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## Endovascular therapy versus no endovascular therapy in patients receiving best medical management for acute isolated occlusion of the posterior cerebral artery : A systematic review and meta-analysis

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## ORIGINAL ARTICLE

# Endovascular therapy versus no endovascular therapy in patients receiving best medical management for acute isolated occlusion of the posterior cerebral artery: A systematic review and meta-analysis

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## Abstract

**Background and purpose:** Endovascular therapy (EVT) is increasingly reported for treatment of isolated posterior cerebral artery (PCA) occlusions although its clinical benefit remains uncertain. This study-level meta-analysis investigated the functional outcomes and safety of EVT and best medical management (BMM) compared to BMM alone for treatment of PCA occlusion stroke.

Anne Berberich and Stephanos Finitis are co-first authors and contributed equally.

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**Methods:** We conducted a literature search in PubMed, Web of Science and Embase for studies in patients with isolated PCA occlusion stroke treated with EVT + BMM or BMM including intravenous thrombolysis. There were no randomized trials and all studies were retrospective. The primary outcome was modified Rankin Scale score of 0–2 at 3 months, while safety outcomes included mortality rate and incidence of symptomatic intracranial hemorrhage (sICH).

**Results:** Twelve studies with a total of 679 patients were included in the meta-analysis: 338 patients with EVT + BMM and 341 patients receiving BMM alone. Good functional outcome at 3 months was achieved in 58.0% (95% confidence interval [CI] 43.83–70.95) of patients receiving EVT + BMM and 48.1% (95% CI 40.35–55.92) of patients who received BMM alone, with respective mortality rates of 12.6% (95% CI 7.30–20.93) and 12.3% (95% CI 8.64–17.33). sICH occurred in 4.2% (95% CI 2.47–7.03) of patients treated with EVT + BMM and 3.2% (95% CI 1.75–5.92) of patients treated with BMM alone. Comparative analyses were performed on studies that included both treatments and these demonstrated no significant differences.

**Conclusions:** Our results demonstrate that EVT represents a safe treatment for patients with isolated PCA occlusion stroke. There were no differences in clinical or safety outcomes between treatments, supporting randomization of future patients into distal vessel occlusion trials.

#### KEYWORDS

distal vessel occlusion, endovascular therapy, intravenous thrombolysis, posterior cerebral artery occlusion, stroke

## INTRODUCTION

Posterior cerebral artery (PCA) infarcts account for approximately 5%–10% of all acute ischemic strokes [1–3]. Patients with PCA occlusion strokes may experience disabling symptoms including visual field defects, cognitive dysfunction, and hemisensory symptoms or hemiparesis in more proximal occlusions [3]. Although clinical symptoms of PCA infarcts may result in a low National Institute of Health Stroke Scale (NIHSS) score, they can severely impact a patient's functional independence and quality of life [1, 4, 5].

Endovascular therapy (EVT) represents a standard treatment for patients with acute ischemic strokes attributable to large vessel occlusions in the anterior circulation [6, 7]. With advances in thrombectomy devices and techniques, the use of EVT is expanding to medium and distal vessel occlusions [8–11]. In addition, EVT is increasingly used to treat patients with isolated occlusions of the PCA. Several recent studies demonstrated the feasibility and safety of EVT in these patients [5, 12–21]. However, randomized clinical trials demonstrating the efficacy of EVT in the treatment of isolated PCA occlusions are lacking.

We performed a study-level systematic review and meta-analysis of publications reporting on treatment of patients with strokes caused by isolated PCA occlusion to investigate the functional outcomes and safety of EVT and best medical management (BMM) compared to BMM alone.

## METHODS

### Systematic review

We conducted a literature review according to the Preferred Reporting Items for Systematic Reviews (PRISMA; Figure S1) [22]. PubMed, Web of Science and Embase databases were explored using the following keywords and their combinations: “posterior cerebral artery”, “thrombectomy”, “endovascular treatment” and “thrombolysis”, from inception until March 15, 2022. The literature search was conducted and publications were analyzed by two authors (A.B. and S.F.). Studies in the English language and series including more than five patients were considered. Studies reporting treatment of acute ischemic stroke due to isolated PCA occlusion with either EVT + BMM or BMM alone, with or without intravenous thrombolysis, (IVT) were included. Studies for which data specific to PCA occlusion could not be extracted were excluded. Possible redundant study populations within distinct publications were excluded. Where authors and/or participating centers were identified in multiple articles, only the most recently published was considered in our analysis.

The primary outcome of interest was (the odds of) a favorable functional outcome, defined as a modified Rankin Scale (mRS) score of 0–2 at 3 months. Secondary safety outcomes included symptomatic intracranial hemorrhage (sICH) and mortality at 3 months. sICH was defined according to the European Cooperative Acute Stroke Study (ECASS) II or III criteria in most of

the studies [5, 13, 15, 16, 19, 23–26]; the studies by Herweh et al. and Brouwer et al. used the Heidelberg bleeding classification for definition of sICH [12, 21, 27]. Information extracted from each study included sample size, age, sex, percentage of patients receiving IVT, NIHSS score at admission, time from onset of symptoms to acute treatment (IVT or puncture), rate of successful reperfusion, rate of sICH, clinical outcomes and mortality at 3 months. Studies were included in the quantitative synopsis if the study followed patients up for at least 3 months using the mRS and reported on adverse events including sICH and mortality. Patients were allocated to groups based on the modality of treatment. Those treated with EVT+BMM with or without bridging IVT comprised the EVT group. Patients who received medical treatment with or without IVT comprised the BMM group.

