Diagnostic accuracy of dynamic contrast-enhanced magnetic resonance imaging for distinguishing pseudoprogression from glioma recurrence: a meta-analysis

Jun Qiu1, Zhen-Chao Tao2, Ke-Xue Deng1, Peng Wang1, Chuan-Yu Chen1, Fang Xiao1, Yi Luo1, Shu-Ya Yuan1, Hao Chen1, Huan Huang1

1Department of Radiology, The First Affiliated Hospital of University of Science and Technology of China, Division of Life Sciences and Medicine, University of Science and Technology of China, Hefei, Anhui 230036, China; 2Department of Radiation Oncology, The First Affiliated Hospital of University of Science and Technology of China, Division of Life Sciences and Medicine, University of Science and Technology of China, Hefei, Anhui 230036, China.

Abstract
Background: It is crucial to differentiate accurately glioma recurrence and pseudoprogression which have entirely different prognosis and require different treatment strategies. This study aimed to assess the diagnostic accuracy of dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) as a tool for distinguishing glioma recurrence and pseudoprogression.

Methods: According to particular criteria of inclusion and exclusion, related studies up to May 1, 2019, were thoroughly searched from several databases including PubMed, Embase, Cochrane Library, and Chinese biomedical databases. The quality assessment of diagnostic accuracy studies was applied to evaluate the quality of the included studies. By using the “mada” package in R, the heterogeneity, overall sensitivity, specificity, and diagnostic odds ratio were calculated. Moreover, funnel plots were used to visualize and estimate the publication bias in this study. The area under the summary receiver operating characteristic (SROC) curve was computed to display the diagnostic efficiency of DCE-MRI.

Results: In the present meta-analysis, a total of 11 studies covering 616 patients were included. The results showed that the pooled sensitivity, specificity, and diagnostic odds ratio were 0.792 (95% confidence interval [CI] 0.707–0.857), 0.779 (95% CI 0.715–0.832), and 16.219 (95% CI 9.123–28.833), respectively. The value of the area under the SROC curve was 0.846. In addition, the SROC curve showed high sensitivities (>0.6) and low false positive rates (<0.5) from most of the included studies, which suggest that the results of our study were reliable. Furthermore, the funnel plot suggested the existence of publication bias.

Conclusions: While the DCE-MRI is not the perfect diagnostic tool for distinguishing glioma recurrence and pseudoprogression, it was capable of improving diagnostic accuracy. Hence, further investigations combining DCE-MRI with other imaging modalities are required to establish an efficient diagnostic method for glioma patients.

Keywords: Meta-analysis; Dynamic contrast-enhanced magnetic resonance imaging; Pseudoprogression; Diagnostic accuracy; Glioma

Introduction
As the most common primary brain tumors, gliomas account for about 80% of all malignant brain tumors as well as 30% of all central nervous system tumors.[1] To date, present standard therapy includes surgical approaches, such as gross total or subtotal excision, followed by concomitant chemo-radiotherapy and temozolomide adjuvant chemotherapy.[2] However, such treatment may cause radiation-induced damage to brain tissue of glioma patients and increase the risk of recurrence. Pseudoprogression is a sub-acute clinical entity, which is characterized by the expansion of existing lesions or the appearance of new lesions within 12 weeks after radiation therapy. In contrast to true tumor progression, the lesions induced by pseudoprogression subsequently stabilize or shrink without further treatment.[3] In several previous reports on glioma patients, the occurrence rate of pseudoprogression is in the range of 15% to 60%.[4–6] In many cases, lesions of pseudoprogression exhibit contrast enhancement on contrast-enhanced magnetic resonance imaging (MRI) or computed tomography, which is similar with those of tumor...
progression.\(^7\)\(^,\)\(^8\) Because therapeutic protocols between recurrences and pseudoprogression are totally different, it is important to explore a method for distinguishing them correctly in the treatment of glioma.

