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META-ANALYSIS

Evaluation of tumor response to antiangiogenic therapy in patients with recurrent gliomas using contrast-enhanced perfusion-weighted magnetic resonance imaging techniques: A meta-analysis

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Author contributions: Kasenene A and Baidya A contributed equally to this work; Kasenene A and Xu HB designed this study; Kasenene A and Baidya A analyzed the data; Kasenene A, Baidya A, Shams S, and Xu HB drafted the paper.

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Abstract

BACKGROUND

It is of vital importance to find radiologic biomarkers that can accurately predict treatment response. Usually, the initiation of antiangiogenic therapy causes a rapid decrease in the contrast enhancing tumor. However, the treatment response is observed only in a fraction of patients due to the partial radiological response secondary to stabilization of abnormal vessels which does not essentially indicate a true antitumor effect. Perfusion-weighted magnetic resonance imaging (PW-MRI) techniques have shown implicitness as a strong imaging biomarker for gliomas since they give hemodynamic information of blood vessels. Hence, there is a rapid expansion of PW-MRI related studies and clinical applications.

AIM

To determine the diagnostic performance of PW-MRI techniques including: (A) dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI); and (B) dynamic susceptibility contrast magnetic resonance imaging (DSC-MRI) for evaluating response to antiangiogenic therapy in patients with recurrent gliomas.

METHODS

Databases such as PubMed (MEDLINE included), EMBASE, and Google Scholar were searched for relevant original articles. The included studies were assessed for methodological quality with the Quality Assessment of Diagnostic Accuracy Studies 2 tool. Medical imaging follow-up or histopathological analysis was used as the reference standard. The data were extracted by two reviewers independently, and then the sensitivity, specificity, summary receiver operating characteristic curve, area under the curve (AUC), and heterogeneity were calculated using Meta-Disc 1.4 software.

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RESULTS
This study analyzed a total of six articles. The overall sensitivity for DCE-MRI and DSC-MRI was 0.69 [95% confidence interval (CI): 0.53-0.82], and the specificity was 0.99 (95%CI: 0.93-1) by a random effects model (DerSimonianee-Laird model). The likelihood ratio (LR) +, LR-, and diagnostic odds ratio (DOR) were 12.84 (4.54-36.28), 0.35 (0.22-0.53), and 24.44 (7.19-83.06), respectively. The AUC (± SE) was 0.9921 (± 0.0120), and the Q* index (± SE) was 0.9640 (± 0.0323). For DSC-MRI, the sensitivity was 0.73, the specificity was 0.98, the LR+ was 7.82, the LR- was 0.32, the DOR was 31.65, the AUC (± SE) was 0.9925 (± 0.0132), and the Q* index was 0.9649 (± 0.0363). For DCE-MRI, the sensitivity was 0.41, the specificity was 0.97, the LR+ was 5.34, the LR- was 0.71, the DOR was 8.76, the AUC (± SE) was 0.9922 (± 0.2218), and the Q* index was 0.8935 (± 0.3037).

CONCLUSION
This meta-analysis demonstrated a beneficial value of PW-MRI (DSC-MRI and DCE-MRI) in monitoring the response of recurrent gliomas to antiangiogenic therapy, with reasonable sensitivity, specificity, +LR, and -LR.

Key words: Glioma; Perfusion-weighted magnetic resonance imaging; Dynamic contrast-enhanced magnetic resonance imaging; Dynamic susceptibility contrast magnetic resonance imaging; Anti-vascular endothelial growth factor; Antiangiogenic; Meta-analysis

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Core tip: Perfusion-weighted magnetic resonance imaging is one of the advanced magnetic resonance (MR) techniques which offer non-invasive and effective ways of grading, differentiating, and assessing therapeutic response and prognosis of brain tumors. This meta-analysis evaluates the clinical applicability of this MR technique in the assessment of the response of recurrent gliomas to antiangiogenic therapy.

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INTRODUCTION

Gliomas are the most common primary brain neoplasms in adults[1]. They overgrow and are very invasive and angiogenic with a high rate of recurrence and dismal median 15-mo survival regardless of multi-modality management including surgical resection, radiotherapy, and chemotherapy[2]. Glioma-associated neovascularization peculiar assembly is an essential factor which contributes to several biological patterns like tumor development, invasiveness, and treatment response[3].

