Original Article

Dynamic susceptibility contrast perfusion in differentiation between recurrence and pseudoprogression in glioblastoma: a systematic review and meta-analysis

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Background: Dynamic susceptibility contrast (DSC) perfusion has emerged as a valuable imaging technique for distinguishing pseudoprogression (PP) from recurrent tumor (RT) in patients with gliomas. However, its diagnostic accuracy, specifically in glioblastoma, remains less clearly defined. This systematic review aimed to evaluate and clarify the diagnostic performance of DSC perfusion in differentiating PP from RT in glioblastoma patients.

Methods: A comprehensive search of the PubMed, Cochrane Library, and Wanfang databases was conducted for relevant articles published up to October 2024. Eligible studies were screened, and data about patient diagnoses were systematically extracted and synthesized.

Results: A total of 13 studies comprising 487 patients met the inclusion criteria, with 318 categorized as RT and 178 as PP. In three studies, both relative cerebral blood volume (rCBV) and relative cerebral blood flow (rCBF) were assessed, whereas the remaining studies relied solely on rCBV. Pooled analyses of rCBV demonstrated a sensitivity of 87% [95% confidence interval (CI): 0.82–0.91], specificity of 83% (95% CI: 0.75–0.89), positive likelihood ratio of 5.14 (95% CI: 3.35–7.89), and negative likelihood ratio of 0.16 (95% CI: 0.11–0.23). None of these measures showed significant heterogeneity (I2=18.92%, 11.76%, 0%, and 0.35%, respectively). The pooled area under the curve (AUC) was 0.92 (95% CI: 0.89–0.94), indicating excellent diagnostic accuracy, with only minimal evidence of publication bias (P=0.051). Due to the limited number of studies (n=3) reporting rCBF-related outcomes, a pooled diagnostic analysis for rCBF could not be performed.

Conclusions: These findings demonstrate that DSC perfusion provides a reliable and effective method for distinguishing PP from RT in the diagnostic evaluation of glioblastoma patients.

Keywords: Recurrence; pseudoprogression (PP); magnetic resonance imaging (MRI); perfusion; glioblastoma

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Introduction

Glioblastoma, classified by the World Health Organization (WHO) as a grade IV glioma, carries an exceptionally poor prognosis (1-3), with median survival ranging from 14 to 15 months and a 5-year survival rate of less than 5% (4,5). Magnetic resonance imaging (MRI) remains the standard modality for both preoperative diagnosis and postoperative surveillance of glioblastoma (6,7). However, abnormal MRI findings observed after treatment, such as those detected on T1-weighted imaging (T1WI), T2-weighted imaging (T2WI), or contrast-enhanced T1WI, can reflect either pseudoprogression (PP) or recurrent tumor (RT) (6,7). PP typically arises as a delayed effect of therapy, most often linked to radiation-induced damage or necrosis (8). Since PP and RT require distinct therapeutic approaches, accurate differentiation between these two entities is crucial for guiding clinical decision-making. Nonetheless, conventional MRI (T1WI, T2WI, and contrast-enhanced T1WI) techniques provide limited discriminatory ability, with diagnostic accuracy rates of only 63–68% (7,8).

Dynamic susceptibility contrast (DSC) perfusion, an MRI-based functional imaging method, has demonstrated improved diagnostic performance in this context, with reported sensitivities and specificities for DSC perfusion in distinguishing PP from RT ranging from 83% to 86% and 83% to 85%, respectively (6,7). The strength of DSC perfusion lies in its capacity to assess microvascular characteristics, including vascular proliferation, perfusion dynamics, and microvascular distribution (6,7). These parameters are particularly informative, as glioblastoma and other high-grade gliomas show significant angiogenesis and microvascular proliferation. In comparison, PP is typically associated with limited small vessel injury and ischemic changes (6,7).

Previous systematic reviews have evaluated DSC perfusion in the broader context of high-grade gliomas (6). However, the diagnostic utility of this technique, specifically in glioblastoma patients, remains insufficiently defined.

To address this gap, the present systematic review was undertaken to comprehensively clarify the diagnostic performance of DSC perfusion in distinguishing PP from RT in glioblastoma. We present this article in accordance with the PRISMA reporting checklist (available at https://qims.amegroups.com/article/view/10.21037/qims-2025-245/rc) (9).