As one of the modern imaging tools, the dynamic contrast-enhanced (DCE)-MRI technique has been extensively applied to tumor diagnosis.\(^9\)\(^,\)\(^10\) Based on the DCE-MRI, the physician can detect the microcirculation in the tissue of patients by analyzing the changes of some pharmacokinetic parameters, which include the extravascular extracellular space per unit volume of tissue (\(V_e\)), the rate transfer constant (\(K_p\)), the blood plasma volume per unit volume of tissue (\(V_p\)), and the volume transfer constant (\(K_{\text{trans}}\)). Some previous research studies have suggested that the parameters provided by DCE-MRI, such as \(V_e\) and \(K_{\text{trans}}\) in pseudoprogression were obviously different from those in true progression.\(^11\)\(^,\)\(^12\) Besides, an earlier study conducted by Biswas et al\(^13\) and Haider et al\(^14\) demonstrated that the parameters provided by DCE-MRI are capable of diagnosing recurrent and radiation injury. Nevertheless, these studies present a major limitation, that is the small sample size.

The purpose of this meta-analysis was to explore the value of DCE-MRI-derived pharmacokinetic parameters in distinguishing glioma recurrence from pseudoprogression for glioma patients.

Methods

Literature search

Based on the PubMed, Embase, Cochrane Library, and Chinese biomedical databases, relevant articles published before May 1, 2019, were searched comprehensively and systematically. In this study, the search strategy was (“glioma” OR “glioblastoma” OR “brain tumour” OR “brain tumor” OR “astrocytoma” OR “neuroectodermal tumor” OR “neuroectodermal tumour” OR “brain neoplasm” OR “neuroglioma” OR “glial tumor” OR “glial tumour” OR “oligodendroglioma” OR “oligodendrocytoma”) AND (“Dynamic contrast enhanced T1 MRI” OR “\(K_{\text{trans}}\)” OR “DCE”) AND (“MRI” OR “magnetic resonance” OR “MR”) AND (“pseudoprogression” OR “recurrence” OR “recurrent” OR “tumor progression” OR “postradiation” OR “radiation necrosis” OR “radiation injury”). Only articles published in English were accepted. At the same time, the relevant references listed in the retrieved articles were also widely scanned to seek other articles of possible eligibility.

Study selection

The included studies were in line with the following criteria:

1. Design of the study: retrospective (R)/prospective (P) study.
2. Patients: expansion of existing lesions or appearance of new lesions in the radiotherapy target area of glioma patients.
3. Diagnostic tool: DCE-MRI.
4. Data: adequate data for calculating true positives (TPs), false positives (FPs), false negatives (FNs), and true negatives (TNs).

The studies with the following characteristics were excluded:

1. Review articles, abstracts, comments, proceedings, meetings, case reports, and letters.
2. Studies highly correlated with glioma but without related data for our analysis.

When contradictory results appeared, full discussions were performed to resolve disagreements.

Data extraction and quality assessment

According to the criteria of study selection, we extracted several types of characteristics from the articles, which included study characteristics (name of the first author, source of publication, year of publication, and study design), patient characteristics (age, sex, and numbers of the population), tumor treatment (radiation therapy dose and chemotherapy drug), and parameters of DCE-MRI. The values of TP, FP, FN, and TN were also calculated. The quality of included studies was evaluated by using the quality assessment of diagnostic accuracy studies (QUADAS-2).\(^15\) The included studies were determined based on the consensus of all authors and analyzed by the Review Manager (version 5.3, Cochrane Collaboration, Oxford, UK).

Statistical analysis

In this meta-analysis, data from each included study were analyzed using the bivariate approach of Reitsma et al\(^16\) in the R package “meta.”\(^17\) Statistical heterogeneity between studies was determined by using Cochran Q-statistic and \(I^2\) statistic. If significant heterogeneity was detected (presence of \(P\) value < 0.05 for the Cochran Q test and \(I^2 > 50\%\)), the DerSimonian and Laird random-effects model was used; in other cases, the Mantel-Haenszel fixed-effects model was applied. Pooled sensitivity, specificity, and their 95% CIs were calculated and shown as forest plots.\(^18\)\(^-\)\(^20\) Besides, the summary receiver operating characteristic (SROC) curve area was also calculated. When the values of area under the curve (AUC) was >0.8, the studied parameters were considered to be of great potential for actual clinical application. In addition, publication bias was explored by constructing a funnel plot to visualize the available data and a regression test for the funnel plot to statistically test any asymmetry in the funnel plot with the “meta” R package.\(^21\) Moreover, Deek funnel plot asymmetry test was also applied to assess the publication bias by using the Stata software (version 12.0).\(^22\)

