

Tissue hypoperfusion after endovascular thrombectomy and functional outcome across heterogeneous imaging definitions: a systematic review and meta-analysis

Fei Xu

Peking University People's Hospital

Lu Cong

Peking University People's Hospital

Dong Wang

Peking University People's Hospital

Yuting Gao

Peking University People's Hospital

Mengyuan Qiu

Peking University People's Hospital

Zunjing Liu

liuzunjing@pku.edu.cn

Peking University People's Hospital

Systematic Review

Keywords: Endovascular thrombectomy, Tissue hypoperfusion, Perfusion imaging, Functional outcome, No reflow phenomenon

Posted Date: October 14th, 2026

DOI: <https://doi.org/10.21203/rs.3.rs-11117693/v1>

License:   This work is licensed under a Creative Commons Attribution 4.0 International License. [Read Full License](#)

Additional Declarations: No competing interests reported.

Abstract

Purpose

Successful macrovascular recanalization after endovascular thrombectomy (EVT) does not invariably result in effective tissue reperfusion. Persistent post-EVT tissue hypoperfusion has been associated with poor outcome but is defined heterogeneously across imaging studies. We investigated whether its prognostic relevance remains consistent across different operational definitions.

Methods

We systematically identified studies enrolling adults with anterior-circulation large vessel occlusion who underwent EVT with successful macrovascular recanalization (mTICI/eTICI $\geq$ 2b), received post-EVT perfusion imaging and had an explicit imaging-based definition of persistent tissue hypoperfusion, impaired microvascular reperfusion, or no reflow. Studies reporting modified Rankin Scale (mRS)-based functional outcomes at approximately 30 or 90 days were included. Random effects meta-analyses were performed using the Hartung-Knapp adjustment.

Results

Six studies (404 patients) were included in the quantitative analysis. Despite substantial heterogeneity in perfusion metrics, spatial definitions, imaging timing, and recanalization thresholds, post-EVT hypoperfusion was associated with lower odds of favorable functional outcome (OR 0.28, 95% CI 0.18-0.46). The association was observed for both mRS 0-2 or mRS 0-1 definitions of favorable outcome. No significant subgroup differences were observed according to perfusion metric or recanalization threshold.

The direction of the association remained consistent in leave-one-out analyses.

Conclusions

The prognostic association of post-EVT tissue hypoperfusion persisted despite substantial heterogeneity in its operational definition, suggesting that its clinical relevance may extend beyond any single imaging surrogate of microvascular no reflow. A broader and standardized operational definition may be useful for prognostic assessment and enrichment of patients for future trials.

Introduction

Endovascular thrombectomy (EVT) has become a standard treatment for acute ischemic stroke caused by anterior circulation large-vessel occlusion with high rates of successful recanalization [1–4]. Nevertheless, a considerable proportion of patients remain disabled or die despite successful angiographic recanalization, reflecting the clinical problem of futile recanalization [5–8]. So, the clinical challenge after EVT is not only limited to reopening the occluded artery but also involves restoring effective downstream tissue perfusion.

Persistent perfusion abnormalities have been observed despite successful macrovascular recanalization [9–11] and may contribute to futile recanalization. The no reflow phenomenon (NRP), traditionally defined as persistent microvascular hypoperfusion despite restoration of upstream blood flow [12], provides a plausible pathophysiological explanation for this observation [13]. Experimental studies have implicated microvascular obstruction [14–16], pericyte-mediated capillary constriction [17–19], endothelial dysfunction [20–21]. However, clinical perfusion imaging cannot directly visualize these microvascular processes and instead characterizes the tissue-level hemodynamic consequences. Definitions of imaging-defined NRP vary in imaging modality, metrics, thresholds, and imaging timing [22–23], and abnormalities labeled as “no reflow” may not necessarily represent the same biological process.

This heterogeneity highlights a distinction between mechanistic specificity and clinical relevance. Although identifying an imaging phenotype that closely reflects genuine microvascular NRP is important for understanding mechanisms and developing targeted therapies, the prognostic relevance of post-EVT hypoperfusion may not depend on its precise biological origin. Even when persistent tissue-level hypoperfusion results from distal embolization rather than microvascular NRP, it still represents ineffective tissue perfusion and identify patients at increased risk of poor recovery. We therefore focused on whether the clinically observable phenotype of persistent post-EVT tissue hypoperfusion has consistent prognostic relevance.

Previous systematic reviews have summarized the available evidence regarding the definition, prevalence, and clinical consequences of imaging NRP phenotype after successful recanalization. Mujanovic et al. [23] reported substantial heterogeneity in the definition of NRP and highlighted the possibility that some imaging-defined cases may reflect distal vascular occlusion rather than genuine microvascular reperfusion failure. A subsequent systematic review and meta-analysis. Pereira da Silva et al. [24] further evaluated the prevalence of NRP and its associations with neurological recovery, hemorrhagic complications, infarct volume, functional outcome and mortality. However, the

extent to which differences in the operational definition of post-EVT hypoperfusion influence its interpretation as a prognostic imaging phenotype remains insufficiently explored.

So we conducted a systematic review and meta-analysis to characterize the operational definitions of post-EVT hypoperfusion and to evaluate whether imaging-defined persistent hypoperfusion after successful recanalization is associated with functional outcome. We further explored whether this prognostic association remained consistent across different definitions of favorable functional outcome and major characteristics of the imaging definitions.