The article by Baik et al. was excluded from the analysis of good clinical outcome because a different definition of favorable functional outcome was used in the study (mRS of 0–1 instead of 0–2) [16]. We obtained supplemental data for the analysis of good clinical outcome by Strambo et al., who also used a different definition of favorable functional outcome in their publication [5]. The article by Baik et al. did not report on the mortality rate and was therefore excluded from the analysis of mortality at 3 months [16].

Quality assessment was performed independently by two authors (A.B. and S.F.) using the Cochrane Risk of Bias tool [28]. Any disagreements were resolved by discussion or by recourse to a third-party reviewer (T.N.N.; Table S1, Figures S2 and S3).

## Statistical analysis

Summary effects were calculated using a random effect model using DerSimonian and Laird estimators with a logit transformation of raw proportions. Individual effect sizes and their sampling variances were calculated using the inverse variance method. Outcomes were presented as proportions with 95% confidence intervals (CIs). Heterogeneity of treatment effect across studies was assessed using the Cochran's  $Q$ -test ( $p$ -value threshold of 0.05), and quantified with the  $I^2$  statistic, with  $I^2 > 50\%$  suggesting substantial heterogeneity. Publication bias was estimated visually by funnel plots. The analysis was performed using the metaphor package of R Statistical Software (version 3.6.2) and STATA 17 Software.

The study was registered in the International Prospective Register of Ongoing Systematic Reviews (PROSPERO; CRD42022310594).

## RESULTS

### Systematic review

We reviewed 441 studies, of which 152 were duplicates. Another 265 studies were excluded because they did not relate to the specific topic and two were excluded because the relevant data could

not be extracted. Another five studies were excluded because of possible redundant study populations, and five studies reported fewer than five patient cases.

Twelve studies were included in the analysis [5, 12–16, 18, 19, 21, 25, 26, 29]. The search strategy is shown in Figure S1. All publications had a retrospective design, no core laboratory and a small sample size. The quality assessment is described in Table S1.

Four of the 12 articles reported on both patients treated with EVT+BMM and patients receiving BMM, including IVT if administered, in both groups [5, 12, 13, 19]. Five studies reported only on patients treated with EVT+BMM [14–16, 18, 21], and three articles described only patients with BMM including IVT for treatment of isolated PCA occlusion [25, 26, 29].

A total of 679 patients were included in the analysis. All patients had isolated occlusions of the PCA in the P1, P2 or P3 segment of the artery.

Endovascular therapy was performed in 338 patients, of whom 147 received IVT. A total of 341 patients were treated with BMM including IVT in 183 patients.

Detailed patient characteristics are summarized for each article in Table 1 (patients treated with EVT+BMM) and Table 2 (patients treated with BMM).

The median NIHSS score ranged from a median of 7 to 14 points in the group of patients treated with EVT+BMM and from 5 to 9 points in the group of patients treated with BMM alone (Tables 1 and 2). Rates of complete reperfusion ranged from 58.8% to 100% in the EVT-treated group in respective studies, defined as a modified Thrombolysis in Cerebral Infarction (mTICI) scale or expanded Thrombolysis in Cerebral Infarction (eTICI) scale of 2b to 3 (Table 1). In comparison, the rate of complete reperfusion was between 43.6% and 66.6% in patients treated with BMM alone, although this was not angiographically proven in most of the cases in this patient group and was only described in a few studies (Table 2).

### Primary endpoint: Favorable outcome

The analysis of favorable functional outcome at 3 months included 340 patients treated with BMM from seven studies and 254 patients treated with EVT+BMM reported in eight studies (Figure 1a for BMM, Figure 1b for EVT+BMM). Favorable functional outcome at 3 months was achieved in 48.1% (95% CI 40.35–55.92) of patients with BMM and in 58.0% (95% CI 43.83–70.95) of patients with EVT+BMM. There was a significant heterogeneity of treatment effects between studies for the pooled analysis of patients treated with EVT+BMM ( $I^2 = 74\%$ ,  $p < 0.01$ ). The study by Baik et al. was excluded from the analysis of good clinical outcome because of its use of a different definition of favorable functional outcome. Excellent functional outcome, defined by an mRS score of 0–1, was achieved in 25 of 48 patients (52%) treated with EVT in this study [16].

For a comparison of good functional outcome between EVT+BMM and BMM alone, we evaluated four studies in which a total of 437

**TABLE 1** Patient characteristics of patients treated with endovascular therapy and best medical management for each study included in this meta-analysis