Thanks to the recognition of different signaling pathways and growth factors imperative in tumor angiogenesis, a couple of new anti-angiogenic drugs have so far been manufactured[4]. Vascular endothelial growth factor (VEGF) is an arch controller of angiogenesis, vessel development, and vessel permeability[5]. The angiogenic action of VEGF is promoted by VEGF receptor-2 (VEGFR-2) which is also the central target for anti-angiogenic therapies, even though added studies have highlighted the significance of signaling *via* VEGFR-1[6].

Bevacizumab (BEV), a humanized monoclonal antibody to the VEGF-A, was the first VEGF inhibitor accredited for cancer treatment by the food and drug authority[7]. Also, other multiple approaches for inhibiting VEGF were researched over the past decade. These approaches include neutralizing antibodies to VEGF[8], low-molecular-weight VEGFR tyrosine kinase inhibitors (TKIs)[9,10], and soluble VEGFR constructs (VEGF-Trap)[11]. Although antiangiogenic drugs result in a rapid decrease in the contrast enhancing tumor, the treatment response is observed in just a fraction of patients, because the radiological response may partially result from stabilization of

abnormal vessels and does not inherently indicate a true antitumor effect[12,13]. Therefore, it is of vital importance to find radiologic biomarkers that can accurately predict treatment response or measure response after the initiation of anti-VEGF therapy[14].

The current imaging modality of choice for clinical use in brain tumors is magnetic resonance imaging (MRI)[15]. Although the conventional MRI techniques show excellent anatomical information of tumors, they cannot evaluate quantitatively the blood vessel physiology and exhibit biological characteristics within the tumor molecules and cells, which play a part in tumor grading[16], treatment evaluation[17], and prognosis prediction[18]. Moreover, non-enhancing regions representative of edema surrounding the tumor cannot be seen on conventional MRI, hampering the total safe tumor excision and treatment response evaluation[19,20]. Perfusion-weighted MRI (PW-MRI) techniques, including dynamic contrast-enhanced MRI (DCE-MRI) and dynamic susceptibility contrast MRI (DSC-MRI), have shown implicitness as a reliable imaging biomarker for gliomas since they give hemodynamic information of blood vessels[21-23]. Hence, there is a rapid expansion of PW-MRI application range which explores the association of imaging parameters and the distinctive features of gliomas non-invasively[24].

Recently, a meta-analysis containing 35 studies assessed the diagnostic accuracy of MRI techniques in the evaluation of treatment responses in patients with high-grade gliomas[25]. In 23 studies, DSC-MRI and DCE-MRI scans were carried out. The sensitivity and specificity of DSC-MRI (18 reviews, 708 patients) were 87% (82-91%) and 86%, respectively. The pooled analysis showed that the sensitivity and specificity of DCE- MRI (five studies, 207 patients) were 92% (73-98%) and 85%, respectively. However, there is no meta-analysis on the use of PW-MRI in the assessment of the response of recurrent gliomas to antiangiogenic therapy. Therefore, we believe that a meta-analysis of the relevant studies is required to better clarify the role of PW-MRI in predicting and assessing the response of recurrent gliomas to antiangiogenic drugs.

MATERIALS AND METHODS

The present Meta-analysis was done as per the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement[26].

Inclusion criteria

Studies included in this analysis fulfilled these requirements: (A) the study researched the performance of DSC-MRI or DCE-MRI for evaluating antiangiogenic therapy response in recurrent glioma patients; (B) the patients underwent tumor resection and chemotherapy treatment before recurrence and were treated with antiangiogenic therapy after recurrence; (C) The reference standard was either pathology reports or clinical observation or by imaging follow-up; and (D) the primary data were enough to compute the true positive (TP), true negative (TN), false positive (FP), and false negative (FN).

Exclusion criteria

The studies were excluded for the following reasons: (A) reviews, pre-clinical studies, titles, abstracts, and expert opinions; (B) studies assessing PW-MRI in glioma grading; and (C) inadequate data to generate a 2 × 2 table.

Study selection

We conducted a comprehensive search in EMBASE, Google Scholar, and Medline (PubMed) for studies up to December 31, 2017 that evaluated the use of PW-MRI in the detection of antiangiogenic response for recurrent gliomas. For PubMed which was the primary database we used to search for studies, MeSH headings used were "MRI", "DCE-MRI", "DSC-MRI", "PW-MRI", "Glioma", "Glioblastoma", "GBM", "Anti-VEGF", "Antiangiogenic", and their combinations.

Data extraction and quality assessment

Data extraction was carried out by two reviewers (Kasenene A and Baidya A) from each of the selected studies using an Excel spreadsheet.