Methods

This systematic review and meta-analysis was made according to PRISMA statement.

2.1 Eligibility criteria

Studies were eligible if they: (1) enrolled adult with anterior-circulation acute ischemic stroke due to large vessel occlusion treated with EVT; (2) included patients with successful macrovascular recanalization, defined as mTICI/eTICI $\geq$ 2b or a stricter threshold specified by the original study; (3) performed post-EVT perfusion imaging; (4) provided an explicit imaging-based definition of tissue hypoperfusion, impaired microvascular reperfusion, or no-reflow; and (5) reported mRS-based functional outcomes at approximately 30 or 90 days. Editorial letters, conference abstracts, case reports, reviews and animal studies, studies without successful recanalization, and studies assessing perfusion only before EVT were excluded.

2.2 Search strategy and study selection

We systematically searched the following databases up to 30, June 2026: PubMed, Embase and Web of Science. The search strategy combined controlled vocabulary (MeSH and Emtree, where appropriate) and free-text terms related to the following keywords: acute ischemic stroke, endovascular thrombectomy, post-EVT persistent hypoperfusion or no-reflow. The complete search strategies for all databases are provided in Supplementary Table S1.

Two authors (X.F. and C.L.) independently screened the retrieved records, assessed full-text articles for eligibility, and extracted data from the included studies. Disagreements were resolved through discussion and when necessary, consultation with a third reviewer (W.D.).

2.3 Data extraction and operational characterization of post-EVT hypoperfusion

We extracted study characteristics, patient population, sample size, recanalization criteria, post-EVT perfusion imaging modality and timing, terminology used to describe abnormal tissue perfusion, operational definition of hypoperfusion, perfusion metrics and thresholds, spatial criteria used to define abnormal perfusion, exclusion of potential alternative causes of hypoperfusion, and functional outcomes. Given substantial variation in terminology and definitions, eligibility was not restricted to studies explicitly using *no reflow* or NRP; comparable post-EVT imaging-defined tissue hypoperfusion, residual hypoperfusion, impaired microvascular reperfusion, and abnormal perfusion were also eligible.

Operational definitions were subsequently characterized according to the perfusion modality, perfusion metric, quantitative threshold, spatial definition, dynamic assessment, timing of post-EVT imaging, exclusion of hemorrhagic transformation or re-occlusion, and angiographic threshold used to define successful recanalization.

2.4 Outcomes

The primary outcome was favorable functional outcome assessed using a modified Rankin Scale (mRS) at follow-up, including functional independence (mRS 0–2) and excellent functional outcome (mRS 0–1). Follow-up assessments were conducted at approximately 30 or 90 days, according to the original study.

As secondary analyses, we separately examined studies defining favorable outcome as mRS 0–2 and studies defining excellent outcome as mRS 0–1. These analyses were performed to assess the consistency of the association across different thresholds of the mRS.

2.5 Subgroup analyses

To explore whether differences in the operational characteristics of post-EVT hypoperfusion affected its association with functional outcome. Exploratory subgroup analyses were performed according to:

1. **Perfusion metric used to define hypoperfusion:** Tmax-based versus rCBF/rCBV-based definitions;
2. **Angiographic threshold used to define successful macrovascular recanalization:** more stringent recanalization thresholds (mTICI/eTICI 2c–3 or mTICI 3) versus broader thresholds (mTICI/eTICI 2b–3).

Due to the limited number of studies within individual subgroups, all subgroup analyses were considered exploratory.

2.6 Statistical analysis

For functional outcomes, odds ratios (ORs) with corresponding 95% confidence intervals (CIs) were used as the summary effect measures. When adjusted ORs were reported, adjusted estimates were preferentially extracted. For studies reporting only raw 2 × 2 data, unadjusted ORs and corresponding 95% CIs were calculated from the reported event data.

Where the reported exposure represented the inverse of the prespecified comparison, the effect estimate was mathematically inverted to ensure a consistent direction of effect across studies. Specifically, all ORs were expressed as the odds of favorable functional outcome among patients with post-EVT hypoperfusion relative to those without hypoperfusion.

Pooled estimates were calculated with 95% CIs, using a random-effects model with restricted maximum likelihood estimation and Hartung–Knapp adjustment. Between-study heterogeneity was assessed using the *Q* test and quantified using the *I*² statistic and τ^2 . Statistical analysis was performed using R 4.5.3 (R Foundation for Statistical Computing, Vienna, Austria) with the meta package. All statistical tests were two-sided, and a *P* value < 0.05 was considered statistically significant.

Results

3.1 Study selection

A total of 900 records were identified through database searches, including PubMed (*n* = 297), Embase (*n* = 293) and Web of Science (*n* = 310). After removing 412 duplicates, 488 records remained for title and abstract screening. Of these, 449 records were excluded based on predefined eligibility criteria, leaving 39 articles for full-text assessment. Subsequently, 22 were excluded, including eight due to insufficient imaging or perfusion data and 14 for not meeting the prespecified population or outcome criteria. 17 studies were included in systematic review, of which six studies were eligible for the quantitative meta-analysis. The study selection process is detailed in Fig. 1.

3.2 Characteristics of included studies and populations

Six studies comprise 404 patients were included. Study characteristics, patient populations and imaging features are summarized in Table 1. All included patients achieved successful macrovascular recanalization, although the angiographic criteria varied across studies, ranging from mTICI 2b–3 to eTICI 2c–3 or mTICI 3. Post-EVT perfusion imaging was performed from the immediate post-procedural period to 72 hours after EVT. The prevalence of tissue-level hypoperfusion after EVT was reported as 20% to 41.7%.

