Rescue Stenting versus Medical Care Alone in Refractory Large Vessel Occlusions: A Systematic Review and Meta-Analysis

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Keywords: Stroke, Thrombectomy, Endovascular Recanalization, Reperfusion

ABSTRACT

Purpose:

Mechanical thrombectomy (MT) failure is associated with very poor prognosis. Permanent intracranial stenting (PIS) may be useful in such refractory occlusions. However, this strategy requires an aggressive antithrombotic regimen that may be harmful in extended strokes. The aim of this study was to compare clinical outcomes between patients with refractory acute large vessel occlusions (LVO) treated by PIS versus patients for whom the procedure was stopped without recanalization.

Methods:

We conducted a systematic review by searching for articles in PubMed, the Cochrane Library and ClinicalTrials.gov from January 2015 to September 2019. Two reviewers independently selected studies comparing PIS after failed MT in addition to usual care versus usual care only. A comparative meta-analysis was performed using random-effects models to estimate odds ratios of favorable clinical outcome at 90 days, defined as a modified Rankin Scale 0-2, mortality and symptomatic intracranial haemorrhage (SICH).

Results:

Four comparative studies were included for a total of 352 patients: 149 in the PIS group versus 203 in the control group. PIS was associated with significantly higher rates of 90-day favorable clinical outcome (Odds Ratio [OR] : 2.87 [95% confidence interval (95% CI) : 1.77-4.66] ; $p<0.001$; I^2: 0%) and lower mortality (OR : 0.39 [0.16-0.93] ; $p=0.03$; I^2: 43%), whereas SICH rates did not significantly differ (OR 0.68 [0.37-1.27] ; $p=0.23$; I^2: 0%).

Conclusion:

From observational study results, attempting PIS after failed MT seems to improve clinical outcomes without increasing the risk of intracranial bleeding. Randomized trials are needed to confirm these results.

INTRODUCTION

Mechanical thrombectomy (MT) for acute ischemic stroke due to large-vessel occlusion (AIS-LVO) is now well established as one of the most efficient treatments in interventional medicine [1, 2]. Indications have greatly expanded in recent years [3, 4], allowing for more patients to benefit from this treatment. However, despite optimized triage and management, a substantial number of patients remains with occlusion or experiences early reocclusion. In randomized trials[1, 5], the rate of MT technical failure, defined as modified thrombolysis in cerebral infarction[6] (mTICI) score IIa or worse, ranges from 10% to 30%, with disastrous consequences in terms of clinical outcomes for these patients[7]. Reasons for MT failure include impossibility to access the target occlusion or, in most cases, failure of clot extraction despite multiple stent retriever or aspiration passes[8–10].

Intracranial atherosclerotic disease-related occlusions account for about 25%[11] to 47%[12] of all intracranial LVOs and seem to be particularly involved in MT failure[13]. Current thrombectomy devices may be excellent for embolectomy but less suitable for removing in situ plaque thromboses. They could even be harmful by causing more plaque activation, which may result in early reocclusion[14]. In interventional cardiology, in which this atherosclerotic mechanism is dominant, direct thromboaspiration has been found inefficient in such cases[15]. Thus, intracranial atherosclerotic acute occlusions could be managed like acute coronary occlusions, with early stenting and antithrombotic management. However, there is a potential risk of intracranial bleeding related to an aggressive antithrombotic regimen[16], which may counterbalance the benefit of vessel patency.

Before the technological breakthrough of stent retrievers in MT, permanent intracranial stenting (PIS) was regularly used as a first-line technique for AIS-LVO, with an acceptable level of safety[17]. Recently, PIS has been increasingly used as a rescue technique for failed recanalization and opened a new path to improve reperfusion rates and clinical outcomes.[18–24] Recent meta-analysis of proportions suggested that PIS could be a safe and effective rescue technique after failed MT[17, 25], however the level of evidence provided by meta-analysis of proportions is low, as they only focus on the experimental group and thus, do not allow direct comparison to a control group. Yet, whether PIS is superior to medical management alone, in refractory LVO remains unknown. Moreover, a large multicenter propensity-score matched cohort study, which was not integrated in previous meta-analyses, has been recently published[26]. Incorporating this study should strengthen the results that may have game-changing implications for this subset of patients.

The aim of this work was to systematically review the literature evaluating the effect of PIS in improving the clinical outcome for patients with refractory LVO in comparison to patients for whom no PIS was attempted and who remained without recanalization.