Authors	Year	n	Age, years; mean (SD)	Female, n/N (%)	NIHSS; median (IQR)	IVT, n/N (%)	Onset-treatment, min;	TICI2b-3	mRS 0-2, n/N (%)	sICH, n/N (%)	Mortality, n/N (%)
Memon et al. [14]	2020	15	64 (17)	9/15 (60)	9 (5-15)	7/15 (46)	Median 303 (IQR 67-756)	TICI 2c-3 12/15 (80)	9/15 (60)	1/15 (6%)	1/15 (6)
Strambo et al. [5]	2020	21	71 (64-78.2)	13/21 (61.9)	7 (5-8.3)	13/21 (62)	Mean 290 (range 198-384)	18/21 (85.7)	13/20 (65)	1/21 (4.7)	4/21 (19)
Nogueira et al. [15]	2020	22	66.2 (14.3)	10/22 (45.4)	14 (8-16)	11/22 (50)	Median 282 (range 210-642)	22/22 (100)	13/22 (59)	0/22 (0)	2/22 (9)
Herweh et al. [12]	2021	23	70 (13.3)	9/23 (39.1)	9 (1-20)	5/23 (21.7)	Mean 353 (range 263)	7/12 (58.3)	10/23 (43.5)	1/23 (4.3)	3/23 (13)
Meyer et al.	2021	143	Median 75 (IQR 62-81)	64/143 (44.7)	7 (4-11)	57/143 (39.8)	Median 197 (IQR 148-277)	125/143 (87.4)	86/109 (78.9)	5/143 (3.4)	12/109 (11)
Baig et al. [18]	2022	21	71.2 (10.2)	12/21 (57.1)	9 (5-15)	10/21 (47.6)	Median 189 (IQR 110-255)	17/21 (80.9)	15/21 (71.4)	1/21 (4.7)	2/21 (16.7)
Cunha et al. [19]	2022	25	Median 80.2 (73.8-83.4)	10/25 (36)	10 (6-14.5)	14/25 (56)	Median 224 (193-269)	17/25 (68)	12/24 (50)	0/25 (0)	0/25 (0)
Baik et al. [16]	2022	48	Median 75 (IQR 62-79)	14/48 (29.1)	9 (6-14)	18/48 (37.5)	Median 187 (IQR 132-328)	33/48 (68.8)	25/48 (52)	3/48 (6.3)	-
Brouwer et al. [21]	2022	20	Median 72 (63-81)	13/20 (65)	13 (5-21)	12 (60)	Mean 216 (181-260)	13/20 (65)	5/20 (25)	0/20 (0)	7/20 (35)

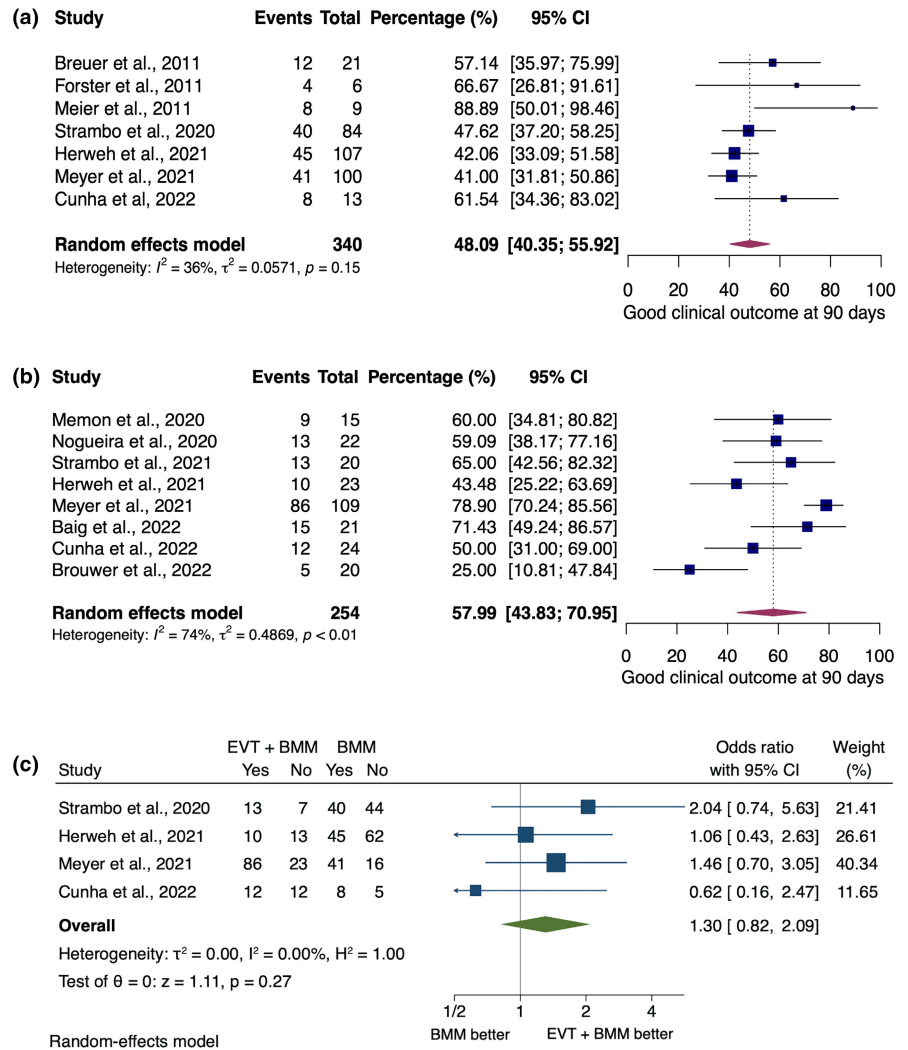
Abbreviations: IQR, interquartile range; IVT, intravenous thrombolysis; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; sICH, symptomatic intracranial hemorrhage; TICI, thrombolysis in cerebral infarction.