Table 1
Characteristics of included studies and populations

Author, year	Country	Study design	Sample size	Mean age	Baseline NIHSS	Successful recanalization	Imaging timing	Outcome	Prevalence
Rivet, 2025 [25]	Australia and New Zealand	post hoc pooled analysis of RCT	150	Not Given	Not Given	eTICI 2c-3	24 ± 6 hours after EVT	90d mRS 0–2	20%
Bai, 2022 [26]	China	Retrospective	63	65 ± 11.2	13	mTICI≥2b	< 72 hours after EVT	90d mRS 0–2	30.20%
ter Schiphorst, 2026 [27]	France	Prospective	71	76 (67–84)	17 (9–22)	mTICI≥2b	shortly and 24 hours after EVT	90d mRS 0–2	21%
Luby, 2022 [28]	Not Given	Not Given	55	67 (55–76)	19 (14–22)	mTICI 3 subgroup (<i>n</i> = 30)	24 hours after EVT	mRS 0–2 at 30d or 90d	20%
Ng, 2026 [29]	Australia	Prospective	29	73 (67–80)	15 (10–19)	eTICI 2c-3	2 hours and 24–48 hours after EVT	90d mRS 0–1	21–24%
Laredo, 2022 [30]	Barcelona	Prospective	36	71 ± 13.5	13 (9–16)	eTICI 2b-3	48 hours after randomization	90d mRS 0–1	41.70%

3.3 Heterogeneity in the operational definitions of post-EVT hypoperfusion

The operational definitions of post-EVT hypoperfusion varied across the included studies (Table 2). Four studies defined abnormal tissue perfusion using delayed perfusion based on a Tmax threshold of >6s, whereas two studies used reductions in relative blood volume or cerebral flow reduction (rCBV/rCBF), with a threshold of > 15% relative to the contralateral mirror region.

Spatial criteria also varied: three studies assessed hypoperfusion within infarcted tissue, two assessed the affected vascular territory, and one was unclear. Assessment ranged from quantitative to combined visual and quantitative approaches, with some studies using serial imaging. Exclusion of hemorrhagic transformation and re-occlusion was inconsistently reported. Recanalization thresholds ranged from mTICI/eTICI 2b-3 to 2c-3, and imaging timing ranged from immediately after EVT to 72 hours. These differences indicate that imaging-defined post-EVT hypoperfusion represents a heterogeneous operational construct rather than a uniform surrogate of microvascular NRP.

Table 2
Operational characteristics of imaging-defined post-EVT hypoperfusion or no-reflow

Author, year	Perfusion modality	Perfusion metric	Threshold	Spatial definition	Dynamic assessment	Hemorrhage excluded	Re-occlusion excluded	Timing	Reperfusion threshold
Rivet, 2025	MRP/CTP	rCBV/rCBF	15% reduction	Infarct-confined	No	Yes	Yes	24hrs	eTICI 2c-3
Bai, 2022	CTP	Tmax	Tmax>6s	Unclear	Yes	Unclear	Yes	< 72 hrs	mTICI 2b-3
ter Schiphorst, 2026	MRP	Tmax	Tmax>6s	Vascular-territory-based	Yes	Yes	Yes	early post-EVT	mTICI 2b-3
Luby, 2022	MRP	Tmax	Tmax>6s	Vascular-territory-based	No	Unclear	No	24hrs	mTICI 3
Ng, 2026	MRP	rCBV/rCBF	15% reduction	Infarct-confined	Yes	Yes	Unclear	24-48hrs	eTICI 2c-3
Laredo, 2022	MRP	Tmax	Tmax>6s	Infarct-confined	No	Unclear	Unclear	48hrs	eTICI 2b-3

3.4 Association between post-EVT hypoperfusion and functional outcome

3.4.1 Primary outcome: favorable functional outcome

Six studies were included in the primary meta-analysis evaluating the association between imaging-defined post-EVT hypoperfusion and favorable functional outcome. Favorable outcome was assessed using dichotomized mRS thresholds as reported in the original studies, including functional independence (mRS 0–2) in four studies and excellent functional outcome (mRS 0–1) in two studies.

Using a random-effects model with restricted maximum-likelihood estimation and Hartung-Knapp adjustment, post-EVT hypoperfusion was significantly associated with lower odds of favorable functional outcome (OR 0.28, 95%CI 0.18–0.46, $P = 0.0010$). The pooled effect estimate, heterogeneity statistics, and corresponding forest plot are presented in Fig. 2.

No statistically significant between-study heterogeneity was detected ($Q = 2.20$, $df = 5$, $P = 0.8212$; $I^2 = 0\%$, 95% CI 0–74.6%). However, given the small number of included studies, the confidence interval around the heterogeneity estimate should be interpreted with caution.

3.4.2 Association according to mRS dichotomization

Stratification by outcome threshold showed an inverse association for both mRS 0–2 and mRS 0–1 (Fig. 3). Among four studies using mRS 0–2, post-EVT hypoperfusion was associated with lower odds of functional independence (OR 0.33, 95% CI 0.20–0.56), whereas the two studies using mRS 0–1 showed a stronger association with excellent functional outcome (OR 0.15, 95% CI 0.09–0.22). The difference between subgroups was statistically significant ($P < 0.01$), but should be interpreted cautiously because only two studies contributed to the mRS 0–1 subgroup.

