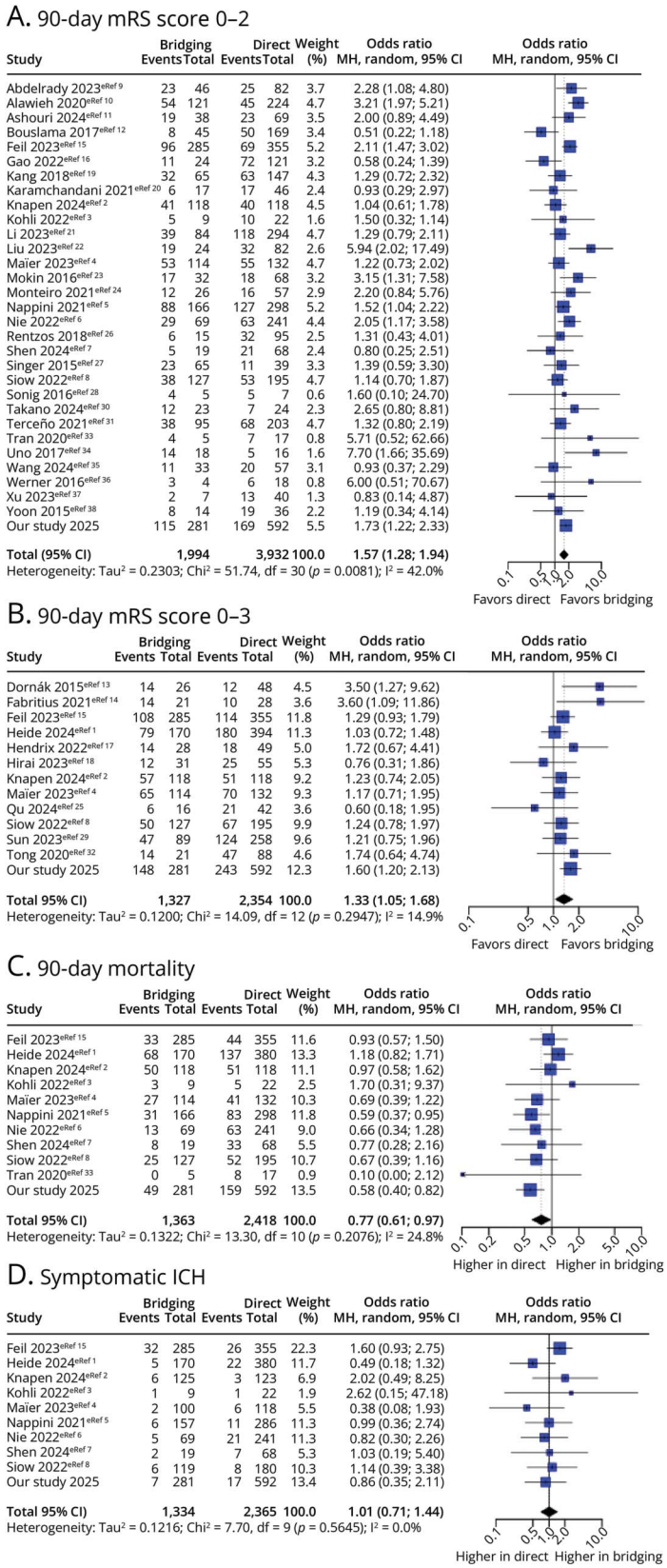
This study provides Class III evidence that in patients with posterior circulation stroke undergoing thrombectomy, previous IVT is associated with better 90-day functional outcomes and lower mortality without increasing hemorrhagic risk.

Discussion

This binational, multicenter study examined real-world outcomes of BT vs DT in posterior circulation LVO strokes. Our findings indicate that BT is associated with improved functional outcomes and reduced mortality, without increasing the risk of sICH, highlighting its safety profile. It is important to note that our study used harmonized data from 2 large, nationwide registries across Taiwan and South Korea. The large sample size, robust methodological adjustments, and addition of an updated meta-analysis further strengthen the evidence supporting BT and enhance the clinical relevance and generalizability.

The 6 randomized controlled trials comparing BT and DT focused on anterior circulation LVO strokes.[1] DIRECT-SAFE was the only trial that included patients with basilar artery

Figure 3 Forest Plots Comparing BT vs DT Based on the Meta-Analysis



Outcomes shown include (A) proportion of patients achieving 90-day mRS score 0–2, (B) 90-day mRS score 0–3, (C) 90-day mortality, and (D) symptomatic ICH in patients receiving BT vs DT. Pooled odds ratios and 95% CIs were calculated using random-effects models. BT = bridging thrombectomy; DT = direct thrombectomy; ICH = intracranial hemorrhage; mRS = modified Rankin Scale.

occlusion.[25] Of interest, in their subgroup analyses, the primary outcome (mRS score 0–2 or return to baseline) strongly favored BT (adjusted OR 0.13, 95% CI 0.01–1.75, comparing DT with BT). However, the CIs were wide because of small sample size (n = 18). In previous observational studies, the results did not universally favor BT. For example, in the Endovascular Treatment in Ischemic Stroke (ETIS) and the Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands (MR CLEAN) registries,[15,16] BT was not associated with better outcomes compared with DT. A potential explanation is the relatively small differences in onset-to-puncture time between the BT and DT groups—6 minutes in ETIS and 126 minutes in MR CLEAN. However, our meta-analysis of available observational studies suggests that BT may still be associated with a higher likelihood of improved functional outcomes compared with DT.