TABLE 2 Patient characteristics of the patients treated with best medical management for each study included in this meta-analysis

Authors	Year	n	Age, years; mean (SD)	Female, n/N (%)	IVT, n/N (%)	NIHSS; median (IQR)	Onset-treatment, min	Recanalization, complete or partial, n/N (%)	mRS 0-2, n/N (%)	sICH, n/N (%)	Mortality, n/N (%)
Breuer et al. [26]	2011	21	Median 72 (IQR 62.5-80)	15/21 (71.4)	21/21 (100)	6.5 (2-15)	-	-	12/21 (57.1)	0/21 (0)	0/21 (0)
Forster et al. [29]	2011	6	75 (7.8)	2/6 (33.3)	6/6 (100)	-	337 (range 196-380)	4/6 (66.6)	4/6 (66.6)	0/6 (0)	0/6 (0)
Meier et al. [13]	2011	9	66 (11.6)	4/9 (44.4)	9/9 (100)	9 (3-15)	180 (range 90-270)	5/9 (55.5)	8/9 (88.8)	0/9 (0)	0/9 (0)
Strambo et al. [5]	2020	34	78.7 (69.5-85.8)	17/34 (50)	34/34 (100)	7 (4.9-12.1)	135 (106.7-175)	17/33 (51.5)	16/34 (47)	1/34 (2.9)	6/34 (17.6)
Strambo et al. 2 [5]	2020	51	76.5 (67.2-81.1)	20 (39.2)	0/51 (0)	7 (4.9-12.1)	-	-	24/50 (48)	0/27 (0)	7/51 (13.7)
Herweh et al. [12]	2021	107	74 (13.1)	51/107 (51)	44/107 (41.1)	7 (1-38)	246 (210)	38/69 (55)	45/107 (42)	3/107 (2.8)	8/107 (7.4)
Meyer et al. [13]	2021	100	Median 75 (IQR 62-81)	50/100 (50)	56/100 (56)	5 (2-10)	Median 154 (IQR 120-218)	41/92 (43.6)	41/100 (71.9)	4/100 (4)	9/51 (17.5)
Cunha et al. [19]	2022	13	Median 74.9 (68.9-82.5)	6/13 (46.2)	13/13 (100)	8 (5.5-10)	138 (112.5-211)	-	8/13 (61.5)	0/13 (0)	2/13 (15.4)

Abbreviations: IVT, intravenous thrombolysis; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; sICH, symptomatic intracranial hemorrhage; TICI, thrombolysis in cerebral infarction.

**FIGURE 1** Favorable functional outcome at 3 months for pooled patient groups treated with either best medical management (a) or endovascular therapy and best medical management (b) and comparative analysis for publications reporting on both treatment modalities (c). A favorable functional outcome was defined as a modified Rankin Scale score of 0–2 at 3 months. Heterogeneity of treatment effect across studies was assessed with a  $p$ -value threshold of 0.05 and with  $I^2 > 50\%$  suggesting substantial heterogeneity. BMM, best medical management; CI, confidence interval; EVT, endovascular therapy; IVT, intravenous thrombolysis [Colour figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]



patients were treated (Figure 1c). No significant differences in frequency of good clinical outcome were found between EVT + BMM or BMM alone (odds ratio [OR] 1.30 [95% CI 0.82–2.09];  $p = 0.27$ ). There was no significant heterogeneity among the studies ( $I^2 = 0\%$ ).

### Secondary outcomes regarding safety

For the analysis of mortality rate after 3 months, 293 patients treated with BMM from seven studies and 290 patients treated with EVT + BMM from eight studies were considered (Figure 2a for BMM, Figure 2b for EVT + BMM). The mortality rate was 12.3% (95% CI 8.64–17.33) of 293 patients treated with BMM and 12.6% (95% CI 7.30–20.93) of 290 patients treated with EVT + BMM, with no significant heterogeneity detected ( $I^2 = 8\%$  and  $I^2 = 49\%$ , respectively; Table 3).

Four studies reported a total of 435 patients with both treatment modalities and these were included in a comparative analysis between EVT + BMM and BMM alone (Figure 2c). No significant difference in mortality rate at 3 months was found between the two treatment groups with an OR of 0.86 (95% CI 0.42–1.76;  $p = 0.68$ ), with no significant heterogeneity detected ( $I^2 = 12.4\%$ ).

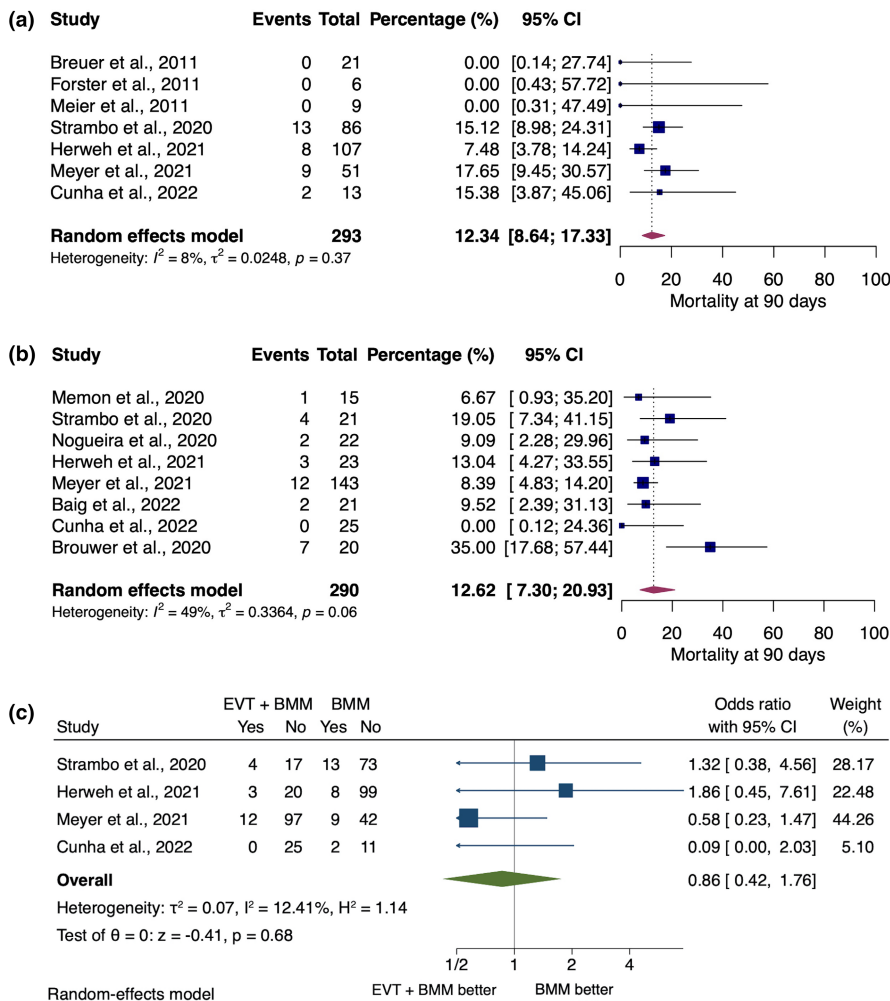
The incidence of sICH was analyzed in seven studies with a total of 321 patients treated with BMM and in nine studies with 338 patients treated with EVT + BMM (Figure 3a for BMM, Figure 3b for EVT + BMM). sICH occurred in 3.2% (95% CI 1.75–5.92) of patients treated with BMM and in 4.2% (95% CI 2.47–7.03) of patients treated with EVT + BMM, with no significant heterogeneity detected ( $I^2 = 0\%$ ).