Results

Study selection and summary of included studies

After a comprehensive and systematic search of multiple databases, a total of 509 records were returned. Initially, a
total of 35 publications were identified as duplicate studies and excluded. Afterward, 463 studies were excluded for diverse reasons (not original researches, not relevant studies, or insufficient data) based on their title, abstract, and full text. Finally, the remaining 11 records were included in this meta-analysis.[7,11,12,23,24] More details of the study selection are depicted in Figure 1.

The main characteristics of studies, patients, tumor treatment, and parameters of DCE-MRI in each included study are presented in Table 1. The included studies consisted of two prospective studies and nine retrospective studies, which were published between 2011 and 2019. Moreover, a total of 616 patients with glioma were included in the studies. The gender ratio among studies was comparable. The clinical or history pathology of patients was used as a reference standard for the included studies. Besides, the TP, TN, FP, and FN of each study are also shown in Table 1.

Quality evaluation
We applied QUADAS-2 to assess the quality of the included studies. The result for evaluation of quality is shown in Figure 2. As we can see, there was only one study with a high-risk bias in the reference standard. For applicability concerns, we found that only one study regarding the selection of patient was treated as a high concern for the reference standard. In addition, the overall attributes of the included studies with high, low, or unclear risk of bias are as shown in a graph [Figure 2]. In general, the quality of the included studies was relatively high with a low-risk bias and applicability concerns and met the requirements of this meta-analysis.

Data analysis
As the heterogeneity between the included studies was significant ($I^2 = 77.5\%$ and Cochran-$Q < 0.05$), the
random-effects model was used in the current analysis. As shown in Figure 3, the overall sensitivity and specificity for differentiating recurrent glioma from pseudoprogression by DCE-MRI were 0.792 (95% CI 0.707–0.857) and 0.779 (95% CI 0.715–0.832), respectively. The analysis of the variability by visual evaluation of the paired forest plots indicated low variability for sensitivity and moderate variability for specificity.

A diagnostic odds ratio of 16.219 (97.5% CI 9.123–28.833) was recorded; this value indicates that the likelihood of the distinction of recurrent glioma from pseudoprogression was approximately 16 times higher using DCE-MRI. The large CI observed was the result of the small study size.

In addition, the SROC curve obtained by the bivariate model is as depicted in Figure 4. The AUC value of the SROC curve was 0.846. Overall, the SROC curve indicated high sensitivities (>0.6) and low FPRs (FPRs = 1–specificity) (<0.5) from most of the included studies.

The slope of the curve was substantially parabolic indicating that sensitivity was dependent on specificity. The sensitivity was very similar across studies while the specificity varied markedly. These results indicate the accuracy of DCE-MRI in the differential diagnostic of recurrent glioma from pseudoprogression.

### Evaluation of study heterogeneity

We performed a crosshair plot to show the sensitivity and FPR of each included study. To acquire a view of the scatter of the study results, each study was plotted as a single sensitivity–FPR point along with 95% CIs. As shown in Figure 5, the crosshair of studies from Suh et al.,[25] Kim et al.[24] and Chung et al.[7] were very close to each other, showing similar sensitivity and specificity; and the specificity of the CIs reported by Suh et al.[25] was wider than those reported by the other two studies. Meanwhile, we also found that the crosshairs of Seeger et al.[29] had a wider confidence interval than Nael et al.[30] and the study of Seeger et al.[29] had a wider specificity for the CIs than Nael et al.[30]. Besides, there were no significant differences between the specificity values of the 11 included studies in our analysis, while the sensitivity values were significantly different from the specificity values. However, the heterogeneity of the included studies was significant ($I^2 = 77.5\%$).