3.5 Exploratory subgroup analyses according to operational characteristics

3.5.1 Perfusion metric

To explore whether the association between post-EVT hypoperfusion and functional outcome differed according to the perfusion metric used to define hypoperfusion, studies were stratified into rCBF/rCBV-based and Tmax-based groups.

An inverse association between post-EVT hypoperfusion and favorable functional outcome was observed in both subgroups (Fig. 4). The test for subgroup differences did not indicate a statistically significant difference between rCBF/rCBV-based and Tmax-based definitions. (P for subgroup differences = 0.76).

Given the limited number of studies within each subgroup, these findings should be interpreted as exploratory.

3.5.2 Recanalization threshold

Studies were further stratified according to the angiographic threshold used to define successful macrovascular recanalization. Studies applying more strict recanalization criteria, including mTICI/eTICI 2c-3/3, were compared with those using broader criteria of mTICI/eTICI 2b-3.

Post-EVT hypoperfusion was associated with lower odds of favorable functional outcome in both subgroups (Supplementary Fig. 1). There was no statistically significant evidence of a statistically significant subgroup difference (P for subgroup differences = 0.79).

3.6 Sensitivity analyses

Leave-one-out analyses were performed to evaluate the robustness of primary pooled estimate. Sequential exclusion of each individual study did not alter the direction or statistical significance of the overall association, with all leave-one-out analyses having statistically significant pooled estimates (all $P < 0.05$, Supplementary Fig. 2). These findings indicate that the observed association between imaging defined post-EVT hypoperfusion and lower odds of favorable functional outcome was not driven by any single study.

Discussion

In this meta-analysis, we examined whether the prognostic relevance of post-EVT tissue hypoperfusion is consistent across different operational definitions. Three main findings emerged. First, post-EVT hypoperfusion was associated with lower odds of favorable functional outcome despite successful macrovascular recanalization, and this association was observed across studies using either mRS 0–1 or mRS 0–2 to define favorable outcome. Second, the included studies differed substantially in perfusion metrics, spatial criteria, assessment timing, and exclusion of alternative causes of persistent hypoperfusion. Third, the direction of the association remained broadly consistent across these definitions, suggesting that the clinical relevance of post-EVT tissue hypoperfusion may extend beyond any single imaging surrogate of microvascular NRP.

The distinction between imaging-defined hypoperfusion and biological NRP is important. Perfusion imaging cannot directly visualize capillary-level failure, and post-EVT hypoperfusion may result from multiple mechanisms, including residual distal arterial obstruction, distal embolization, early re-occlusion, edema-related vascular compression, infarct evolution [23, 31–32]. These mechanisms may coexist and may not be distinguishable using a single perfusion parameter.

Substantial heterogeneity was also observed in how tissue hypoperfusion was defined. Four studies used Tmax-based criteria, whereas two studies defined hypoperfusion according to reductions in rCBF or rCBV. The parameters characterize different aspects of tissue hemodynamics: Tmax is a model derived timing parameter that reflects delayed contrast transit, whereas rCBF and rCBV reflect relative measures in tissue blood flow or blood volume, respectively [33–34]. Spatial definitions also differed, with some studies focusing on hypoperfusion within infarcted tissue and others assessing broader vascular territories. This distinction may be clinically relevant because territorial hypoperfusion can reflect distal embolization or incomplete downstream reperfusion, whereas hypoperfusion within the ischemic tissue may more closely reflect microvascular reperfusion failure [29]. Similarly, imaging was performed from the immediate post-procedural period to 72 hours after EVT, during which delayed reperfusion, infarct evolution, edema, or microvascular injury may alter perfusion patterns. Indeed, recent literature has highlighted the dynamic nature of tissue-level reperfusion after EVT, including both delayed reperfusion and delayed hypoperfusion [29, 35–36]. These temporal differences may partly explain the variability in reported incidence and effect estimates across previous studies.

These findings should be interpreted in the context of the recently published meta-analysis by Eichel et al. [37]. Their study synthesized eight post-EVT perfusion imaging cohorts involving 670 patients and demonstrated a strong association between residual hypoperfusion and functional independence (pooled OR 0.28, 95% CI 0.15–0.51), while proposing candidate perfusion thresholds and a 30-120-minute acquisition window for future patient selection [37]. Our study addresses a complementary question. Rather than seeking a single optimal threshold or imaging window, we specifically examined whether the prognostic association of post-EVT tissue hypoperfusion persists across heterogeneous operational definitions used in contemporary clinical studies. An important implication of our findings is that

prognostic utility does not necessarily require perfect mechanistic specificity. A broader tissue-level hypoperfusion phenotype may retain clinical value even when its precise biological substrate cannot be resolved by routine imaging.

This framework may have practical implications for future post-EVT trials. Angiographic reperfusion grades describe macrovascular recanalization and may not fully capture downstream tissue perfusion. Post-EVT hypoperfusion could therefore serve as a complementary imaging phenotype for identifying patients at high risk of poor recovery and potentially enriching trials of adjunctive therapies. Recent works have similarly highlighted persistent tissue hypoperfusion as a potential biomarker for identifying patients who may benefit from adjunctive therapies after EVT [37–38]. Importantly, the optimal intervention may depend on the underlying mechanism: therapies targeting residual or distal thromboembolic obstruction may differ from those targeting endothelial dysfunction, inflammation, or pericyte-mediated capillary constriction. Thus, broad tissue-level phenotyping may be useful for clinical risk stratification, whereas mechanistically specific imaging or biomarkers may be required for treatment selection.