The extracted data included general characteristics (*i.e*., first author and year of publication for each study, country, number of patients, median age, study design, imaging modality, imaging biomarkers, MR scanner tesla intensity, type of anti-angiogenic therapy given, and the treatment response gold standard used), TP, TN, FP, and FN. Disagreements between investigators concerning outcomes of interest were reviewed later, and the consensus was reached by discussion.

The Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) tool[27] was

used to assess the quality of the included studies, where we scored all 14 QUDAS items used to determine the risk of bias as "low risk", "high risk", or "uncertain risk".

Statistical analysis

We constructed 2 × 2 tables for each study independently. Data from the original publications were used to calculate the sensitivity, specificity, positive likelihood ratio (LR+), negative likelihood ratio (LR-), diagnostic odds ratio (DOR), 95% confidence intervals (CI), summary receiver operating characteristic (SROC) curves, and Q* index. Wherever any of TP, FP, FN, and TN values was zero, we added 0.5 to every cell of each study.

We adopted a random effects model (DerSimonianee-Laird model) in this study because of the difference in sample size, anti-angiogenic therapy, and reference standards among the included studies.

The analysis was done using Meta-Disc (version 1.4) software and Microsoft Excel 2016 (Microsoft, Seattle, WA, USA)[28].

RESULTS

Search strategy and study selection

This meta-analysis included studies which met the selection criteria successfully and were published before December 31, 2017. The search strategy generated a total of 133 clinical studies, of which 44 were investigated further. Out of the 44 studies, we excluded 38 studies, and finally, in this meta-analysis, we included only six studies. The flowchart outlining the process of study selection and exclusion reasons is showed in Figure 1.

Quality assessment

The quality assessment was performed as per the QUADAS-2 tool and the findings are shown in Table 1. Among the six included studies, four were conducted prospectively, and two were conducted retrospectively. None of the included studies checked all 14 QUDAS risk assessment items.

Characteristics of the studies

The characteristics and the clinical responses of the six studies encompassed in this meta-analysis are delineated in Tables 2 and 3. The studies were all in English, containing 120 patients all together with their age ranging from 25-78 years. The sample size of the studies was 10 to 36 patients.

There were two studies on DCE-MRI, two studies on DSC-MRI, and two combined both. All studies performed a sequential DCE-MRI, DSC-MRI, or both before and after the antiangiogenic treatment. Four different types of antiangiogenic therapies were used as the treatment of choice whereby BEV, which is a recombinant humanized monoclonal antibody targeting the VEGF, was used in three studies. VEGF Trap, which acts as a trap by inhibiting the activity of the VEGF subtypes VEGF-A and VEGF-B, was used in one study. Pazopanib, a potent and selective multi-targeted receptor TKI which stops the growth of the tumor and halts angiogenesis, was used in one study. Tivozanib, which is also a TKI, was used in the remaining one study. In four studies, a decrease in volume transfer constant (K^{trans}) value was used as the cutoff criterion for response to antiangiogenic therapy. The other studies relied on a reduction of relative cerebral blood volume (rCBV), extracellular volume fraction (EES V_e) value, vessel leakage reduction, decrease in tumor volume, tissue oxygenation, or vasogenic edema criteria for therapy response.

Data analysis

DSC-MRI and DCE-MRI: Due to the heterogeneity across all six included studies which evaluated DCE-MRI or DSC-MRI or both, a random effects model (DerSimonianee-Laird model) was used to compute the sensitivity, specificity, LR+, LR-, and DOR (Figures 2-4). The overall sensitivity of DCE-MRI and DSC-MRI was 69%. The specificity was 99%. The detailed sensitivity, specificity, LR+, LR-, and DOR with 95%CI for individual studies are presented in Table 4.

The SROC curves with the Q* index are shown in Figure 5. Of all six studies, the area under the curve (AUC) (± SE) was 0.9921 (± 0.0120), and the Q* index was 0.9640 (± 0.0323).