MATERIAL AND METHODS

This systematic review and meta-analysis was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[27]. The protocol was registered at PROSPERO (CRD42019133434).

Search strategy

We conducted an electronic search of MEDLINE via PubMed and the Cochrane Library with the search algorithm reported in **Electronic Supplementary Material**. The search was initially conducted in April 2019, then updated in September 2019. The search was restricted from January 2015, when endovascular treatment for AIS was generally accepted and routinely performed. We also manually searched the table of contents of the 10 most implicated journals in endovascular stroke medicine (*Stroke, JAMA Neurology, Journal of Neurointerventional Surgery, Journal of Neurosurgery, Clinical Neuroradiology , Journal of Neuroradiology, Interventional Neuroradiology, International Journal of Stroke, Journal of Stroke Cerebrovascular Diseases and European Journal of Neurology*) for any additional reference. A search in ClinicalTrials.gov was also performed and the reference lists of eligible full-text manuscripts were checked for additional references.

Eligibility criteria and selection process

The following inclusion criteria were defined before reviewing: 1) studies comparing patients who underwent PIS in the 48 hr after an ischemic stroke with LVO and after at least one MT attempt to patients receiving only usual care for refractory occlusions; 2) peer-reviewed publication as stated by the journal; 3) minimum of 5 patients included; and 4) available modified Rankin Scale (mRS) score at 90 days. Exclusion criteria were 1) lack of a control group, 2) tandem (extracranial + intracranial) occlusions, 3) non-English language, 4) non-human study, and 5) inclusion period before the standard use of stent retrievers in MT. When several articles originated from the same center and included overlapping populations, only the most relevant article with the largest population was retained. Two reviewers independently evaluated eligibility criteria for all references retrieved by the search. Any disagreements were discussed to achieve consensus.

Data extraction

Two investigators independently extracted data for each included study from full texts, figures, tables and supplemental materials if available. Any disagreements were discussed to achieve consensus. The following data were extracted:

- Publication characteristics: year of publication and journal.
- Study design: randomized trial, prospective or retrospective cohort, case–control study and sample size.
- Patient baseline characteristics: sex, age, past medical history, National Institute of Health Stroke Scale (NIHSS) score at admission, initial Alberta Stroke Program Early Computed Tomography (ASPECT) score and use of intravenous tissue plasminogen activator (IV-tPA).

- Procedural parameters: number of MT attempts (with a stent retriever or direct thromboaspiration), antithrombotic management and other rescue interventions besides stenting.
- Outcomes of interest: favorable clinical outcome defined as a mRS score 0 to 2 at 90 days, defined as the primary outcome; successful reperfusion; mortality; and SICH as defined in the European Cooperative Acute Stroke Study[28]. For each outcome of interest, we collected the corresponding number of events in each group and the number of patients analyzed in each group.

Risk of bias assessment

Risk of bias was evaluated by both reviewers by using the Newcastle–Ottawa Quality Assessment Form for Cohort and Case-control Studies[29]. Any disagreements were discussed to achieve consensus.

Statistical analysis

All continuous data are described with means (SD) or medians (quartile 1 [Q1]–Q3 or range) and qualitative data with frequencies (%). Associations between PIS and outcomes are expressed as odds ratios (ORs) and 95% confidence intervals (CIs). We first evaluated characteristics of included studies to assess whether they were sufficiently close to allow meta-analyses We conducted random-effects meta-analyses considering the presumed heterogeneity of the included studies. However, a sensitivity analysis with fixed-effect models was performed. For each meta-analysis, heterogeneity was evaluated with the Cochran Q and I^2 statistics and the between-study variance τ^2. We planned to perform evaluation of small study effects including publication bias using funnel plots and Egger tests but this was not possible because of the low number of identified studies. For all analyses, $p < 0.05$ was considered statistically significant. Meta-analyses were performed with Review Manager (RevMan) v5.3 (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014). For zero events, Revman automatically applies a correction for trials with 0 in one arm only. The correction consists in adding 0.5 to each of the cells of the 2x2 table to calculate odds ratios.

RESULTS

Selection process

In total, 1168 records were identified by the search and were screened for eligibility. After initial screening, 25 were considered for full-text review (**Figure 1**) and finally, 4 comparative studies (352 patients) were included.