Methods

This systematic review was registered on the INPLASY platform (https://inplasy.com/, Number: INPLASY2024100123).

Study inclusion

A comprehensive search of the PubMed, Cochrane Library, and Wanfang databases was conducted to identify relevant studies published up to October 2024. The search strategy employed the following terms: (((((perfusion) OR (PWI)) AND ((DSC) OR (dynamic susceptibility contrast))) AND (((recurrent) OR (recurrence)) OR (progression))) AND (((pseudoprogression) OR (necrosis)) OR (radiation injury))) AND (glioblastoma).

Studies were eligible for inclusion if they met the following criteria: (I) diagnostic studies evaluating the differentiation of PP from RT in glioblastoma; (II) use of DSC perfusion as the diagnostic method; and (III) enrollment of ≥20 patients. The exclusion criteria were as follows: absence of extractable raw diagnostic data, reviews, case series, or studies involving non-human participants.

Data extraction

Two investigators independently extracted data from all eligible studies, with discrepancies resolved by consultation with a third investigator. Extracted information included: first author, country, publication year, study design, sample size, blinding status, MRI field strength, diagnostic reference standards, and diagnostic outcomes.

Quality analyses

The methodological quality of the included studies was evaluated using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool (10).

Statistical analysis

Diagnostic performance metrics, including pooled sensitivity, specificity, positive likelihood ratio (PLR), and negative likelihood ratio (NLR), were calculated. High diagnostic accuracy was defined as an NLR <0.2 combined with a PLR >5. Summary receiver operating characteristic (SROC) curves analyses were performed, with an area under the curve (AUC) >0.8 considered indicative of strong diagnostic accuracy. Fagan plots were used to assess prior and diagnostic probabilities. Heterogeneity across studies was examined using Cochran's Q test and I^2 statistics,