DSC-MRI: Four included studies evaluated DSC-MRI. Also, the random effects model (DerSimonianee-Laird model) was used to calculate sensitivity, specificity, LR+, LR-, and DOR (Figures 6-8). The sensitivity of DSC-MRI to assess antiangiogenic treatment response in gliomas was 73%. The specificity was 98%. The pooled LR+ was

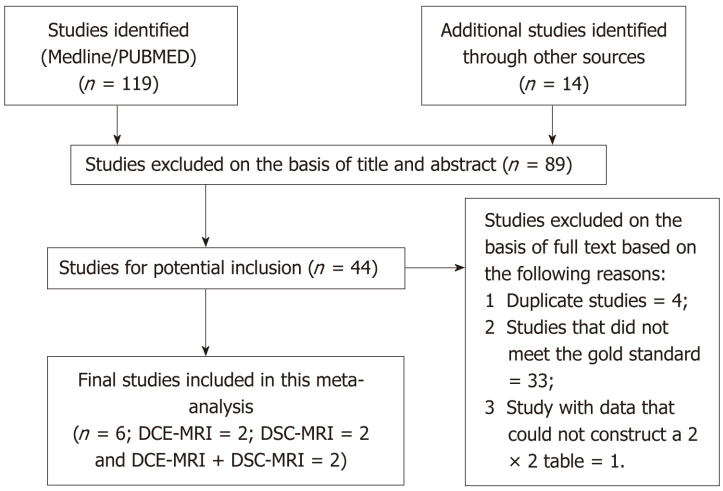


Figure 1 Flowchart outlining the study selection process according to the Preferred Reporting Items for Systematic Reviews guidelines. DCE-MRI: Dynamic contrast-enhanced magnetic resonance imaging; DSC-MRI: Dynamic susceptibility contrast magnetic resonance imaging.

7.82; LR- was 0.32. The pooled DOR was 31.65.

The SROC curves with the Q* index are shown in Figure 9. Of all four studies, the AUC (± SE) was 0.9925 (± 0.0132), and the Q* index was 0.9649 (± 0.0363).

DCE-MRI: Four included studies evaluated DCE-MRI, again the random effects model (DerSimonianee-Laird model) was used to calculate sensitivity, specificity, LR+, LR-, and DOR (Figures 10-12). The sensitivity of DCE-MRI to assess antiangiogenic treatment response in gliomas ranged from 21% to 64%. The specificity was 97%. The pooled LR+ was 5.34; LR- was 0.71. The pooled DOR was 8.76.

The SROC curves with the Q* index are shown in Figure 13. Of all four studies, the AUC (± SE) was 0.9922 (± 0.2218), and the Q* index was 0.8935 (± 0.3037).

DISCUSSION

PW-MRI is a non-invasive imaging technique which is increasingly used in clinical evaluation and treatment response assessment of brain tumors. The current meta-analysis was conducted to assess the diagnostic performance of PW-MRI techniques (DCE-MRI and DSC-MRI) in the evaluation of glioma response to antiangiogenic therapy.

The overall sensitivity and specificity for DSC-MRI and DCE-MRI were 0.69 and 0.99, respectively. Although the pooled sensitivity for the present study was relatively low, the statistical results still showed that PW-MRI (DSC-MRI and DCE-MRI) techniques are effective ways to assess the response of gliomas to antiangiogenic therapy. On the SROC, the summary points were closer to the left hand, and the AUC was 0.9921, which indicates an excellent diagnostic accuracy. Likelihood ratios are other measures of the diagnostic accuracy, with LR greater than 1 meaning that the test result is associated with the disease presence, and the LR ratio less than 1 meaning that the test result is related to the disease absence. The higher the LR are from 1, the stronger the evidence for the presence or absence of disease; LR > 10 and < 0.1 are thought to provide strong evidence to declare the presence or absence of the disease in most cases[34]. The LR+ for the DSC-MRI and DCE-MRI group was 12.84, indicating that there were an approximately 13 times chance of PWI-MRI showing clinically meaningful changes as the result of antiangiogenic therapy. On the other hand, the LR- was 0.35, meaning it was below the cut-off value, indicating a chance of not showing any changes was approximately 0.4 times.

Moreover, for the DSC-MRI group, the sensitivity and specificity were 0.73 and 0.98, respectively, where the sensitivity was slightly higher than in the DSC-MRI and DCE-MRI group. The pooled LR+ was 7.82, which means the chance of DSC-MRI indicating the changes associated with antiangiogenic therapy was approximately 8 times; LR- was 0.32 and below the cut-off point, which suggests that the chance of DSC-MRI not showing treatment-associated changes was 0.3 times, and AUC was 0.9925, indicating an excellent diagnostic accuracy. While for the DCE-MRI group, the sensitivity and specificity were 0.41 and 0.97, respectively; the sensitivity of the DCE-