### Publication bias

As shown in Figure 6, the publication bias of this meta-analysis was assessed by constructing funnel plots. The result for the bias test from the “meta” R package showed that the included studies’ outcomes exhibited publication bias ($t = 3.21; P = 0.005$). Meanwhile, Deek test showed a similar result ($P = 0.01$) [Figure 7], suggesting publication bias in the outcomes of the included studies.

### Discussion

The misdiagnosis of pseudoprogression or true progression might lead to wrong clinical treatment decisions and unnecessary surgery; thus, it is urgent to explore an accurate method to distinguish pseudoprogression from tumor recurrence in glioma treatment. As known, changes in the contrast-enhancement area on MRI are commonly used as an indicator for the therapy response or tumor relapse in patients, but conventional MRI cannot correctly differentiate tumor recurrence from pseudoprogression.

As with the development of MRI technology, several advanced MRI modalities appeared in recent years, such as...
the DCE-MRI and dynamic susceptibility contrast (DSC)-MRI. Compared with the DSC-MRI, the DCE-MRI has distinct advantages with greater spatial resolution, better estimations of vascular leakiness, and less artifact from sources of susceptibility. Some clinical studies indicated that DCE-MRI might provide useful information for the prognosis of glioma models or patients. A research of Hou et al. revealed that DCE-MRI could be used to evaluate the hypoxia status of the glioma model. Meanwhile, a previous study conducted by Thomas et al. revealed that the lower mean and 90th percentile values for both $V_p$ and $K_{trans}$ showed a correlation with pseudoprogression. Besides, the study also suggested that the parameters of DCE-MRI, $V_p$ ratio, and $K_{trans}$ ratio could be used as predictors for the determination of lesion etiology.

In this study, our findings suggest that DCE-MRI could aid in distinguishing recurrence from pseudoprogression in glioma patients. The DCE-MRI showed high sensitivity (0.792) and specificity (0.779). These data indicate that the DCE-MRI could be used as a diagnostic tool for differentiating recurrent and pseudoprogression in patients with glioma.

There are several strengths in this meta-analysis. First, to reduce the risk of selection bias, the study selection, data extraction as well as evaluation of the risk of bias were conducted by the three authors respectively and independently. Besides, all the included studies were highly correlated with the diagnostic value of DCE-MRI for recurrence, radiation injury, or/and pseudoprogression in glioma patients. In addition, this meta-analysis assessed the
Furthermore, this meta-analysis is rigorously in compliance with the preferred reporting items for systematic reviews and meta-analyses protocols.[35,36] However, our meta-analysis still presents some limitations. There is obvious heterogeneity across the included studies in the current meta-analysis; thus, the results from the analysis should be explained more cautiously. First, the number of studies that meet the inclusion criteria of this meta-analysis is limited, and the small number of cases may slightly reduce the reliability of the results. Second, most of the included studies were retrospective researches, except for two that were prospective researches. Third, the various clinical characteristics of the study cases, such as age, radiotherapy dose, and chemotherapy, could be significant sources of heterogeneity because treatment methods and age are correlated with recurrence and pseudoprogression in glioma. Finally, this meta-analysis only included English language literature, which might lead to missing some other articles and hence result in the publication bias in this meta-analysis. Nevertheless, we believe the results of this study are valuable as the exclusion of non-English publications from systematic reviews had a minimal effect on overall conclusions.[37]

**Figure 3:** Paired forest plots indicating the sensitivity and the specificity of the DCE for differentiating recurrent glioma from pseudoprogression. DCE: Dynamic contrast-enhanced.

**Figure 4:** SROC curve with individual study outcomes. SROC: Summary receiver operating characteristic.

diagnostic value of DCE-MRI for distinguishing glioma recurrence from pseudoprogression in patients.
Figure 5: Crosshair plot of individual study outcomes representing the sensitivity and FPR (FPR = 1 – specificity) (A) and a plot with confidence regions (B) for each study. FPR: False positive rate.