This study has some limitations. First, only six studies were included, limiting the precision of pooled estimates and statistical power for subgroup analyses, so these analyses should be considered exploratory. Second, substantial heterogeneity existed in the operational definitions of post-EVT hypoperfusion. Although this heterogeneity was a central focus of the present study, it also limits the extent to which a single pooled effect can be interpreted as representing a uniform biological phenomenon. Third, both adjusted and unadjusted effect estimates were included, and residual confounding cannot be excluded. Finally, formal assessment of publication bias was not performed because the small number of studies makes funnel plots and statistical tests for small-study effects unreliable.

Conclusion

Post-EVT tissue hypoperfusion remains a heterogeneous imaging construct rather than a uniformly defined surrogate for microvascular NRP. Nevertheless, across different perfusion metrics, spatial definitions, and imaging time points, imaging-defined hypoperfusion after successful macrovascular recanalization was associated with lower odds of favorable functional outcome.

These findings support the use of a broader, clinically operational phenotype for prognostic assessment and patient enrichment in future trials, while mechanistic studies are needed to distinguish distal vascular obstruction, and true microvascular NRP, which may require different therapeutic strategies.

Declarations

Author Contribution

F.X. and L.C. conceived the conceptual framework, screened the retrieved records, assessed full-text articles for eligibility, and extracted data from the included studies. D.W. resolved any discrepancies. Y.T.G. and M.Y.Q. undertook the literature review. Z.J.L. contributed to critical revision. All authors read and approved the final manuscript.

Data Availability

All data used in this systematic review and meta-analysis were derived from previously published studies and are publicly available in the corresponding original publications. The data extracted for the quantitative synthesis and the statistical analyses are presented in the manuscript and Supplementary Information.

Ethical approval and informed consent

This meta-analysis is based on secondary analysis of previously published data. No individual patient data were collected, and thus no ethical approval or patient consent was required.

Acknowledgements

F.X. and L.C. conceived the conceptual framework, screened the retrieved records, assessed full-text articles for eligibility, and extracted data from the included studies. D.W. resolved any discrepancies. Y.T.G. and M.Y.Q. undertook the literature review. Z.J.L. contributed to critical revision. All authors read and approved the final manuscript.

Funding

This work was supported by the National Natural Science Foundation of China (Grant No.52573148).

Conflicts of interest

The authors declare that they have no competing interests.

References

1. Berkhemer OA, Fransen PS, Beumer D, et al. A randomized trial of intraarterial treatment for acute ischemic stroke. *N Engl J Med*. 2015;372(1):11–20.
2. Goyal M, Demchuk AM, Menon BK, et al. Randomized assessment of rapid endovascular treatment of ischemic stroke. *N Engl J Med*. 2015;372(11):1019–30.
3. Campbell BC, Mitchell PJ, Kleinig TJ, et al. Endovascular therapy for ischemic stroke with perfusion-imaging selection. *N Engl J Med*. 2015;372(11):1009–18.
4. 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):1723–31.
5. Nie X, Pu Y, Zhang Z, Liu X, Duan W, Liu L. Futile Recanalization after Endovascular Therapy in Acute Ischemic Stroke. *Biomed Res Int*. 2018;2018:5879548. Published 2018 May 9.
6. Deng G, Chu YH, Xiao J, et al. Risk Factors, Pathophysiologic Mechanisms, and Potential Treatment Strategies of Futile Recanalization after Endovascular Therapy in Acute Ischemic Stroke. *Aging Dis*. 2023;14(6):2096–112. Published 2023 Dec 1.
7. Shen H, Killingsworth MC, Bhaskar SMM. Comprehensive Meta-Analysis of Futile Recanalization in Acute Ischemic Stroke Patients Undergoing Endovascular Thrombectomy: Prevalence, Factors, and Clinical Outcomes. *Life (Basel)*. 2023;13(10):1965. Published 2023 Sep 26.
8. Chacon A, Hijazi D, Tffaily A, et al. From Recanalization to Failed Recovery: No Reflow, No Rescue, and No Regrow After Thrombectomy. *Transl Stroke Res*. 2026;17(4):96. Published 2026 Aug 7.
9. Mujanovic A, Imhof A, Zheng S, et al. Perfusion Abnormalities on 24-Hour Perfusion Imaging in Patients With Complete Endovascular Reperfusion. *Stroke*. 2024;55(9):2315–24.
10. Horie N, Inoue M, Morimoto T, et al. Recanalization Does Not Always Equate to Reperfusion: No-Reflow Phenomenon After Successful Thrombectomy. *Stroke*. 2025;56(1):183–9.
11. Barbagallo M, Zahn M, Zimmermann J, et al. Reperfusion failure after successful thrombectomy of large vessel occlusion stroke: clinical and imaging evidence. *Front Neurol*. 2025;16:1639880. Published 2025 Aug 22.
12. Ames A 3rd, Wright RL, Kowada M, Thurston JM, Majno G. Cerebral ischemia. II. The no-reflow phenomenon. *Am J Pathol*. 1968;52(2):437–53.
13. Sun F, Zhou J, Chen X, et al. No-reflow after recanalization in ischemic stroke: From pathomechanisms to therapeutic strategies. *J Cereb Blood Flow Metab*. 2024;44(6):857–80.
14. Desilles JP, Syvannarath V, Di Meglio L, et al. Downstream Microvascular Thrombosis in Cortical Venules Is an Early Response to Proximal Cerebral Arterial Occlusion. *J Am Heart Assoc*. 2018;7(5):e007804. Published 2018 Mar 1.
15. El Amki M, Glück C, Binder N, et al. Neutrophils Obstructing Brain Capillaries Are a Major Cause of No-Reflow in Ischemic Stroke. *Cell Rep*. 2020;33(2):108260. 10.1016/j.celrep.2020.108260IF: 7.7 Q1.
16. Kang L, Yu H, Yang X, et al. Neutrophil extracellular traps released by neutrophils impair revascularization and vascular remodeling after stroke. *Nat Commun*. 2020;11(1):2488. Published 2020 May 19.
17. Yemisci M, Gursoy-Ozdemir Y, Vural A, Can A, Topalkara K, Dalkara T. Pericyte contraction induced by oxidative-nitrative stress impairs capillary reflow despite successful opening of an occluded cerebral artery. *Nat Med*. 2009;15(9):1031–7.
18. Hall CN, Reynell C, Gesslein B, et al. Capillary pericytes regulate cerebral blood flow in health and disease. *Nature*. 2014;508(7494):55–60.
19. Zhong X, Ye Z, Liu L, et al. Spatiotemporal dynamics of brain pericytes in ischemic stroke. *J Neuroinflammation*. 2026;23(1):116. Published 2026 Mar 4.
20. Granger DN, Kvietys PR. Reperfusion therapy-What's with the obstructed, leaky and broken capillaries? *Pathophysiology*. 2017;24(4):213–28.
21. Luo X, Zhang S, Wang L, Li J. Pathological roles of mitochondrial dysfunction in endothelial cells during the cerebral no-reflow phenomenon: A review. *Med (Baltim)*. 2024;103(51):e40951.
22. Mutimer CA, Mujanovic A, Kaesmacher J, et al. Comparison of Perfusion Imaging Definitions of the No-Reflow Phenomenon after Thrombectomy-What Is the Best Perfusion Imaging Definition? *Ann Neurol*. 2024;96(6):1104–14.