Table 1 Quality assessment of the included studies

Study	Risk of bias			Applicability concerns			
	Patient selection	Index test	Reference standard	Flow and timing	Patient selection	Index test	Reference standard
Iwamoto *et al*[29], 2010	L	U	H	L	L	L	L
Piludu *et al*[30], 2015	L	U	U	L	L	L	L
Kalpathy-Cramer *et al*[31], 2017	L	U	U	L	L	L	L
O'Neill *et al*[32], 2016	L	U	H	L	L	L	L
Schmainda *et al*[4], 2014	L	U	U	L	L	L	L
Hilario *et al*[33], 2016	L	U	U	L	L	L	L

L: Low risk; U: Unclear risk; H: High risk.

group was lower as compared to the previous two groups, and this might be due to the patient sample size variation among the studies in this group. The LR+ was 5.34, indicating a 5 times chance of showing treatment-associated changes; LR- was 0.71 and below the cut-off value, indicating a 0.7 times chance of not showing anything, and the AUC was 0.9922, indicating a higher diagnostic accuracy. All of these values suggest that both DSC-MRI and DCE-MRI have diagnostic value in treatment evaluation of recurrent gliomas.

Limitations

First, some included studies were too small, which may have led to imprecise and inconclusive results. Second, only articles published in English were included, which may have led to publication bias. Third, there was verification bias or workup bias, because patients were subjected to different reference tests and antiangiogenic medications.

Conclusion

Regardless of some limitations, this meta-analysis demonstrated a beneficial value of PW-MRI (DSC-MRI and DCE-MRI) in monitoring the response to antiangiogenic therapy in recurrent gliomas, with reasonable sensitivity, specificity, +LR, and -LR.

Table 2 The basic characteristics of the included studies

Studies	Country	Patients, *n*	Median age	Study design	Imaging modality	Imaging biomarkers	MR scanner tesla	Anti-angiogenic treatment	Clinical question	Standard reference	TP	FP	FN	TN
Iwamoto *et al*[29], 2010	United States	11	53 (29-73)	Pro-spective	DSC, DCE	Ktrans, rCBV	NR	Pazopanib	DSC and DCE *vs* response	Macdonald criteria RANO criteria	1	0	6	4
Piludu *et al*[30], 2015	Germany	27	54 (33-77)	Pro-spective	DCE	nIAUGC, Ktrans	3.0 T	Bevacizumab	DCE *vs* response	RANO criteria	6	0	5	16
Kalpathy-Cramer *et al*[31], 2017	United States	10	62 (51-74)	Pro-spective	DSC, DCE	Ktrans, rCBV, rCBF	3.0 T	Tivozanib	DSC and DCE *vs* response	RANO criteria	1	1	4	4
O'Neill *et al*[32], 2016	United States	12	NR	Pro-spective	DCE	Ktrans, Ve	1.5 T	VEGF Trap	DCE *vs* response	Macdonald criteria	1	0	0	11
Schmainda *et al*[4], 2014	United States	36	34 (30-68)	Retro-spective	DSC	rCBV, stdrCBV	1.5 T or 3.0 T	Bevacizumab	DSC *vs* response	Macdonald criteria RANO criteria	6	0	0	30
Hilario *et al*[33], 2016	Spain	24	52.5 (31-74)	Retro-spective	DSC	Leakage volume (CBV-LCCBV)	1.5 T	Bevacizumab	DSC *vs* response	RANO criteria	14	0	0	10

TP: True positive; FP: False positive; TN: True negative; FN: False negative; DCE: dynamic contrast-enhanced; DSC: Dynamic susceptibility.

Table 3 Clinical responses of gliomas to antiangiogenic treatments

Study	Patient, *n*	RANO criteria				Macdonald criteria			
		Responders		Non-responders		Responders		Non-responders	
		CR	PR	SD	PD	CR	PR	SD	PD
O'Neill *et al*[32], 2016	12	-	-	-	-	0	1	0	11
Piludu *et al*[30], 2015	27	0	6	5	16	-	-	-	-
Schmainda *et al*[4], 2014	36	0	6	0	30	-	-	-	-
Iwamoto *et al*[29], 2010	11	-	-	-	-	0	1	6	4
Hilario *et al*[33], 2016	24	0	14	0	10	-	-	-	-
Kalpathy-Cramer *et al*[31], 2017	10	1	1	4	4	-	-	-	-

CR: Complete response; PR: Partial response; SD: Stable disease; PD: Progressive disease. *Response as defined using the Macdonald criteria and Response Assessment in Neuro-Oncology (RANO) working group guidelines.