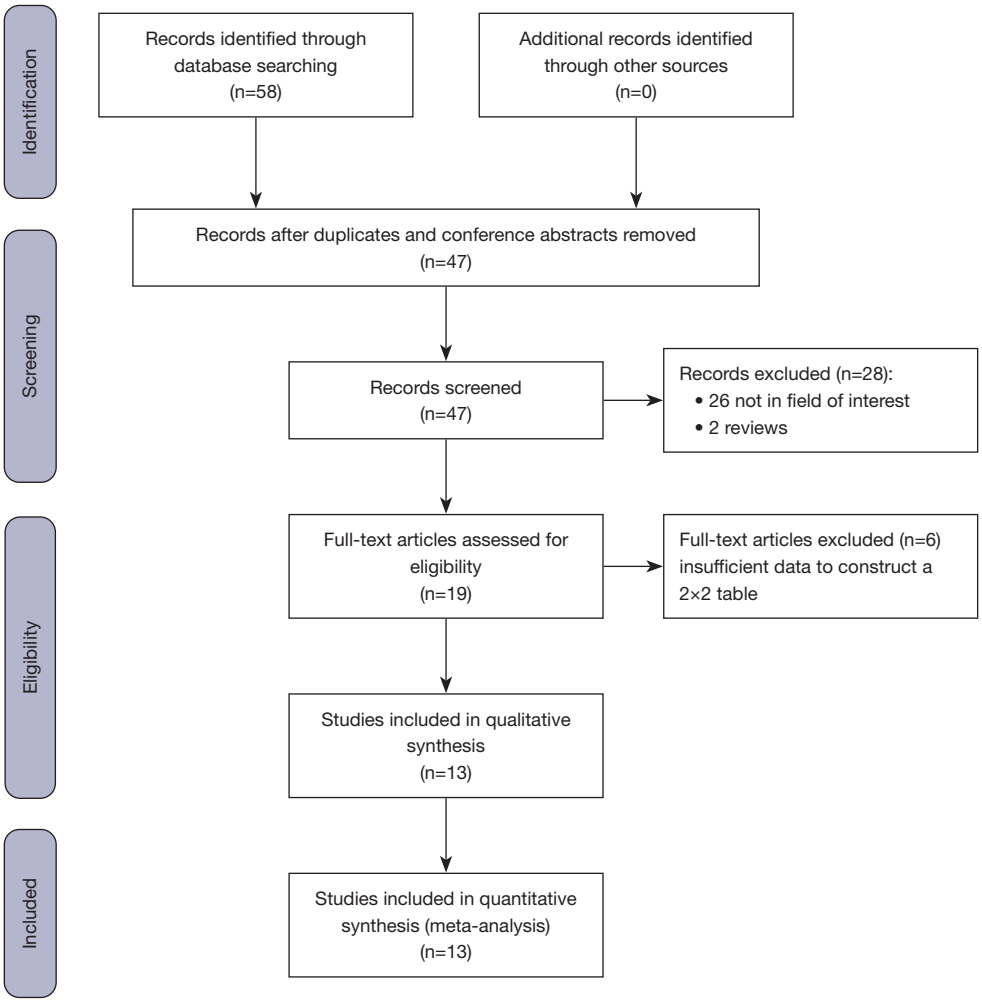

Figure 1 The study selection process for this meta-analysis.

with I^2 values >50% indicating substantial heterogeneity. Leave-one-out sensitivity analyses were applied to identify potential sources of heterogeneity. Publication bias was assessed using Deeks' funnel plots, with statistical significance defined as P<0.05. All analyses were conducted using Stata 12.0 (StataCorp., College Station, TX, USA).

Results

Study selection

The initial database search yielded 58 potentially relevant articles, of which 13 met the inclusion criteria and were incorporated into the final analysis (11-23). The study selection process is summarized in *Figure 1*. In total, 487 patients were included across these studies, with 318 classified as RT and 178 as PP. RT diagnoses were confirmed exclusively through pathological evaluation, whereas PP diagnoses were verified either by pathology or through MRI follow-up (11-23). Among the included studies, three used both relative cerebral blood volume (rCBV) and relative cerebral blood flow (rCBF) for diagnostic assessment (15,17,21), whereas the remainder relied solely on rCBV (*Table 1*). The extracted raw data about diagnostic performance are summarized in *Table 2*.