There are several potential reasons why BT achieves better outcomes in patients with posterior circulation LVO stroke. First, patients undergoing BT typically receive faster treatment, including both thrombolysis and puncture times. Given the central principal of "time is brain" in the acute stroke care, these findings are not surprising in nonrandomized, observational studies. Second, IVT can partially dissolve the thrombus and soften hard clots, even if not completely, before thrombectomy is performed.[26] This may be particularly relevant in the context of posterior circulation stroke, where intracranial atherosclerotic disease is more prevalent, especially in Asian populations.[4] This was echoed by the multinational study[14] showing that the BT group was only associated with improved functional outcomes in patients with underlying atherosclerosis. Patients with intracranial atherosclerotic disease often develop more collateral vessels, and it is speculated that IV thrombolytic agents may be delivered through these vessels, enabling them to dissolve distal thrombi more effectively.[27] Third, thrombolytic agents may enhance microcirculation and help prevent the no-reflow phenomenon, even after successful recanalization of the LVO, although this hypothesis remains under debate.[28,29]

Our analysis demonstrates that the effectiveness of BT is most pronounced when the onset-to-puncture time is within 400 minutes, beyond which the effects diminish. These findings align with Kaesmacher's meta-analysis of clinical trials on anterior circulation LVO strokes, which showed that the benefit of BT was time-dependent and decreased when the onset-to-needle time exceeded 2 hours and 20 minutes.[30] Notably, unlike in Kaesmacher's study, we were unable to calculate the "hypothetical" onset-to-needle time for the DT group because of the nonrandomized nature of our study and the significant time discrepancy between the 2 groups. Therefore, we could only use the onset-to-puncture time to determine the threshold beyond which the effects of BT are no longer evident.

Compared with anterior circulation stroke, the longer therapeutic window for BT in posterior circulation stroke suggests that the decision to administer IVT is less controversial in this patient group. In other words, for patients with posterior circulation stroke who present to the emergency department within the IVT time window, our data indicate that BT is superior to DT. The recently published EXPECTS trial demonstrated that IVT may be beneficial for posterior circulation strokes even in 4.5 to 24 hours after onset, indicating a potential for extending treatment time window.[31] However, it is important to note that the trial mainly included patients with relatively mild strokes (median NIHSS score 3) who were not planned for thrombectomy. Whether BT can be extended to patients presenting beyond 4.5 hours who are eligible for thrombectomy remains an open question.

In this study, BT demonstrated a comparable rate of sICH to DT (2.5% vs 2.9%), which was lower than in previous randomized trials of anterior circulation LVO stroke (5.4% vs 4.3%).[1] Notably, the meta-analysis of EVT trials of BA occlusion showed a significantly higher rates of sICH in the EVT group compared with controls (5% vs <1%).[10] Nonetheless, the sICH rate observed in our study (<3%) was lower than the 5% reported in those trials, reinforcing the safety of BT in posterior circulation stroke and alleviating concerns about increased hemorrhagic risk associated with IVT.

The updated meta-analysis, incorporating 39 studies and over 7,000 patients, provides a comprehensive synthesis of existing evidence. A previous meta-analysis of the same topic included only 17 studies, and 3,278 patients showed that BT was associated with a higher proportion of mRS score 0–2 (OR 1.83, 95% CI 1.54–2.19), but not mRS score 0–3 outcomes (OR 1.18, 95% CI 0.96–1.45).[32] Our expanded data set demonstrates greater statistical power and reduced heterogeneity. For example, we demonstrated that the BT is also associated with a higher proportion of mRS score 0–3 outcomes. These findings underscore the robustness and external validity of our study conclusions.

The strengths of this study lie in its large sample size, cross-country collaboration, and robust methodological approaches, including propensity score matching and sensitivity analyses. The harmonized data set from 2 distinct registries enhances the generalizability of our findings while the inclusion of an updated meta-analysis strengthens their external validity. However, several limitations must be acknowledged. The first major limitation is the clear time imbalance between the BT and DT group. To address this, we performed extensive statistical adjustments, including covariate adjustment, propensity score matching, and sensitivity analyses. Nevertheless, some covariates, particularly previous stroke and use of oral anticoagulants, remained imbalanced between groups, with standardized mean differences exceeding 0.2. These residual imbalances may introduce unmeasured confounding and limit the internal validity of the propensity-matched comparisons. Second, the extent of early infarction—such as the pc-ASPECTS[33] or the Basilar Artery on Computed Tomography Angiography score[34]—was not

registered prospectively across the entire cohort. Although we retrospectively assessed pc-ASPECTS in a subset of 197 Taiwanese patients, this partial data may not fully capture infarct burden across all study sites. Given the potential for prolonged time to treatment in the DT group to result in larger infarcts, the absence of comprehensive baseline imaging data remains a key limitation. Our future studies should incorporate standardized imaging assessment to better account for early ischemic damage. Third, our data set did not collect collateral status or specific occlusion sites, such as proximal, middle, or distal BA occlusions. In clinical trials, EVT has shown greater benefit in more proximal BA occlusions.[10] However, we were unable to determine whether this benefit is enhanced with the addition of IVT. Fourth, our study predominantly included East Asian populations, where intracranial atherosclerosis is more prevalent; thus, the results may not fully generalize to populations with different stroke etiologies. Fifth, outcome assessors were also not formally blinded, although 90-day mRS score was evaluated by trained case managers independent of treatment decisions, which helped minimize potential bias. Finally, our meta-analysis was limited to study-level data. Individual patient data, necessary for more granular adjustments, such as accounting for time differences between BT and DT groups, were not available.

In conclusion, our study provides strong evidence to support the use of BT in posterior circulation strokes, especially if the patients presented early within the standard time window of IVT. Efforts to improve the recognition and rapid treatment of posterior circulation strokes are critical to maximizing therapeutic outcomes. Future randomized controlled trials are needed to confirm these findings.

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