Four studies reporting a total of 494 patients with both treatment modalities were included for comparative analysis (Figure 3c). The rate of sICH was similar in the two treatment groups (OR 1.12 [95% CI 0.40–3.16];  $p = 0.83$ ,  $I^2 = 0\%$ ). No significant heterogeneity was detected among studies for mortality and sICH analyses. We also found no evidence suggestive of publication bias by visually examining the respective funnel plots (Figure S4).

### DISCUSSION

This systematic review and meta-analysis showed that, overall, in patients presenting with isolated acute PCA occlusion stroke, a favorable functional outcome at 3 months was achieved in 48.1%





**FIGURE 2** Mortality rate at 3 months for pooled patient groups treated with either best medical management (a) or endovascular therapy and best medical management (b) and comparative analysis for publications reporting on both treatment modalities (c). Heterogeneity of treatment effect across studies was assessed with a  $p$ -value threshold of 0.05 and with  $I^2 > 50\%$  suggesting substantial heterogeneity. BMM, best medical management; CI, confidence interval; EVT, endovascular therapy; IVT, intravenous thrombolysis [Colour figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]

**TABLE 3** Overview of included studies in respective analyses and outcomes of interest

Outcomes	Patient groups	Number of patients (studies)	Percentage or relative effect (95% CI)	Heterogeneity
mRS score 0–2	BMM	340 (7)	48.1% (40.35–55.92)	$I^2 = 36\%$ , $p = 0.15$
mRS score 0–2	EVT+BMM	254 (8)	58.0% (43.83–70.95)	$I^2 = 74\%$ , $p < 0.01$
mRS score 0–2	BMM vs. EVT+BMM	437 (4)	OR 1.30 (0.82–2.09)	$I^2 = 0\%$ , $p = 0.27$
Mortality	BMM	293 (7)	12.3% (8.64–17.33)	$I^2 = 8\%$ , $p = 0.37$
Mortality	EVT+BMM	290 (8)	12.6% (7.30–20.93)	$I^2 = 49\%$ , $p = 0.06$
Mortality	BMM vs. EVT+BMM	435 (4)	OR 0.86 (0.42–1.76)	$I^2 = 12\%$ , $p = 0.7$
sICH	BMM	321 (7)	3.2% (1.75–5.92)	$I^2 = 0\%$ , $p = 0.98$
sICH	EVT+BMM	338 (9)	4.2% (2.47–7.03)	$I^2 = 0\%$ , $p = 0.99$
sICH	BMM vs. EVT+BMM	494 (4)	OR 1.12 (0.40–3.16)	$I^2 = 0\%$ , $p = 0.83$

Abbreviations: BMM, best medical management; EVT, endovascular therapy; mRS, modified Rankin Scale; OR, odds ratio; sICH, symptomatic intracranial hemorrhage.