Study characteristics

Table 1 summarizes the characteristics of each included study. Briefly, the Baracchini et al.[19] study was a prospective single-center cohort study performed from 2014 to 2016 that included 109 patients who underwent stent retriever thrombectomy and were divided into 4 groups: 1) successful reperfusion, 2) successful reperfusion after rescue intra-arterial tirofiban infusion only, 3) PIS after failed MT, and 4) no successful reperfusion. Only data from groups 3 and 4 were considered for this meta-analysis. The Chang et al.[20] study was a large multicenter prospective cohort study including 148 patients with MT failure who received rescue stenting or no rescue stenting. The Cornelissen et al.[21] study was a retrospective single-center cohort study that compared outcomes in 26 patients included after failed clot extraction attempts with the Embotrap device, who received PIS or remained with persistent LVO. Finally, the Peng et al.[26] study was a multicenter retrospective cohort study that initially included 90 consecutive patients in the rescue stenting group and 117 patients in the control group. However, considering that both groups were not exactly comparable, and especially for crucial parameters such as baseline NIHSS and ASPECT scores, authors performed a propensity score matching in order to obtain the best balance possible. After propensity score matching, 66 patients were included in each group; and we used the data from this matched population in this meta-analysis.

The methodological quality of included studies was judged “fair” and “good” according to the Newcastle–Ottawa Quality Assessment Form.

Baseline characteristics

Of the 352 patients included in analysis, 149 underwent PIS after failed MT attempts (PIS group) and 203 did not undergo rescue stenting (control group). All recorded baseline characteristics, including major confounding factors such as NIHSS score at admission, use of IV-tPA or site of occlusion, were similar between the two groups (**Table 1**). Only one study included patients with posterior circulation occlusions. The 4 studies used a wide variety of antithrombotic protocols and different types of interventions before and after stenting, that were summarized in **Table 2**. Of note, only the studies of Chang et al.[20] and Peng et al.[26] gave detailed informations regarding additional interventions during the procedures for the PIS and the control groups altogether.

Outcomes

Favorable clinical outcome at 90 days was significantly more frequent in the PIS than control group (OR, 2.87; 95% CI, 1.77-4.66), with low heterogeneity across studies (p_{het}=0.41, I^2 = 0%, τ^2 = 0.00) (**Figure 2**). Mortality was significantly lower in the PIS group (OR, 0.39; 95% CI, 0.16-0.93; I^2 = 43%) but SICH rates did not

significantly differ between the groups (OR, 0.68; 95% CI, 0.37-1.27; I^2 = 0%). Sensitivity analyses with fixed-effects models gave consistent results, except for mortality. Successful mTICI≥IIb reperfusion rates after rescue stenting ranged from 64.6% to 91.7%.

Delays

Times from symptoms' onset to arterial puncture were similar between both groups across studies and ranged from an average of 196.1 (+/- 48.1) to 289 minutes (+/- 90.9).Two studies specifically evaluated the delays from arterial puncture to successful recanalization after stenting and found an average of 113 (+/- 53) minutes in the Chang et al.[20] study and 83.3 (+/- 50.1) minutes in the study of Cornelissen et al.[21]

DISCUSSION

The interest over PIS as a rescue technique after failed MT is rapidly growing[17, 19–21, 25], owing to the positive clinical findings in everyday practice. Even though, no randomized controlled trials have been conducted so far, several comparative observational studies have been published. Of note, a recent and the largest one to date, is a multicenter Chinese cohort study[26] that performed a propensity-score matching, which is the most robust pairing method for observational studies, that limits indication bias to its minimum and provides top-level comparability. The results of this study were in line with previous comparative studies and were incorporated in this meta-analysis. Our current meta-analysis includes studies comparing clinical outcomes of rescue PIS to no additional endovascular interventions. PIS was associated with improved clinical outcome at 90 days and lower mortality as compared with no recanalization. Although PIS requires an aggressive antiplatelet regimen (**Table 2.**) to ensure stent patency, it did not seem to result in increased rates of SICH.