Figure 6: Funnel plot.
Furthermore, as the sample size of the included studies is relatively small, we did not perform subgroup analysis.

In summary, DCE-MRI showed the potential for improvement of the diagnostic accuracy in distinguishing glioma recurrence from pseudoprogression. However, owing to the drawbacks of our study as listed earlier, additional studies with larger sample sizes would be required to obtain a more credible result. Moreover, further investigations on diagnosis efficiency of combining the DCE-MRI with other imaging modalities might aid in establishing an efficient diagnostic method for distinguishing glioma recurrence from pseudoprogression in glioma patients.

**Conflicts of interest**

None.

**References**

1. Ostrom QT, Gittleman H, Liao P, Rouse C, Chen Y, Dowling J, et al. CBTRUS statistical report: primary brain and central nervous system tumors diagnosed in the United States in 2007-2011. Neuro Oncol 2014;16(Suppl 4):v1–v63. doi: 10.1093/neo/mou223.
2. Stupp R, Mason WP, van den Bent MJ, Weller M, Fisher B, Taphoorn MJ, et al. Radiotherapy plus concomitant and adjuvant temozolomide for glioblastoma: optimum area under the curve method derived from dynamic contrast-enhanced T1-weighted perfusion MR imaging. Radiology 2013;267:561–568. doi: 10.1148/radiol.13130016.
3. Wen PY, Macdonald DR, Reardon DA, Cloughesy TF, Sorensen AG, van den Bent MJ, Taal W. Updated response assessment criteria for high-grade gliomas: response assessment in neuro-oncology working group. J Clin Oncol 2011;29:252. doi: 10.1200/JCO.2009.26.3341.
4. Fink J, Born D, Chamberlain MC. Pseudoprogression: relevance with respect to treatment of high-grade gliomas. Curr Treat Options Oncol 2011;12:240–252. doi: 10.1007/s11864-011-0157-1.
5. van West SE, de Bruin HG, van de Langen JT, Swaak-Krauten AT, van den Bent MJ, Taal W. Incidence of pseudoprogression in low-grade gliomas treated with radiotherapy. Neuro Oncol 2017;19:719–725. doi: 10.1093/neuonc/nov194.
6. Kruser TJ, Mehta MP, Robins H. Pseudoprogression after glioma therapy: a comprehensive review. Expert Rev Neurother 2013;13:389–403. doi: 10.1586/ern.13.7.
7. Chung WJ, Kim HS, Kim N, Choi CG, Kim SJ. Recurrent glioblastoma: optimum area under the curve method derived from dynamic contrast-enhanced T1-weighted perfusion MR imaging. Radiology 2013;267:561–568. doi: 10.1148/radiol.13130016.
8. Reddy K, Westerly D, Chen C. MRI patterns of T1 enhancing radiation necrosis versus tumour recurrence in high-grade gliomas. J Med Imaging Radiat Oncol 2013;57:349–355. doi: 10.1111/j.1754-9485.2012.02472.x.
9. Heye AK, Culling RD, Valdés Hernández MDC, Thripplenton MJ, Wardlaw JM. Assessment of blood-brain barrier disruption using dynamic contrast-enhanced MRI. A systematic review. Neuroimage Clin 2014;6:262–274. doi: 10.1016/j.nicl.2014.09.002.
10. Leach MO, Morgan B, Tofts PS, Buckley DL, Huang W, Horsfield MA, et al. Imaging vascular function for early stage clinical trials using dynamic contrast-enhanced magnetic resonance imaging. Eur Radiol 2012;22:1451–1464. doi: 10.1007/s00330-012-2446-x.
11. Yan TJ, Park C-K, Kim TM, Lee S-H, Kim J-H, Sohn C-H, et al. Glioblastoma treated with concurrent radiation therapy and temozolomide chemotherapy: differentiation of true progression from pseudoprogression with quantitative dynamic contrast-enhanced MR imaging. Radiology 2015;274:830–840. doi: 10.1148/radiol.14123632.