Table 4 True positive, false positive, true negative, and false negative as well as the sensitivity, specificity, likelihood ratio, and diagnostic odds ratio for the meta-analysis of antiangiogenic treatment evaluation

Study	TP	FP	FN	TN	Sensitivity (95%CI)	Specificity (95%CI)	LR+ (95%CI)	LR- (95%CI)	DOR (95%CI)
Iwamoto *et al*[29], 2010	1	0	4	6	0.2 (0.01-0.72)	1 (0.54-1)	3.5 (0.17-70.94)	0.81 (0.49-1.340)	4.33 (0.14-132.32)
Piludu *et al*[30], 2015	6	0	5	16	0.55 (0.23-0.83)	1 (0.79-1)	18.42 (1.14-296.83)	0.47 (0.25-0.880	39 (1.88-810.44)
Kalpathy-Cramer *et al*[31], 2017	1	1	4	4	0.2 (0.01-0.72)	0.8 (0.28-0.99)	1 (0.08-11.93)	1 (0.54-1.86)	1 (0.05-22.18)

O'Neill *et al*[32], 2016	1	0	0	11	1 (0.03-1)	1 (0.72-1)	18 (1.06-304.71)	0.26 (0.02-2.89)	69 (0.96-4951.23)
Schmainda *et al*[4], 2014	6	0	0	30	1 (0.54-1)	1 (0.88-1)	57.57 (3.65-906.93)	0.07 (0.01-1.05)	793 (14.37-43,746.61)
Hilario *et al*[33], 2016	14	0	0	10	1 (0.77-1)	1 (0.69-1)	21.27 (1.42-319.53)	0.03 (0-0.53)	609 (911.16-33,236.62)
Pooled results	29	1	13	77	0.69 (0.53-0.82)	0.99 (0.93-1)	12.84 (4.54-36.28)	0.35 (0.22-0.53)	24.44 (7.19-83.06)
Heterogeneity test					I^2 = 81.30%, P = 0.0001	I^2 = 12.2%, P = 0.3369	I^2 = 19.1%, P = 0.2892	I^2 = 81.5%, P = 0.0001	I^2 = 53.5%, P = 0.0563

TP: True positive; FP: False positive; TN: True negative; FN: False negative; LR+: Positive likelihood ratio; LR-: Negative likelihood ratio; DOR: Diagnostic odds ratio; CI: Confidence interval.

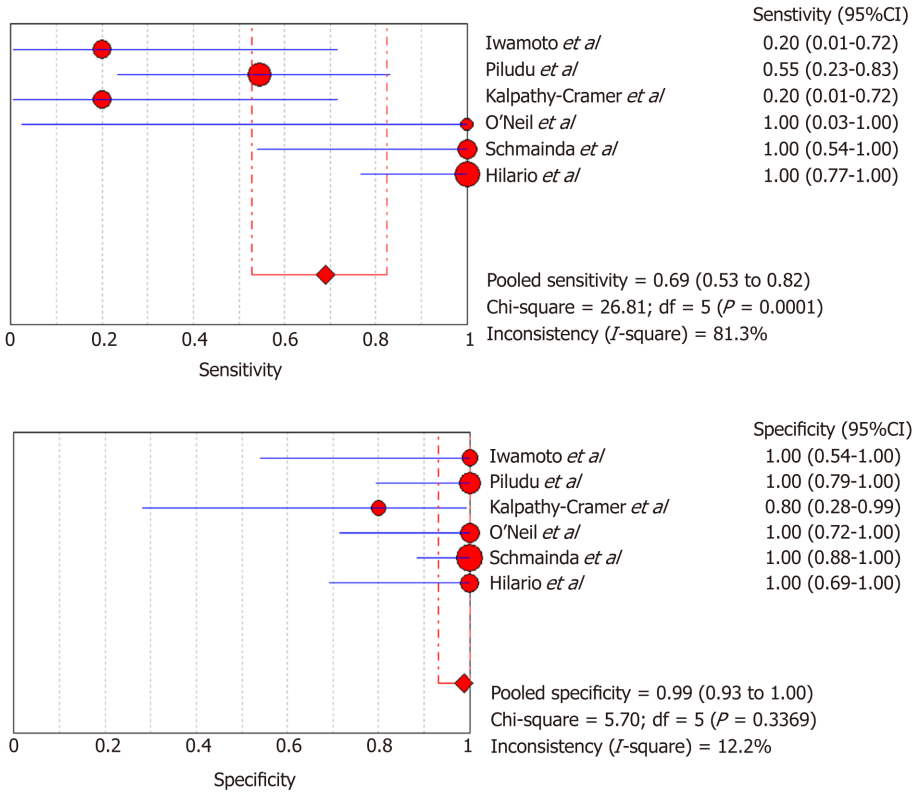
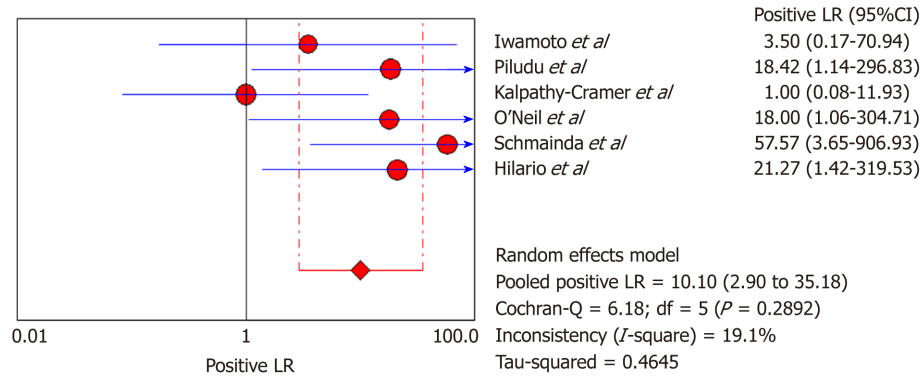