Risk of bias assessments are presented in *Figure 2A*,*2B*. Seven studies did not specify whether patient enrollment was consecutive (11,14,16,17,19,21,22), and eight did not clarify whether MRI evaluations were performed under blinded conditions (11,12,14,16,17,20,22,23).

Table 1 Characteristics of studies included in meta-analysis

Studies	Year	Country	Study design	Blind	Patients (n)	Field strength	Reference standards	Diagnostic tools			
								rCBV	Cutoff	rCBF	Cutoff
Barajas (11)	2009	USA	Retrospective	Unclear	57	1.5	P, F	Yes	1.75	No	–
Cha (12)	2014	Korea	Retrospective	Unclear	35	3	P, F	Yes	1.8	No	–
Choi (13)	2013	Korea	Retrospective	Yes	62	3	P, F	Yes	NR	No	–
Di Costanzo (14)	2014	Italy	Retrospective	Unclear	29	3	P, F	Yes	<2	No	–
Feng (15)	2022	China	Prospective	Yes	46	3	P, F	Yes	3.25	Yes	1.67
Hojjati (16)	2018	USA	Retrospective	Unclear	22	3	P, F	Yes	3.32	No	–
Hu (17)	2011	USA	Retrospective	Unclear	31	NR	P, F	Yes	1.14	Yes	0.98
Jajodia (18)	2022	India	Retrospective	Yes	44	1.5	P, F	Yes	3.4	No	–
Jovanovic (19)	2017	Serbia	Prospective	Yes	31	3	P, F	Yes	2.89	No	–
Maiter (20)	2022	UK	Retrospective	Unclear	32	3	P, F	Yes	3	No	–
Manning (21)	2020	USA	Retrospective	Yes	32	3	P, F	Yes	1.335	Yes	1.335
Nael (22)	2018	USA	Retrospective	Unclear	46	3	P, F	Yes	2.2	No	–
Young (23)	2013	USA	Retrospective	Unclear	20	1.5/3	P, F	Yes	2.4	No	–

F, follow-up; NR, not reported; P, pathological; rCBF, relative cerebral blood flow; rCBV, relative cerebral blood volume.