Refractory LVO remains a major concern in the era of MT because it is associated with an unfavorable prognosis as confirmed by data from the control groups in our included studies. After an average of 3.5 intracranial MT passes, successful reperfusion could never be achieved, and persistent occlusion was confirmed at the end of procedures in all studies (0% of mTICI≥ IIb in the control groups). Rates of functional independence at 90 days ranged from 17.4% to 22% and mortality rates from 19% to 43.9%. These rates are consistent with data from patients included in the control arms of the 5 first randomized trials evaluating MT[1]. In comparison, attempting PIS permitted successful reperfusion of most refractory LVOs, resulting in an increased rate of favorable clinical outcome, more in line with those expected in the general setting of MT. The more MT is attempted, the less probability of achieving reperfusion, which leads to deteriorated clinical outcomes. Some observational studies have even suggested that beyond 5 attempts, the probability of achieving reperfusion decreases drastically and that, even when achieved, does not result in improved outcomes when compared to patients without recanalization. [30] This finding suggests that if PIS is considered, it should be promptly initiated to avoid futile recanalization that could be detrimental to patients under dual antiplatelet therapy.

As expected, SICH rates in these studies were high, about three-fold higher than in the HERMES pooled population[1]. Indeed, MT failure is a well-known risk factor for SICH[31] and in many PIS cases, antiglycoprotein IIb/IIa agents were used before stenting, which also have known risks for haemorrhagic transformations, especially in extended stroke. Even though the level of evidence is low, we did not observe an additional risk in patients receiving PIS as compared with the control group. However, this observation should be carefully interpreted since additional IA antithrombotics were also used in the control groups which may have overestimated the rates of SICHs. Moreover, the included studies mostly used CT-based protocols when AIS was suspected, which may not be the best way to evaluate the extent of infarctions, especially at the hyperacute phase. The two largest studies provided an estimation of the infarction volume using the ASPECT score; and these ASPECTs were rather high in patients included. This suggests that patients from these studies were selected for rescue stenting with special attention to this parameter; and that if PIS was to be performed in lower ASPECT groups, SICHs would probably be more frequent. As such, the initial volume of infarction should be viewed as a critical factor to consider before placing a patient under strong antiplatelet therapy in the setting of

PIS. Furthermore, the featured studies included AIS within 6 hours from symptoms' onset to puncture; therefore these results may only be applicable to this subset of patients and not to late-onset strokes. Studies that disclosed the times from puncture to reperfusion when PIS was performed showed that these procedures were rather long, which is a natural consequence of the refractory nature of these occlusions. Longer procedures did not result in worse outcomes or increased SICHs in the PIS group; however one must consider that beyond 6 hours from symptoms onset, PIS has not yet been sufficiently studied, and could arguably be harmful by promoting SICHs in late infarcts.

Within each study, baseline characteristics of patients did not differ between those with PIS and those without recanalization. These populations also seemed quite comparable to the population included in the 5 main randomized trials of MT[1]. Although the reports lacked information regarding the AIS etiology, a fair proportion probably resulted from intracranial atherosclerotic disease, especially considering the over-representation of the Asian patient population in this meta-analysis[20, 26].

This study has several limitations. First, the small sample size of included studies and the observational design intrinsically limit the level of evidence. Although the groups were comparable, we cannot exclude confounding or indication bias because the decision to undergo PIS was solely at the operator's discretion and was not protocol-based. No information was available regarding the parameters used for patient selection and specifically infarct size and how this was integrated in decision-making for intracranial stenting. Another limitation is related to the high heterogeneity in antithrombotic management across studies and other interventions besides PIS such as balloon angioplasty.

Nevertheless, this comparative meta-analysis of observational studies provides additional evidence to answer the question of whether the benefit of vessel patency through rescue stenting outweighs the risk of intracranial haemorrhage in refractory LVOs.

CONCLUSION

Although the prevalence of refractory LVO is decreasing in the modern era of MT with improved techniques, the prognosis remains unfavorable. PIS may be an efficient rescue technique, allowing for important improvements in clinical outcome in this subgroup of patients. Although PIS requires strong antithrombotic therapy, no differences in SICHs were found between groups. However, given the level of evidence, decisions to undergo the procedure should be carefully evaluated and on a patient-level basis, with special attention to the extent of infarction before stenting as well as the delay from symptoms' onset. This work warrants randomized studies to confirm these assumptions and identify the patients who could benefit most from these findings.

COMPLIANCE WITH ETHICAL STANDARDS

Funding: None

Conflict of Interest: The author declares conflicts of interests.

Dr. Sourour reports a conflict of interest with Medtronic, Balt Extrusion, Microvention (consultant), Stock/Stock Options: Medina. Prof. Clarençon reports a conflict of interest with Medtronic, Guerbet, Balt Extrusion (payment for readings), Codman Neurovascular (core lab). The other authors report no conflicts of interest.