12. Thomas AA, Arevalo-Perez J, Kaley T, Iyo J, Peck KK, Shi W, et al. Dynamic contrast enhanced T1 MRI perfusion differentiates pseudoprogression from recurrent glioblastoma. J Neurooncol 2015;125:183–190. doi: 10.1007/s11060-015-1893-z.
13. Bisdas S, Naegeli T, Ritz R, Dimonstheni A, Pfannenberg C, Reimold M, et al. Distinguishing recurrent high-grade gliomas from radiation injury: a pilot study using dynamic contrast-enhanced MRI imaging. Acad Radiol 2011;18:575–583. doi: 10.1016/j.acra.2011.01.018.
14. Haider MA, Chung P, Sweet J, Tao A, Jhaveri K, Ménard C, et al. Dynamic contrast-enhanced magnetic resonance imaging for localization of recurrent prostate cancer after external beam radiotherapy. Int J Radiat Oncol Biol Phys 2008;70:425–430. doi: 10.1016/j.ijrobp.2007.06.029.
15. Whiting PF, Rutjes AW, Westwood ME, Mallett S, Deeks JJ, Reitsma JB, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. Ann Intern Med 2011;155:529–536. doi: 10.7326/0003-4819-155-8-20110810-00009.
16. Reitsma JB, Glas AS, Rutjes AW, Scholten RJ, Bossuyt PM, Zwinderman AH. Bivariate analysis of sensitivity and specificity produces informative summary measures in diagnostic reviews. J Clin Epidemiol 2005;58:982–990. doi: 10.1016/j.jclinepi.2005.02.022.
17. Deoer P, Holling H. Meta-analysis of Diagnostic Accuracy with Mada. Available from: https://rrdr.io/rorge/mada/binst/doc/mada. pdf. Accessed May 25, 2020.
18. Zhao N, Abraira V, Muriel A, Khan K, Coomarasamy A. Meta-Dis: a software for meta-analysis of test accuracy data. BMC Med Res Methodol 2006;6:31. doi: 10.1186/1471-2288-6-31.
19. Honest H, Khan KS. Reporting of measures of accuracy in systematic reviews of diagnostic literature. BMC Health Serv Res 2002;2:4. doi: 10.1186/1472-6963-2-4.
20. DerSimonian R, Laird N. Meta-analysis in clinical trials revisited. Control Clin Trials 2015;45:139–145. doi: 10.1016/j.cct.2015.09.002.
21. Schwarzer G, Carpenter JR, Rücker G. Meta-analysis with R. Cham: Springer; 2015.
22. Deeks JJ, Giftplak P, Irwig L. The performance of tests of publication bias and other sample size effects in systematic reviews of diagnostic test accuracy was assessed. J Clin Epidemiol 2005;58:882–893. doi: 10.1016/j.jclinepi.2005.01.016.
23. Hamilton JD, Lin J, Ison C, Leeds NE, Jackson EF, Fuller GN, et al. Dynamic contrast-enhanced perfusion processing for neuroradiologists: model-dependent analysis may not be necessary for determining recurrent high-grade glioma versus treatment effect. AJNR Am J Neuroradiol 2015;36:686–693. doi: 10.3174/ajnr.A4190.
24. Kim HS, Goh MJ, Kim N, Choi CG, Kim SJ, Kim JB. Which combination of MR imaging modalities is best for predicting recurrent glioblastoma? Study of diagnostic accuracy and reproducibility. Radiology 2014;273:831–843. doi: 10.1148/radiol.14132868.
25. Sun CH, Kim HS, Choi YJ, Kim N, Kim SJ. Prediction of pseudoprogression in patients with glioblastomas using the initial and final area under the curves ratio derived from dynamic contrast-enhanced T1-weighted perfusion MR imaging. AJNR Am J Neuroradiol 2013;34:2278–2286. doi: 10.3174/ajnr.A3634.
26. Narang J, Jain R, Arbab AS, Mikkelsen T, Scarpacci L, Rosenblum ML, et al. Differentiating treatment-induced necrosis from recurrent/
progressive brain tumor using nonmodel-based semiquantitative indices derived from dynamic contrast-enhanced T1-weighted MR perfusion. Neuro Oncol 2011;13:1037–1046. doi: 10.1093/neuonc/nor075.