Table 2 Raw data of diagnostic performance of studies included in this meta-analysis

Studies	rCBV				rCBF			
	True positive	False positive	False negative	True negative	True positive	False positive	False negative	True negative
Barajas (11)	36	6	10	14	–	–	–	–
Cha (12)	9	4	2	20	–	–	–	–
Choi (13)	28	9	6	19	–	–	–	–
Di Costanzo (14)	18	1	3	7	–	–	–	–
Feng (15)	27	2	4	13	26	1	5	14
Hojjati (16)	18	1	0	3	–	–	–	–
Hu (17)	13	1	2	15	13	3	2	13
Jajodia (18)	23	2	5	14	–	–	–	–
Jovanovic (19)	20	0	0	11	–	–	–	–
Maiter (20)	17	4	2	9	–	–	–	–
Manning (21)	22	1	3	6	21	1	4	6
Nael (22)	27	1	7	11	–	–	–	–
Young (23)	16	1	0	3	–	–	–	–

rCBF, relative cerebral blood flow; rCBV, relative cerebral blood volume.

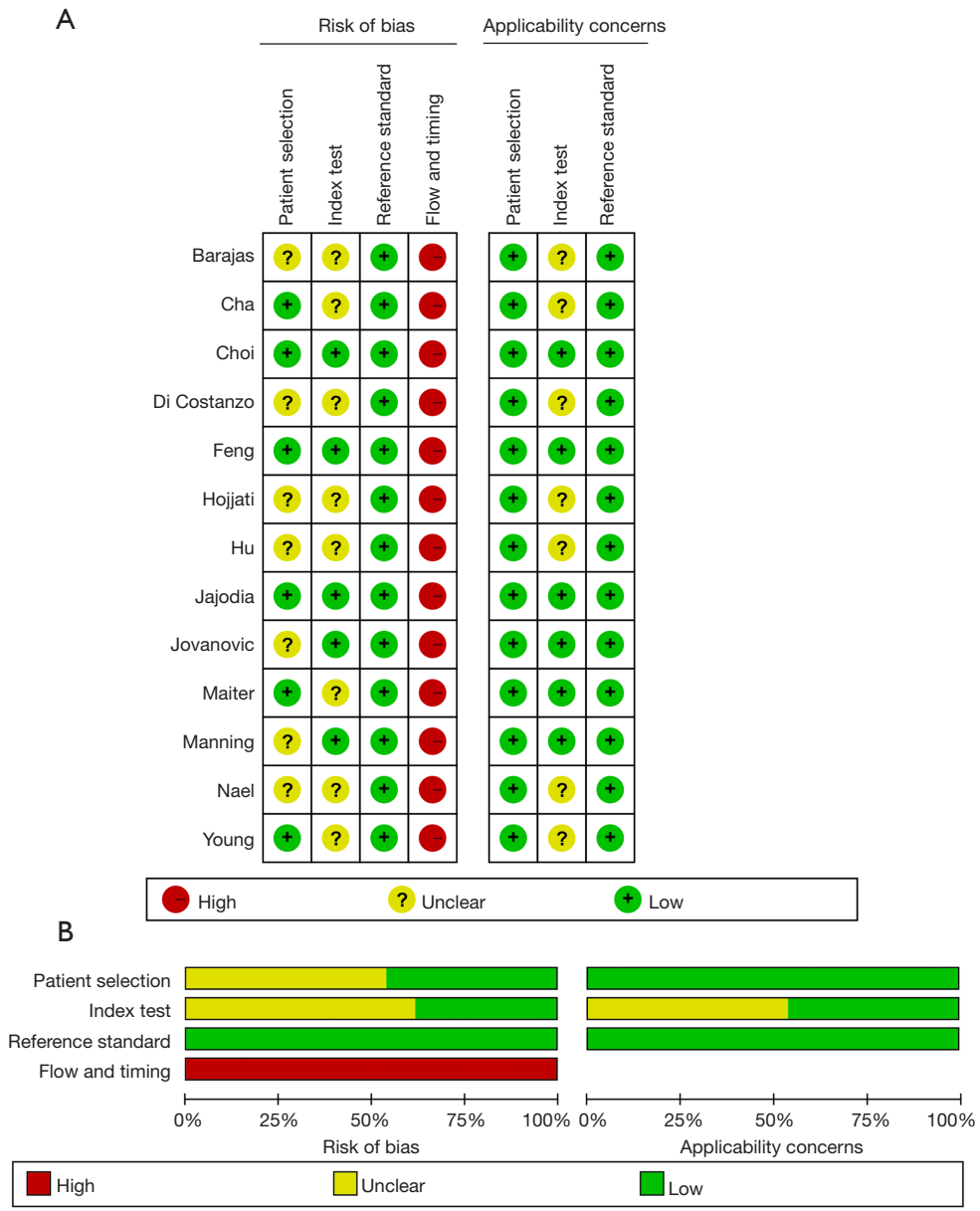

Figure 2 Quality assessment of the included studies according to the QUADAS-2 criteria. (A) The quality assessment of each included study. (B) The summary of the quality assessment. QUADAS-2, Quality Assessment of Diagnostic Accuracy Studies.

Diagnostic performance

All included studies provided rCBV-related diagnostic outcomes, with pooled analyses exhibiting respective sensitivity, specificity, PLR, and NLR values of 87% [95% confidence interval (CI): 82–91%, *Figure 3A*], 83% (95% CI: 75–89%, *Figure 3B*), 5.14 (95% CI: 3.35–7.89, *Figure 3C*), and 0.16 (95% CI: 0.11–0.23, *Figure 3D*), respectively. None of these parameters showed substantial heterogeneity (I^2=18.92%, 11.76%, 0%, and 0.35%, respectively), eliminating the need for sensitivity analyses. The pooled AUC for rCBV-based diagnostic performance was 0.92 (95% CI: 0.89–0.94, *Figure 4*), indicating excellent diagnostic accuracy. Fagan plot analysis demonstrated a pre-test probability of 20%, with post-test probabilities of 4% for NLR and 56% for PLR, respectively (*Figure 5*). The