Ethical approval: For this type of study formal consent is not required.

Informed consent: Not required

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TABLE AND FIGURE LEGENDS

Figure 1. Flowchart of the selection of articles.

MT: mechanical thrombectomy; mRS: modified Rankin Scale

Figure 2. Forest plots for favorable clinical outcome (modified Rankin Scale score 0–2) at 90 days, mortality and symptomatic intracranial haemorrhage (SICH)

Barrachini 2017[19] ; Chang 2018[20] ; Cornelissen[21] ; Peng[26] ; 95% CI : 95% Confidence Interval ; M-H : Mantel-Haenszel

Table 1. Summary of the included study characteristics and main baseline characteristics of included patients with permanent intracranial stenting (PIS group) or usual care (control group)

SD: standard deviation ; NIHSS: National Institute of Health Stroke Scale ; ICA: internal carotid artery ; IQR: interquartile range ; MCA: middle cerebral artery ; M1: first segment of the MCA ; M2: second segment of the MCA ; IV-tPA: intravenous tissue plasminogen activator ; ASPECT: Alberta Stroke Program Early Computed Tomography Score ; mL: milliliter.

Table 2. Summary of additional interventions and antithrombotic protocols used in included studies.

IA: intra-arterial; IV: intravenous; †: Timing of additional interventions (before or after stenting) not disclosed; rtPA: recombinant tissue plasminogen activator, *No information regarding these additional interventions were available for the control group

384 **Table 1.** Summary of the included study characteristics and main baseline characteristics of included patients with permanent intracranial

385 stenting (PIS group) or usual care (control group)

Study	**Country**	**Period of inclusion**	**Study design**	**Number of patients in each group**	**Main baseline characteristics of patients in the PIS and control groups**
Baracchini et al. 2017	Italy	2014-2016	Prospective single-center cohort study	PIS group: 23 Control group: 23	Mean age, years (SD): 70 (16.9) vs 74 (8.3) Median NIHSS score (range): 16 (4-26) vs 18 (5-20) Occlusion site: intracranial ICA and/or MCA in all cases IV-tPA, No. (%): 4/23 (17.4%) vs 10/23 (43.5%)
Chang et al. 2018	South Korea	2010-2015	Prospective multicenter cohort study	PIS group: 48 Control group: 100	Mean age, years (SD): 63.7 (16.8) vs 68.0 (12.1) Median NIHSS score (IQR): 14 (8) vs 15 (6) Median ASPECT score (+/-IQR): 8 (1.75) vs 8 (2) Occlusion site: intracranial ICA and/or MCA in all cases IV-tPA, No. (%): 22/48 (45.8%) vs 46/100 (46.0%)
Cornelissen et al. 2018	Sweden	2013-2017	Retrospective single-center cohort study	PIS group: 12 Control group: 14	Mean age, years (SD): 65.2 (13.9) vs 67.3 (9.5) Median NIHSS score (range): 16.5 (5–22) vs 16.5 (8–22) Infarct volume, mL (SD): 14.9 (22.3) vs 30.1 (36)

					Occlusion site: No. (%): • PIS group: basilar: 2/12 (16.7%), vertebral: 1/12 (8.3%), ICA: 1/12 (8.3%), M1: 8/12 (66%) • Control group: basilar: 4/14 (28.6%), M1: 9/14 (64.3%), M2: 1/14 (7.1%) IV-tPA, No. (%): 3/12 (25%) vs 6/14 (42.9%)
Peng et al. 2019	China	2015-2018	Retrospective multicenter case-control study	PIS group: 66 Control group: 66	Median age, (IQR): 66 (55-76) vs 67 (56-75) Median NIHSS score (IQR): 16 (12-21) vs 18 (13-21) Median ASPECT score (IQR): 9 (8-10) vs 9 (8-10) Occlusion site: intracranial ICA and/or MCA in all cases IV-tPA, No. (%): 20/66 (30.3%) vs 22/66 (33.3%)

386 SD: standard deviation ; NIHSS: National Institute of Health Stroke Scale ; ICA: internal carotid artery ; IQR: interquartile range ; MCA: middle
387 cerebral artery ; M1: first segment of the MCA ; M2: second segment of the MCA ; IV-tPA: intravenous tissue plasminogen activator ; ASPECT:
388 Alberta Stroke Program Early Computed Tomography Score ; mL: milliliter.