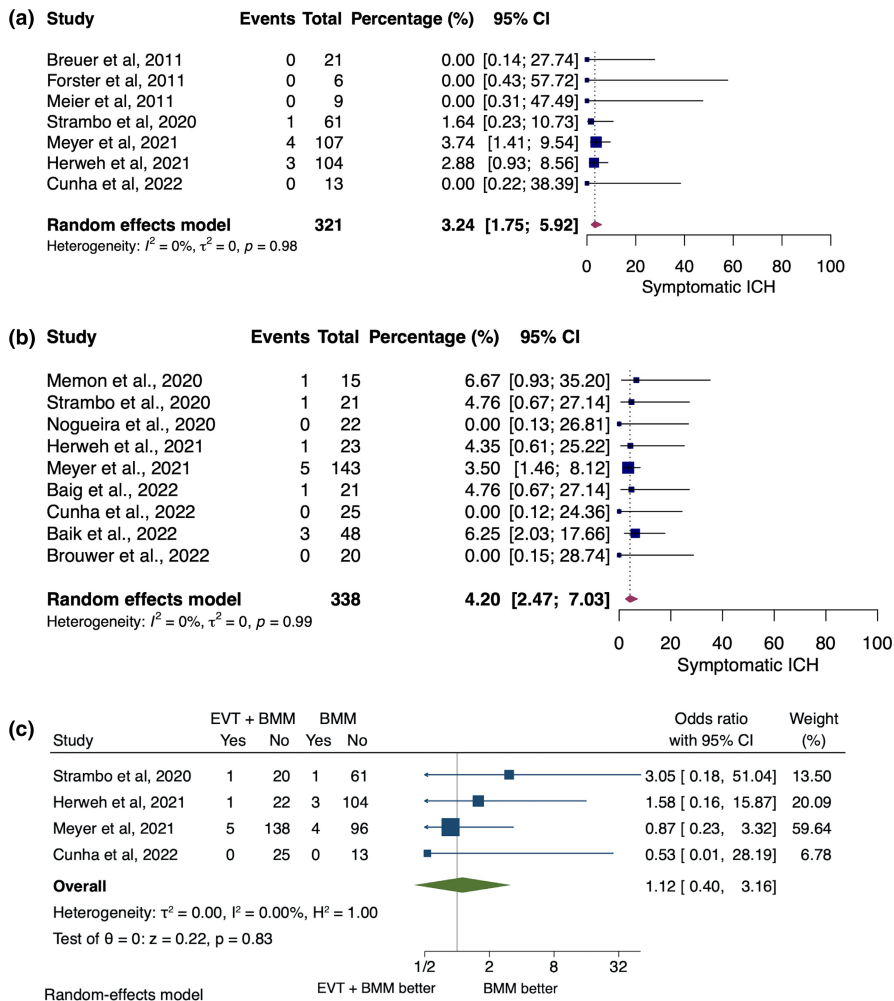
(95% CI 40.35–55.92) of patients treated with BMM and in 58.0% (95% CI 43.83–70.95) of patients treated with EVT+BMM. We did not identify any significant difference in the meta-analysis of studies comprising both EVT and BMM groups. There was no difference in sICH or mortality between the EVT and BMM groups in the isolated analyses for each treatment regimen or in the comparative meta-analysis. These results are consistent with the respective

conclusions reported in the studies included in this meta-analysis [5, 12, 13, 17, 19].

One explanation for the lack of differences between EVT+BMM and BMM alone may be that we performed a study-level meta-analysis and, therefore, the included patients were not balanced between treatment groups in terms of age, baseline symptom severity or location of occlusion in the PCA (proximal or distal segment of



**FIGURE 3** Symptomatic intracranial hemorrhage for pooled patient groups treated with either best medical management (a) or endovascular therapy and best medical management (b) and comparative analysis for publications reporting on both treatment modalities (c). Heterogeneity of treatment effect across studies was assessed with *p*-value threshold of 0.05 and with  $I^2 > 50\%$  suggesting substantial heterogeneity. BMM, best medical management; C.I., confidence interval; EVT, endovascular therapy; IVT, intravenous thrombolysis [Colour figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]



the artery). Also, there was a heterogeneity of treatment effects between studies for the pooled analysis of favorable functional outcomes of patients treated with EVT + BMM.

The median NIHSS score was higher in the EVT group, ranging from a median NIHSS score of 7–14 points compared with a median NIHSS score of 5–9 points in the BMM group. As no clear recommendation for the treatment of patients with PCA occlusions exists, the higher NIHSS score in the EVT group might indicate that patients with a high NIHSS score were considered in particular for EVT. Although the EVT group comprised patients with more severe symptoms, 58% of these patients had a favorable functional outcome and 12% of patients died at 3 months. Of note, Meyer et al. found a significant treatment effect of EVT in the subgroup of patients with an NIHSS score of 10 points or higher at admission and in patients not eligible for IVT [13]. Therefore, the results may indicate that EVT is a reasonable treatment option for at least some patients with isolated PCA occlusion.

It is also possible that mRS score is less effective in discriminating differential treatment effects at 3 months in this patient population presenting with milder deficit compared with most patients with anterior circulation large vessel occlusion, or with deficits such as visual field loss or cognitive impairment that may be disabling without a major impact on the mRS. Consequently, other primary endpoints, such as change in NIHSS score or adjusted NIHSS score at 24 h or

hospital discharge could be considered as alternative outcome measures in future studies [30].

Complete reperfusion was achieved more frequently in patients treated with EVT + BMM, with rates of complete reperfusion ranging from 58.8% to 100% in the respective studies compared with recanalization rates of 43.6%–66.6% observed in patients treated with BMM alone, although this was not angiographically proven for the latter group in most of the cases. Meyer et al. and Herweh et al. reported that successful recanalization more often resulted in early neurological improvement, although this was not reflected in improvement of mRS score at 3 months [12, 13].

Regarding the safety of mechanical thrombectomy for isolated PCA occlusions, we found no difference in the incidence of sICH or mortality between patients treated with EVT + BMM and those treated with BMM alone. The rate of sICH was low in both groups: 4.2% (95% CI 2.47–7.03) in patients treated with EVT + BMM and 3.2% (95% CI 1.75–5.92) in patients treated with BMM alone (OR 1.12, 95% CI 0.40–3.16 in the comparative meta-analysis), and the mortality rate was similarly low: 12.6% in the EVT-treated group and 12.3% in the BMM-treated group. These results highlight that mechanical thrombectomy is a safe treatment option in patients with isolated PCA occlusion stroke. The similar clinical and safety outcomes between BMM alone and EVT + BMM support

the randomization of patients with isolated PCA occlusion into ongoing trials on distal vessel occlusion stroke (NCT05029414, NCT05151172, NCT 05030142) [31].