23. Mujanovic A, Ng F, Meinel TR, et al. No-reflow phenomenon in stroke patients: A systematic literature review and meta-analysis of clinical data. *Int J Stroke*. 2024;19(1):58–67.
24. Pereira da Silva AM, Ribeiro Gonçalves O, Falcão L, et al. Association between the no-reflow phenomenon and clinical outcomes after endovascular treatment for acute ischemic stroke: A systematic review and meta-analysis. *Eur Stroke J*. 2026;11(1):23969873251376846.
25. Rivet S, Churilov L, Yassi N, et al. Persistent Tissue-Level Hypoperfusion (No-Reflow) Negates the Clinical Benefit of Successful Thrombectomy. *Stroke*. 2025;56(6):1451–9.
26. Bai X, Yu F, Tian Q, et al. Clinical Significance and Influencing Factors of Microvascular Tissue Reperfusion After Macrovascular Recanalization. *Transl Stroke Res*. 2023;14(4):446–54.
27. Ter Schiphorst A, Seners P, Dargazanli C, et al. Hypoperfusion on Early MRI Despite Successful Thrombectomy: A Prospective Imaging and Inflammatory Biomarkers Study. *Stroke*. 2026;57(3):745–57.
28. Luby M, Merino JG, Davis R, et al. Association of Multiple Passes during Mechanical Thrombectomy with Incomplete Reperfusion and Lesion Growth. *Cerebrovasc Dis*. 2022;51(3):394–402.
29. Ng FC, Rivet S, Churilov L, et al. Temporal Dynamics of the No-Reflow Phenomenon on Serial Perfusion MRI After Thrombectomy. *Neurology*. 2026;106(7):e214673.
30. Laredo C, Rodríguez A, Oleaga L, et al. Adjunct Thrombolysis Enhances Brain Reperfusion following Successful Thrombectomy. *Ann Neurol*. 2022;92(5):860–70.
31. Mujanovic A, Kurmann CC, Manhart M, et al. Value of Immediate Flat Panel Perfusion Imaging after Endovascular Therapy (AFTERMATH): A Proof of Concept Study. *AJNR Am J Neuroradiol*. 2024;45(2):163–70. Published 2024 Feb 7.
32. Qiao Y, Ter Schiphorst A, Xu Y, Baron JC, Zhao W. Revisiting Incomplete Tissue-Level Reperfusion Following Successful Thrombectomy for Acute Ischemic Stroke. *Ann Neurol*. 2026;99(3):668–83.
33. Wintermark M, Flanders AE, Velthuis B, et al. Perfusion-CT assessment of infarct core and penumbra: receiver operating characteristic curve analysis in 130 patients suspected of acute hemispheric stroke. *Stroke*. 2006;37(4):979–85.
34. Copen WA, Schaefer PW, Wu O. MR perfusion imaging in acute ischemic stroke. *Neuroimaging Clin N Am*. 2011;21(2):259–x.
35. Mujanovic A, Kammer C, Kurmann CC, et al. Association of Intravenous Thrombolysis with Delayed Reperfusion After Incomplete Mechanical Thrombectomy. *Clin Neuroradiol*. 2023;33(1):87–98.
36. Mujanovic A, Yogendrakumar V, Ng FC, et al. Effect of Thrombolytics on Delayed Reperfusion After Incomplete Thrombectomy: Target Trial Emulation. *Neurology*. 2025;104(10):e213641.
37. Eichel R, Teitcher M, Mausbach S et al. Post-endovascular thrombectomy perfusion imaging (CT and MR) as a prognostic biomarker and patient-selection tool for adjuvant therapy: A systematic review, meta-analysis, and clinical threshold framework. *J Stroke Cerebrovasc Dis*. Published online August 17, 2026.
38. Renú A, Fernández-Couto MD, de la Riva P, et al. Adjunctive Intra-Arterial Alteplase After Successful Thrombectomy for Acute Ischemic Stroke: The CHOICE-2 Randomized Clinical Trial. *JAMA*. 2026;335(21):1859–69.