27. Zakhari N, Taccone MS, Torres CH, Chakraborty S, Sinclair J, Woulfe J, et al. Prospective comparative diagnostic accuracy evaluation of dynamic contrast-enhanced (DCE) vs. dynamic susceptibility contrast (DSC) MR perfusion in differentiating tumor recurrence from radiation necrosis in treated high-grade gliomas. J Magn Reson Imaging 2019;50:573–582. doi: 10.1002/jmri.26621.

28. Nam JG, Kang KM, Choi SH, Lim WH, Yoo RE, Kim JH, et al. Comparison between the prebolus T1 measurement and the fixed T1 value in dynamic contrast-enhanced MR imaging for the differentiation of true progression from pseudoprogression in glioblastoma treated with concurrent radiation therapy and temozolomide chemotherapy. AJNR Am J Neuroradiol 2017;38:2243–2250. doi: 10.3174/ajnr.A5417.

29. Nael K, Bauer AH, Hormigo A, Lemoine M, Germano IM, Puig J, et al. Multiparametric MRI for differentiation of radiation necrosis from recurrent tumor in patients with treated glioblastoma. AJR Am J Roentgenol 2018;210:18–23. doi: 10.2214/AJR.17.18003.

30. Seeger A, Braun C, Skardelly M, Paulsen F, Schittenhelm J, Ernemann U, et al. Quantification of cerebral blood flow, cerebral blood volume, and blood-brain-barrier leakage with DCE-MRI. Magn Reson Med 2009;62:205–217. doi: 10.1002/mrm.22005.

31. Sourbron S, Ingrisch M, Sievert A, Reiser M, Herrmann K. Prognostic value of preoperative dynamic contrast-enhanced MRI perfusion parameters for high-grade glioma patients. Neuroradiology 2016;58:1197–1208. doi: 10.1007/s00234-016-1741-7.

32. Ali MM, Janic B, Babajani-Feremi A, Varma NRS, Iskander ASM, Anagl J, et al. Changes in vascular permeability and expression of different angiogenic factors following anti-angiogenic treatment in rat glioma. PLoS One 2010;5:e8727. doi: 10.1371/journal.pone.0008727.

33. Ali MM, Janic B, Babajani-Feremi A, Varma NRS, Iskander ASM, Anagl J, et al. Changes in vascular permeability and expression of different angiogenic factors following anti-angiogenic treatment in rat glioma. PLoS One 2010;5:e8727. doi: 10.1371/journal.pone.0008727.

34. Hou W, Xue Y, Tang W, Pan H, Xu M, Li X, et al. Evaluation of tumor hypoxia in C6 glioma rat model with dynamic contrast-enhanced magnetic resonance imaging. Acad Radiol 2019;26:e224–e232. doi: 10.1016/j.acra.2018.09.011.

35. Shamseer L, Moher D, Clarke M, Gherdi D, Liberati A, Petticrew M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ 2015;350:g7647. doi: 10.1136/bmj.g7647.

36. Moher D, Shamseer L, Clarke M, Gherdi D, Liberati A, Petticrew M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Syst Rev 2015;4:1. doi: 10.1186/s13063-014-0316-6.

37. Nussbaumer-Streit B, Klerings I, Dobrescu AI, Persad E, Stevens A, Garrity C, et al. Excluding non-English publications from evidence-syntheses did not change conclusions: a meta-epidemiological study. J Clin Epidemiol 2020;118:42–54. doi: 10.1016/j.jclinepi.2019.10.011.

How to cite this article: Qiu J, Tao ZC, Deng KX, Wang P, Chen CY, Xiao F, Luo Y, Yuan SY, Chen H, Huang H. Diagnostic accuracy of dynamic contrast-enhanced magnetic resonance imaging for distinguishing pseudoprogression from glioma recurrence: a meta-analysis. Chin Med J 2021;134(21). doi: 10.1097/CM9.0000000000001445