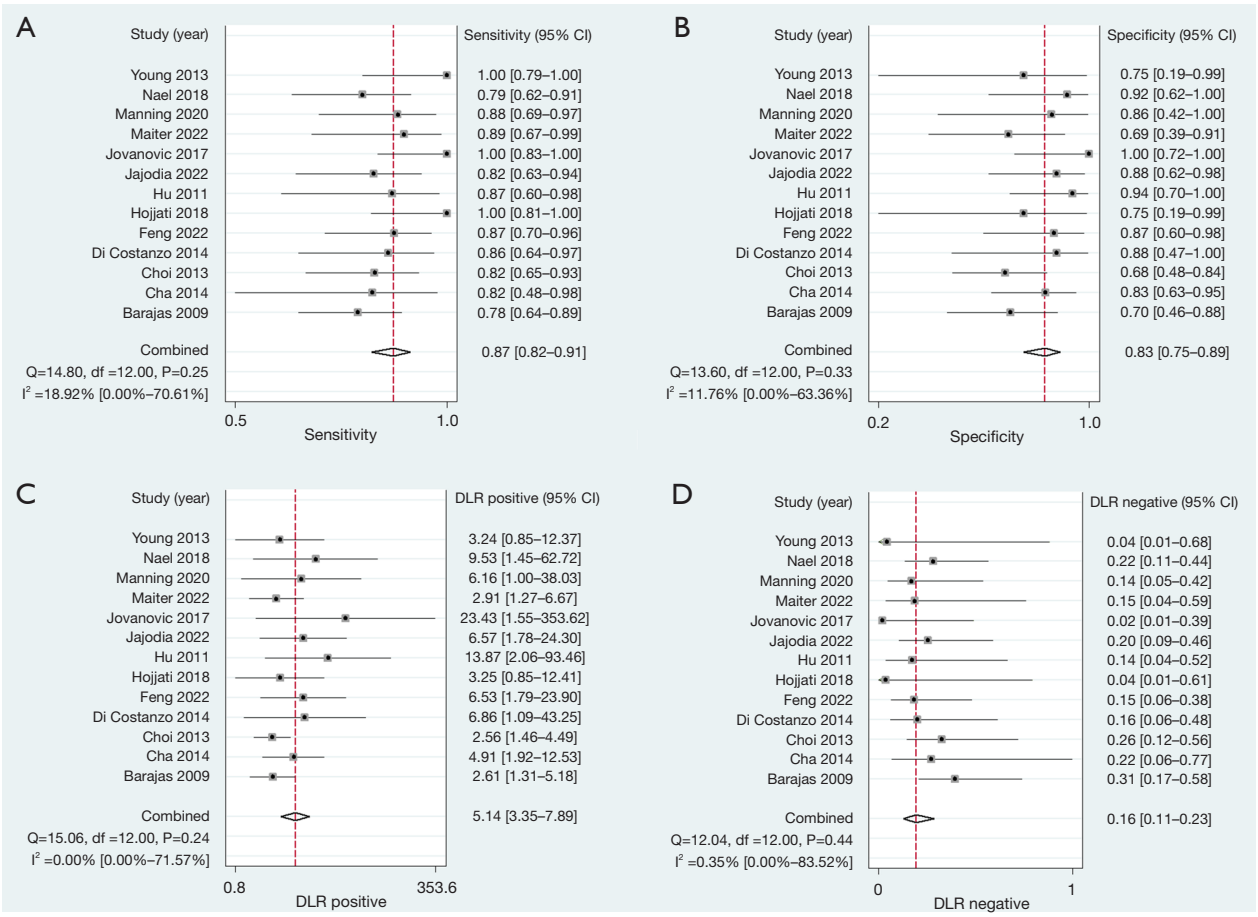

Figure 3 The results of pooled (A) sensitivity, (B) specificity, (C) PLR, and (D) NLR for this meta-analysis. CI, confidence interval; DLR, diagnostic likelihood ratio; NLR, negative likelihood ratio; PLR, positive likelihood ratio.

likelihood of publication bias in this meta-analysis was not significant (P=0.051).

As only three studies reported diagnostic outcomes for rCBF, pooled analyses for this parameter were not possible.

Discussion

In patients with glioma, PP and RT often present with overlapping features on conventional MRI, despite apparent biological differences in their angiogenic profiles (24). MRI perfusion provides further insight by characterizing microvascular distribution within the lesion, offering a means of differentiating these entities (24). RT is typically associated with immature vascular networks, increased neovascular density, and elevated expression of vascular endothelial growth factor. In contrast, PP is characterized by vascular endothelial cell apoptosis, leading to reduced perfusion (25). As the most aggressive WHO grade IV glioma, glioblastoma is particularly characterized by high levels of blood perfusion (26).

The current systematic review evaluated the diagnostic performance of DSC perfusion in distinguishing PP from RT in glioblastoma. In the present study, rCBV, the most commonly employed DSC perfusion parameter, demonstrated strong diagnostic accuracy with an AUC of 0.92, sensitivity of 87%, and specificity of 83%. These findings indicate that rCBV is a reliable marker for differentiating PP from RT in this patient population. Moreover, the observed PLR (5.14) and NLR (0.16) values suggest that rCBV offers clinically meaningful predictive power: values above the diagnostic threshold corresponded to a 5-fold higher likelihood of a lesion being RT rather

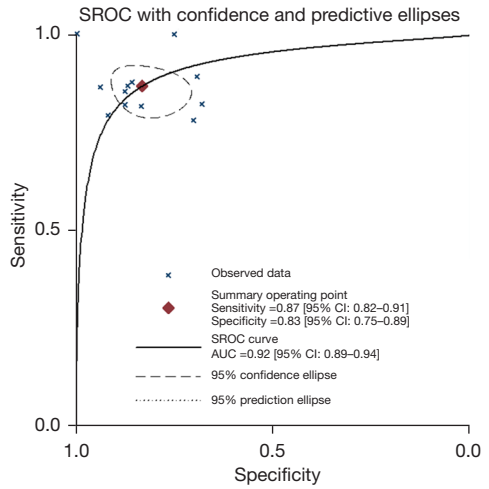

Figure 4 The SROC curve of this meta-analysis. AUC, area under the curve; SROC, summary receiver operating characteristic.