This meta-analysis has several limitations. All included studies were retrospective and non-randomized. Since there is no recommendation for a standard treatment in patients with isolated PCA occlusion, selection bias for the particular treatment cannot be excluded, nor can publication bias, although we assessed the heterogeneity of treatment effects across studies. The latter is particularly relevant because we also included studies reporting on patients treated only with EVT+BMM or only with BMM including IVT. Furthermore, patients in the respective treatment groups were not balanced for baseline characteristics or location of isolated PCA occlusion (posterior communicating segment, P1 to P3 segment) in our study-level analysis.

In conclusion, to our knowledge, this is the largest study to date to systematically review patients with isolated PCA occlusion stroke treated with EVT and medical management compared to medical management alone, and may serve as a basis on which to guide clinical practice in this patient population. Our data confirmed that EVT is a safe and feasible treatment option for these patients. We could not demonstrate a significant difference in the frequency of favorable functional outcomes at 3 months between EVT+BMM and BMM alone. Further analysis of individual patient-level data controlling for baseline characteristics would provide more detailed information on treatment effects in subgroups of patients and permit stratified guidance on the treatment of patients with isolated PCA occlusion stroke until randomized clinical trial data become available to more definitively answer the question about the efficacy of EVT in this patient population.

## AUTHOR CONTRIBUTIONS

**Anne Berberich:** Conceptualization (equal); investigation (lead); methodology (equal); validation (lead); writing – original draft (lead). **Stephanos Finitis:** Conceptualization (lead); data curation (lead); formal analysis (lead); investigation (lead); methodology (lead); supervision (lead); visualization (lead); writing – review and editing (lead). **Davide Strambo:** Data curation (equal); validation (equal); writing – review and editing (equal). **Patrik Michel:** Validation (equal); writing – review and editing (equal). **Christian Herweh:** Validation (equal); writing – review and editing (equal). **Lukas Meyer:** Validation (equal); writing – review and editing (equal). **Uta Hanning:** Validation (equal); writing – review and editing (equal). **Daniel Strbian:** Validation (equal); writing – review and editing (equal). **Mohamad Abdalkader:** Validation (equal); writing – review and editing (equal). **Raul G Nogueira:** Validation (equal); writing – review and editing (equal). **Volker Puetz:** Visualization (equal); writing – review and editing (equal). **Daniel Kaiser:** Validation (equal); writing – review and editing (equal). **Marta Olive-Gadea:** Validation (equal); writing – review and editing (equal). **Marc Ribó:** Validation (equal); writing – review and editing (equal). **Isabel Fragata:** Validation (equal); writing – review and editing (equal). **João Pedro Marto:** Validation (equal); writing – review and editing (equal). **Michele Romoli:** Validation

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## CONFLICT OF INTEREST

Thanh Nguyen reports research support from Medtronic and SVIN, unrelated to the present work. Simon Nagel reports consulting fees for Brainomix and lecture fees from BMS Pfizer and Böhringer Ingelheim, outside the scope of this study. Peter Ringleb reports consulting and lecture fees from Boehringer Ingelheim, Bayer and BMS, and lecture fees from Pfizer, outside this work. Daniel Kaiser reports a research collaboration with Brainomix with no payment and outside the scope of this study. Raul Nogueira reports consulting fees for advisory roles with Anaconda, Biogen, Cerenovus, Genentech, Philips, Hybernia, Imperative Care, Medtronic, Phenox, Philips, Prolong Pharmaceuticals, Stryker Neurovascular, Shanghai Wallaby and Synchron, and stock options for advisory roles with Astrocyte, Brainomix, Cerebrotech, Ceretrieve, Corindus Vascular Robotics, Vesalio, Viz-AI, RapidPulse and Perfuze. Raul Nogueira is one of the Principal Investigators of the “Endovascular Therapy for Low NIHSS Ischemic Strokes (ENDOLOW)” trial. Funding for this project was provided by Cerenovus. Raul Nogueira is an investor in Viz-AI, Perfuze, Cerebrotech, Reist/Q'Apel Medical, Truvic, Vastrax and Viseon.

## DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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## REFERENCES

1. Ntaios G, Spengos K, Vemmou AM, et al. Long-term outcome in posterior cerebral artery stroke. *Eur J Neurol*. 2011;18(8):1074-1080.
2. Cereda C, Carrera E. Posterior cerebral artery territory infarctions. *Front Neurol Neurosci*. 2012;30:128-131.