389 **Table 2.** Summary of additional interventions and antithrombotic protocols used in included studies.

Study names	Additional interventions before stenting	Antithrombotic protocol before stenting	Additional interventions after stenting	Antithrombotic regimen after stenting
Baracchini et al. 2017*	Balloon angioplasty IA antiglycoprotein IIb/IIIa	IA bolus (25 µg/kg in 3 min) of antiglycoprotein IIb/IIIa (tirofiban)	Balloon angioplasty for residual stenosis	12-hr IV infusion (0.1 µg/kg/min) of tirofiban then switch to dual antiplatelet therapy for 3 months
Chang et al. 2018	†Balloon angioplasty: 15/48 (31.3%) in PIS group versus 4/100 (4%) in control group IA antiglycoprotein IIb/IIIa: 34/48 (70.8%) in PIS group versus 14/100 (14%) in control group IA urokinase : 7/48 (14.6%) in PIS group versus 16/100 (16%) in control group			Not available
Cornelissen et al. 2018*	None	IV bolus of antiglycoprotein IIb/IIIa (abiciximab) or aspirin	Balloon angioplasty	Dual antiplatelet therapy for 3–6 months then aspirin for life
Peng et al. 2019	†Balloon angioplasty: 18/66 (27.3%) in PIS group versus 20/66 (30.3%) in control group IA Tirofiban: 18/66 (27.3%) in PIS group versus 16/66 (24.2%) in control group IA urokinase or rtPA: 7/66 (10.6%) in PIS group versus 5/66 (7.6%) in control group			Not available; At the operator's discretion

IA: intra-arterial; IV: intravenous; †: Timing of additional interventions (before or after stenting) not disclosed; rtPA: recombinant tissue plasminogen activator; *No information regarding these additional interventions were available for the control group