Figures

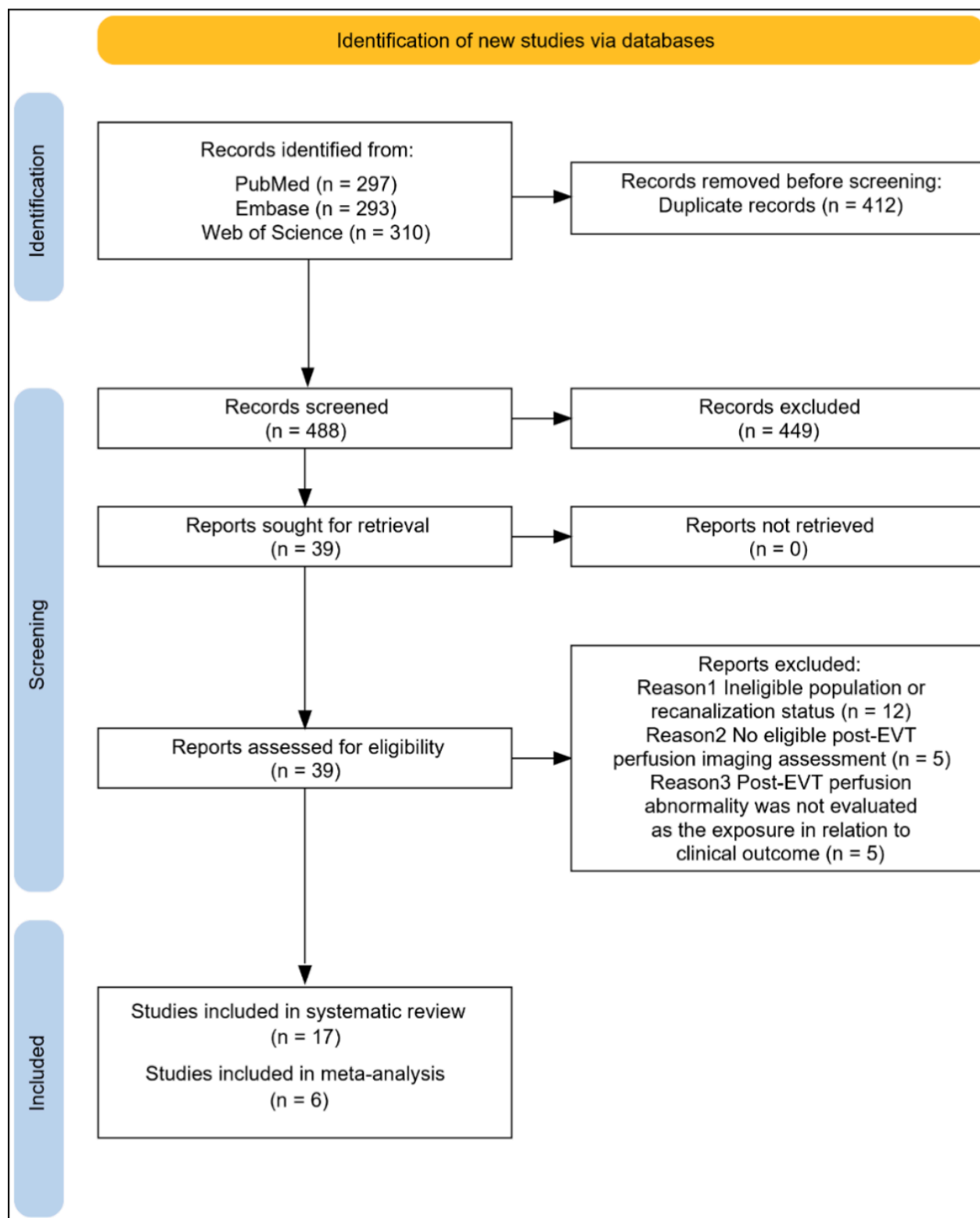


Figure 1

PRISMA flow diagram

Records identified from PubMed, Embase, and Web of Science were screened for eligibility. Seventeen studies were included in the systematic review, of which six were included in the meta-analysis.