Figure 2 Sensitivity and specificity of dynamic contrast-enhanced magnetic resonance imaging and dynamic susceptibility contrast magnetic resonance imaging in the evaluation of response to antiangiogenic therapy in recurrent gliomas.



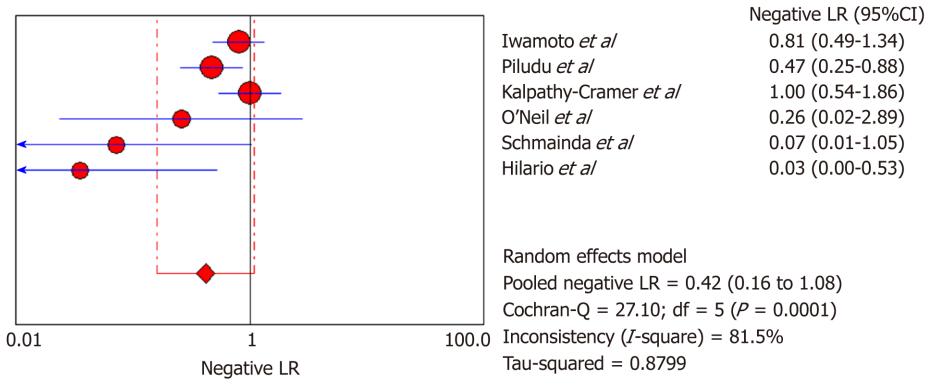


Figure 3 Likelihood ratio + and likelihood ratio - of dynamic contrast-enhanced magnetic resonance imaging and dynamic susceptibility contrast magnetic resonance imaging in the evaluation of response to antiangiogenic therapy in recurrent gliomas.

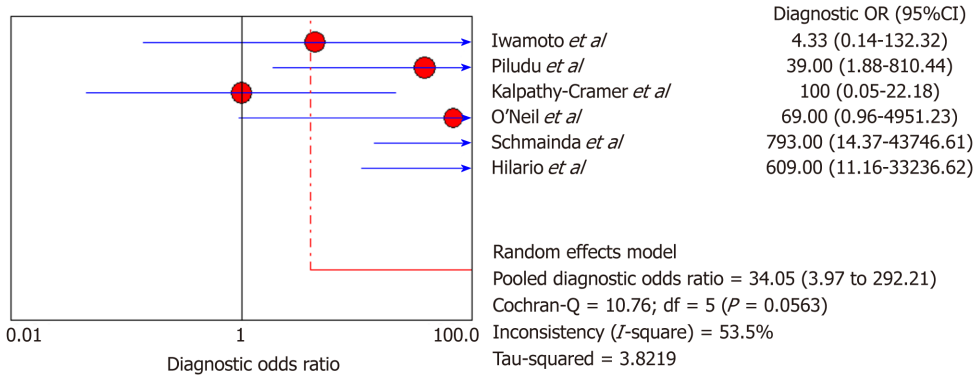


Figure 4 Diagnostic odds ratio of dynamic contrast-enhanced magnetic resonance imaging and dynamic susceptibility contrast magnetic resonance imaging in the evaluation of response to antiangiogenic therapy in recurrent gliomas.