Figure 1

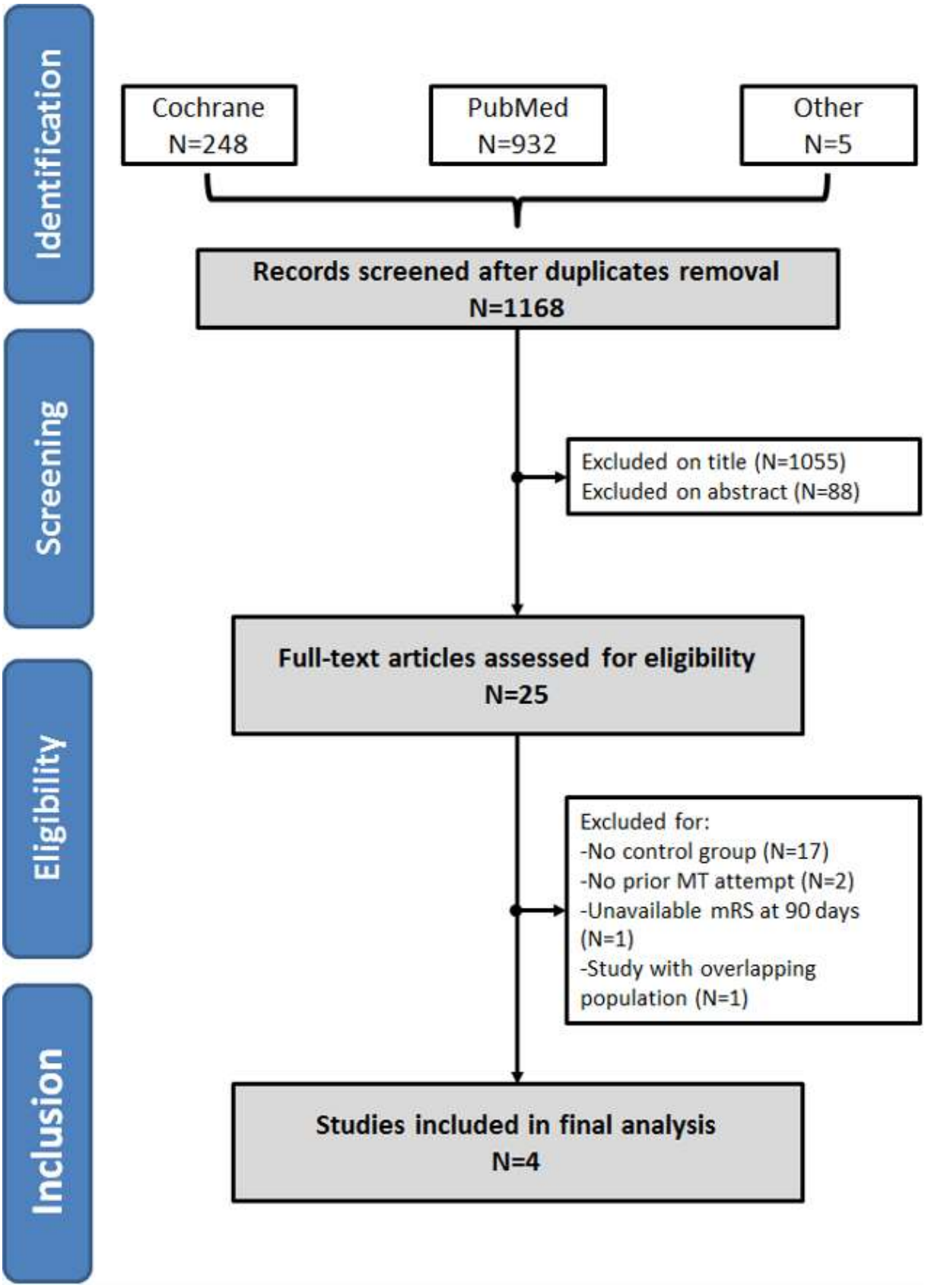
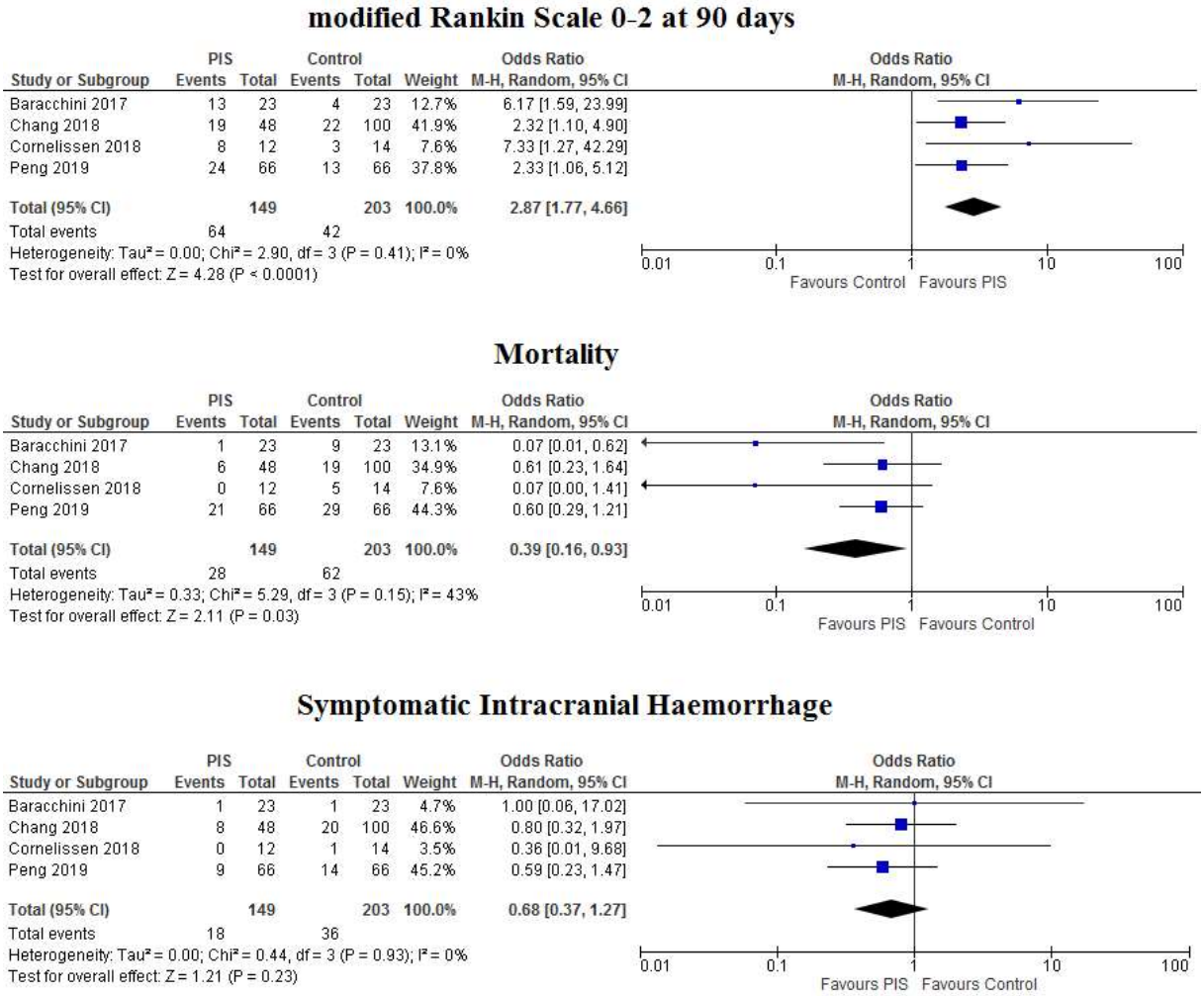