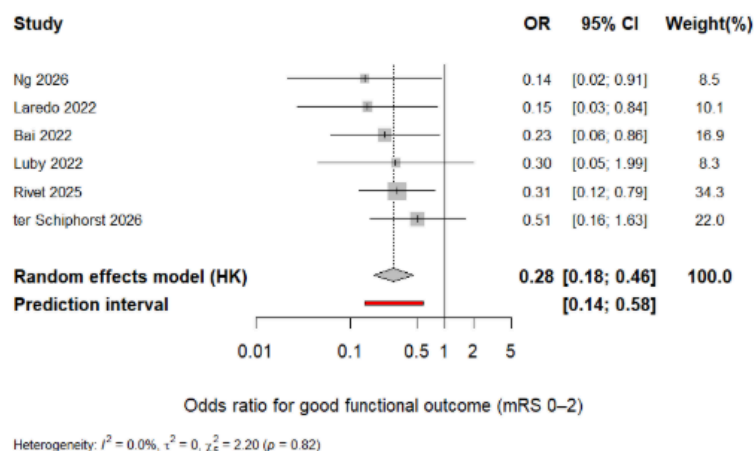


Figure 2

Forest plot of the association between post-EVT hypoperfusion and favorable functional outcome.

Odds ratios (ORs) were pooled using a random-effects model with Hartung–Knapp adjustment. The pooled estimate was OR 0.28 (95% CI 0.18–0.46).

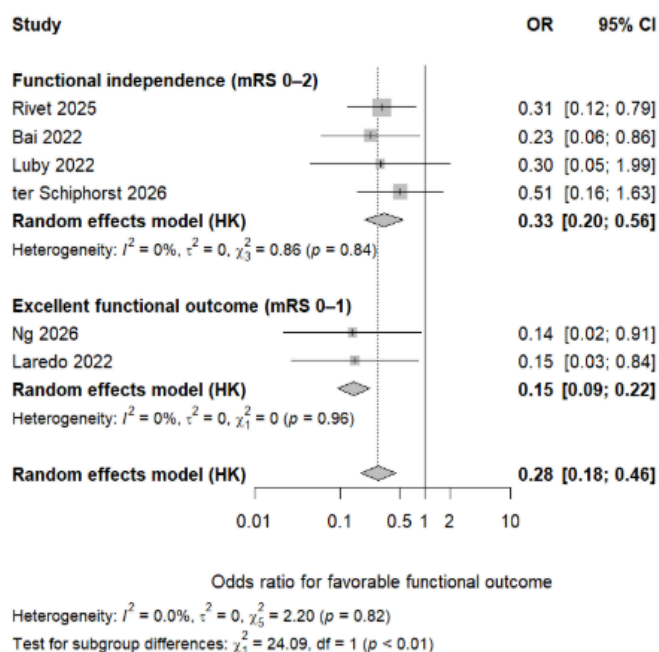


Figure 3

Forest plot of the association between post-EVT hypoperfusion and 90-day functional independence and excellence functional outcome

In the functional independence (mRS 0–2) subgroup, the pooled OR was 0.33 (95% CI: 0.20–0.56; $I^2 = 0\%$). In the excellent functional outcome (mRS 0–1) subgroup, the pooled OR was 0.15 (95% CI: 0.09–0.22; $I^2 = 0\%$). The overall pooled OR was 0.28 (95% CI: 0.18–0.46; $I^2 = 0\%$). A statistically significant difference between subgroups was observed ($p < 0.01$).

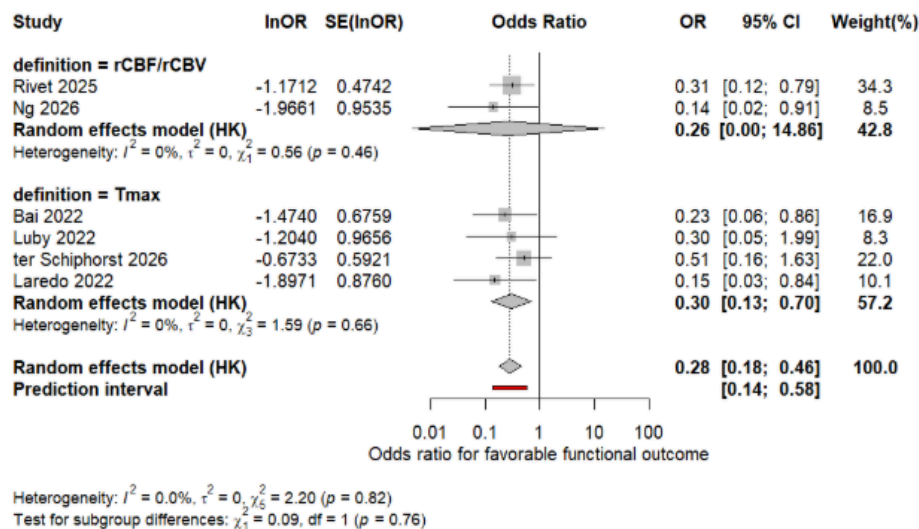


Figure 4

Subgroup analysis of the association between different perfusion metrics and favorable functional outcome

In the rCBF/rCBV subgroup, the pooled OR was 0.26 (95% CI: 0.00–14.86; $I^2 = 0\%$). In the Tmax subgroup, the pooled OR was 0.30 (95% CI: 0.13–0.70; $I^2 = 0\%$). The overall pooled OR was 0.28 (95% CI: 0.18–0.46; $I^2 = 0\%$), with a prediction interval of 0.14 to 0.58. No statistically significant difference between subgroups was observed ($p = 0.76$).

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [SupplementaryTableS1.xlsx](#)
- [SupplementaryFigureS1.tiff](#)
- [SupplementaryFigureS2.tiff](#)