3. Brandt T, Steinke W, Thie A, Pessin MS, Caplan LR. Posterior cerebral artery territory infarcts: clinical features, infarct topography, causes and outcome. Multicenter results and a review of the literature. *Cerebrovasc Dis*. 2000;10(3):170-182.
4. Ng YS, Stein J, Salles SS, Black-Schaffer RM. Clinical characteristics and rehabilitation outcomes of patients with posterior cerebral artery stroke. *Arch Phys Med Rehabil*. 2005;86(11):2138-2143.
5. Strambo D, Bartolini B, Beaud V, et al. Thrombectomy and thrombolysis of isolated posterior cerebral artery occlusion: cognitive, visual, and disability outcomes. *Stroke*. 2020;51(1):254-261.
6. Goyal M, Menon BK, van Zwam WH, et al. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. *Lancet*. 2016;387(10029):1723-1731.
7. Eskey CJ, Meyers PM, Nguyen TN, et al. Indications for the performance of intracranial endovascular neurointerventional procedures: a scientific statement from the American Heart Association. *Circulation*. 2018;137(21):e661-e689.
8. Saver JL, Chapot R, Agid R, et al. Thrombectomy for distal, medium vessel occlusions: a consensus statement on present knowledge and promising directions. *Stroke*. 2020;51(9):2872-2884.
9. Perez-Garcia C, Moreu M, Rosati S, et al. Mechanical thrombectomy in medium vessel occlusions: blind exchange with minipinning technique versus mini stent retriever alone. *Stroke*. 2020;51(11):3224-3231.
10. Puetz V, Strbian D, Nguyen TN, Nagel S. Editorial: challenges in posterior circulation ischemic stroke. *Front Neurol*. 2021;12:789836.
11. Abdalkader MSA, Dmytriw AA, Brinjikji W, Dabus G, Raz E, et al. Mechanical thrombectomy of the fetal posterior cerebral artery. Stroke: vascular and interventional. *Neurology*. 2021;2021(1):e000115.
12. Herweh C, Abdalkader M, Nguyen TN, et al. Mechanical thrombectomy in isolated occlusion of the proximal posterior cerebral artery. *Front Neurol*. 2021;12:697348.
13. Meyer L, Stracke CP, Jungi N, et al. Thrombectomy for primary distal posterior cerebral artery occlusion stroke: the TOPMOST study. *JAMA Neurol*. 2021;78(4):434-444.
14. Memon MZ, Kushnirsky M, Brunet MC, Saini V, Koch S, Yavagal DR. Mechanical thrombectomy in isolated large vessel posterior cerebral artery occlusions. *Neuroradiology*. 2021;63(1):111-116.
15. Nogueira RG, Mohammaden MH, Haussen DC, et al. Endovascular therapy in the distal neurovascular territory: results of a large prospective registry. *J Neurointerv Surg*. 2021;13(11):979-984.
16. Baik SH, Jung C, Kim BM, Kim DJ. Mechanical thrombectomy for acute posterior cerebral artery stroke; feasibility and predictors of outcome. *Neuroradiology*. 2022;64(7):1419-1427. doi:10.1007/s00234-022-02910-3
17. Monteiro A, Khan S, Waqas M, et al. Mechanical thrombectomy versus intravenous alteplase alone in acute isolated posterior cerebral artery occlusion: a systematic review. *J Neurointerv Surg*. 2021;14:564-567.
18. Baig AA, Monteiro A, Waqas M, et al. Acute isolated posterior cerebral artery stroke treated with mechanical thrombectomy: a single-center experience and review of the literature. *Interv Neuroradiol*. 2022;15910199211070949. doi:10.1177/15910199211070949. Online ahead of print.
19. Cunha B, Baptista M, Pamplona J, et al. Acute treatment of isolated posterior cerebral artery occlusion: single center experience. *J Stroke Cerebrovasc Dis*. 2022;31(2):106239.
20. Miszczuk M, Bauknecht HC, Kleine JF, et al. Mechanical thrombectomy of acute distal posterior cerebral artery occlusions. *J Clin Neurosci*. 2021;88:57-62.
21. Brouwer J, Ergezen S, Mulder M, et al. Endovascular treatment for isolated posterior cerebral artery occlusion stroke in the MR CLEAN registry. *J Neurointerv Surg*. 2022;neurintsurg-2021-018505. doi:10.1136/neurintsurg-2021-018505. Online ahead of print.
22. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. *BMJ*. 2009;339:b2700.
23. Hacke W, Kaste M, Fieschi C, et al. Randomised double-blind placebo-controlled trial of thrombolytic therapy with intravenous alteplase in acute ischaemic stroke (ECASS II). Second European-Australasian acute stroke study investigators. *Lancet*. 1998;352(9136):1245-1251.
24. Hacke W, Kaste M, Bluhmki E, et al. Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke. *N Engl J Med*. 2008;359(13):1317-1329.
25. Meier N, Fischer U, Schroth G, et al. Outcome after thrombolysis for acute isolated posterior cerebral artery occlusion. *Cerebrovasc Dis*. 2011;32(1):79-88.
26. Breuer L, Huttner HB, Jentsch K, et al. Intravenous thrombolysis in posterior cerebral artery infarctions. *Cerebrovasc Dis*. 2011;31(5):448-454.
27. von Kummer R, Broderick JP, Campbell BC, et al. The Heidelberg bleeding classification: classification of bleeding events after ischemic stroke and reperfusion therapy. *Stroke*. 2015;46(10):2981-2986.
28. Higgins JP, Altman DG, Gotzsche PC, et al. The cochrane collaboration's tool for assessing risk of bias in randomised trials. *BMJ*. 2011;343:d5928.
29. Forster A, Gass A, Kern R, Wolf ME, Hennerici MG, Szabo K. MR imaging-guided intravenous thrombolysis in posterior cerebral artery stroke. *AJNR Am J Neuroradiol*. 2011;32(2):419-421.
30. Mistry EA, Yeatts S, de Havenon A, et al. Predicting 90-day outcome after thrombectomy: baseline-adjusted 24-hour NIHSS is more powerful than NIHSS score change. *Stroke*. 2021;52(8):2547-2553.
31. Campbell BCV, Nguyen TN. Advances in stroke: treatments-interventional. *Stroke*. 2022;53(1):264-267.

## SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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