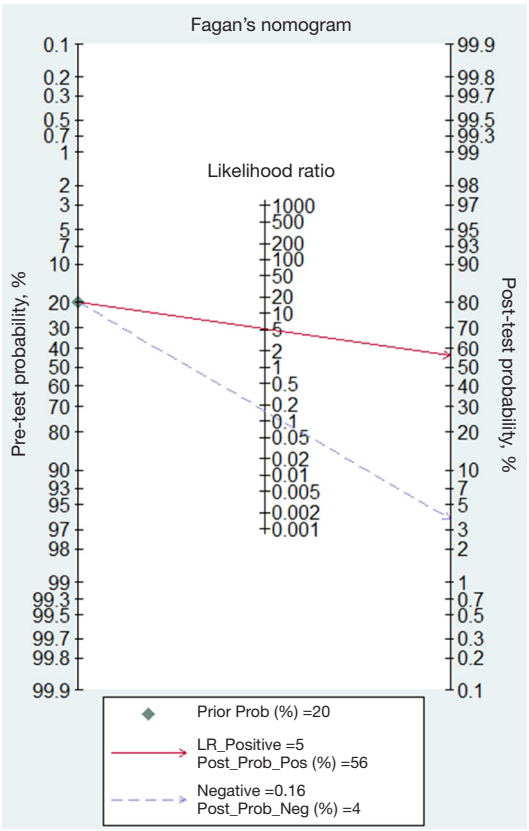

Figure 5 The Fagan plot of this meta-analysis. LR, likelihood ratio.

than PP, whereas values below the threshold were associated with a more than 80% probability of PP.

The rCBF represents another DSC perfusion parameter that has previously been identified as a valuable marker for distinguishing RT from PP in patients with high-grade gliomas, with one systematic review reporting an AUC of 0.92 (6). In the present analysis, however, only three included studies reported rCBF-related outcomes, preventing the performance of pooled analyses for this parameter.

Arterial spin labeling (ASL) perfusion is a non-contrast enhanced MRI technique that measures tissue perfusion using water molecules in arterial blood as endogenous tracers, unaffected by the integrity of the blood–brain barrier (27). Compared with DSC perfusion, ASL provides a non-invasive means of evaluating perfusion status. A previous meta-analysis reported an AUC of 0.88 for ASL in differentiating RT from PP in patients with glioma, indicating high diagnostic accuracy (28). However, ASL has certain limitations including prolonged acquisition times and lower spatial resolution compared with DSC perfusion (29).

DSC perfusion offers a broader range of diagnostic parameters than ASL perfusion (29,30), whereas ASL relies exclusively on CBF as a diagnostic index (28-30); DSC perfusion incorporates both rCBV and rCBF in addition to time to peak (TTP) and mean transit time (MTT) parameters (6), which can further enhance diagnostic discrimination.

Zhang *et al.* (7) and Gu *et al.* (6) previously performed a meta-analysis evaluating the differentiation between PP and RT among glioma and high-grade glioma patients, yielding AUC values of 0.91 and 0.92, respectively (6,7). These meta-analyses, however, included gliomas of varying WHO grades and were susceptible to some degree of selection bias. Here, the present meta-analysis specifically focused on glioblastoma patients, thus limiting the potential for selection bias and ensuring greater result reliability.

This study has several limitations. First, the majority of the studies were retrospective in nature, and many provided limited information regarding blinding procedures, introducing a considerable risk of bias within this systematic review. Second, variability in MRI acquisition parameters across studies may have contributed to heterogeneity and potential bias in the pooled results. Third, the overall number of eligible studies was relatively small, which

restricted the ability to conduct pooled analyses for rCBF-related diagnostic outcomes.

Conclusions

This systematic review demonstrates that DSC perfusion, particularly through the use of rCBV, provides a reliable and accurate method for differentiating PP from RT in patients with glioblastoma.

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Footnote

Reporting Checklist: The authors have completed the PRISMA reporting checklist. Available at https://qims.amegroups.com/article/view/10.21037/qims-2025-245/rc

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-2025-245/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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