Identification
Screening
Eligibility
Inclusion
Cochrane
N=248
PubMed
N=932
Other
N=5
Records screened after duplicates removal
N=1168
Excluded on title (N=1055)
Excluded on abstract (N=88)
Full-text articles assessed for eligibility
N=25
Excluded for:
-No control group (N=17)
-No prior MT attempt (N=2)
-Unavailable mRS at 90 days (N=1)
-Study with overlapping population (N=1)
Studies included in final analysis
N=4

Figure 2:


modified Rankin Scale 0-2 at 90 days
PIS
Control
Odds Ratio
Odds Ratio
Study or Subgroup Events Total Events Total Weight M-H, Random, 95% CI
M-H, Random, 95% CI
Baracchini 2017 13 23 4 23 12.7% 6.17 [1.59, 23.99]
Chang 2018 19 48 22 100 41.9% 2.32 [1.10, 4.90]
Cornelissen 2018 8 12 3 14 7.6% 7.33 [1.27, 42.29]
Peng 2019 24 66 13 66 37.8% 2.33 [1.06, 5.12]
Total (95% CI) 149 203 100.0% 2.87 [1.77, 4.66]
Total events 64 42
Heterogeneity: Tau² = 0.00; Chi² = 2.90, df = 3 (P = 0.41); I² = 0%
Test for overall effect: Z = 4.28 (P < 0.0001)
0.01 0.1 1 10 100
Favours Control Favours PIS
Mortality
PIS
Control
Odds Ratio
Odds Ratio
Study or Subgroup Events Total Events Total Weight M-H, Random, 95% CI
M-H, Random, 95% CI
Baracchini 2017 1 23 9 23 13.1% 0.07 [0.01, 0.62]
Chang 2018 6 48 19 100 34.9% 0.61 [0.23, 1.64]
Cornelissen 2018 0 12 5 14 7.6% 0.07 [0.00, 1.41]
Peng 2019 21 66 29 66 44.3% 0.60 [0.29, 1.21]
Total (95% CI) 149 203 100.0% 0.39 [0.16, 0.93]
Total events 28 62
Heterogeneity: Tau² = 0.33; Chi² = 5.29, df = 3 (P = 0.15); I² = 43%
Test for overall effect: Z = 2.11 (P = 0.03)
0.01 0.1 1 10 100
Favours PIS Favours Control
Symptomatic Intracranial Haemorrhage
PIS
Control
Odds Ratio
Odds Ratio
Study or Subgroup Events Total Events Total Weight M-H, Random, 95% CI
M-H, Random, 95% CI
Baracchini 2017 1 23 1 23 4.7% 1.00 [0.06, 17.02]
Chang 2018 8 48 20 100 46.6% 0.80 [0.32, 1.97]
Cornelissen 2018 0 12 1 14 3.5% 0.36 [0.01, 9.68]
Peng 2019 9 66 14 66 45.2% 0.59 [0.23, 1.47]
Total (95% CI) 149 203 100.0% 0.68 [0.37, 1.27]
Total events 18 36
Heterogeneity: Tau² = 0.00; Chi² = 0.44, df = 3 (P = 0.93); I² = 0%
Test for overall effect: Z = 1.21 (P = 0.23)
0.01 0.1 1 10 100
Favours PIS Favours Control