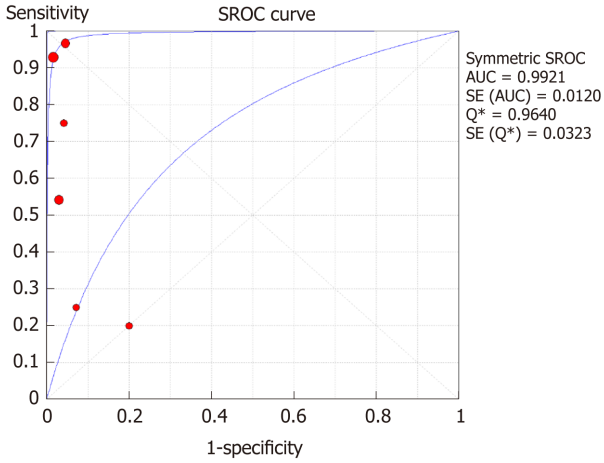


Figure 5 Summary receiver operating characteristic curve for dynamic contrast-enhanced magnetic resonance imaging and dynamic susceptibility contrast magnetic resonance imaging. Solid circle represents each study in the meta-analysis, and the circle size indicates the study size. SROC: Summary receiver operating characteristic.

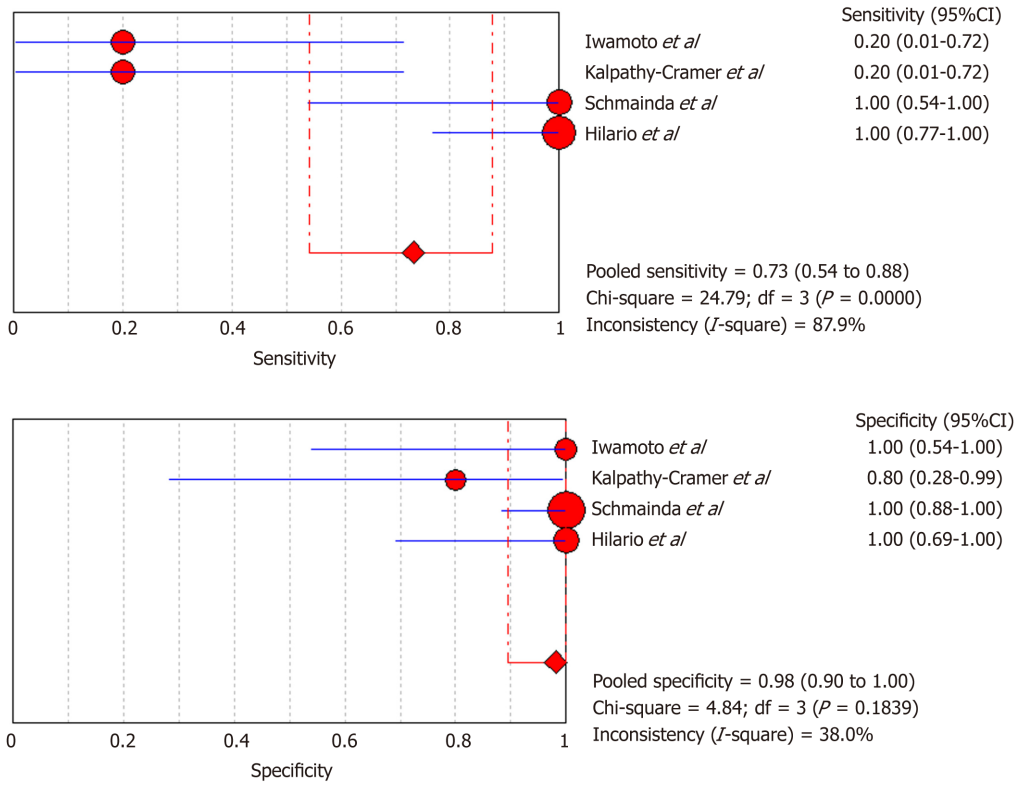


Figure 6 Sensitivity and specificity of dynamic susceptibility contrast magnetic resonance imaging in the evaluation of response to antiangiogenic therapy in recurrent gliomas.

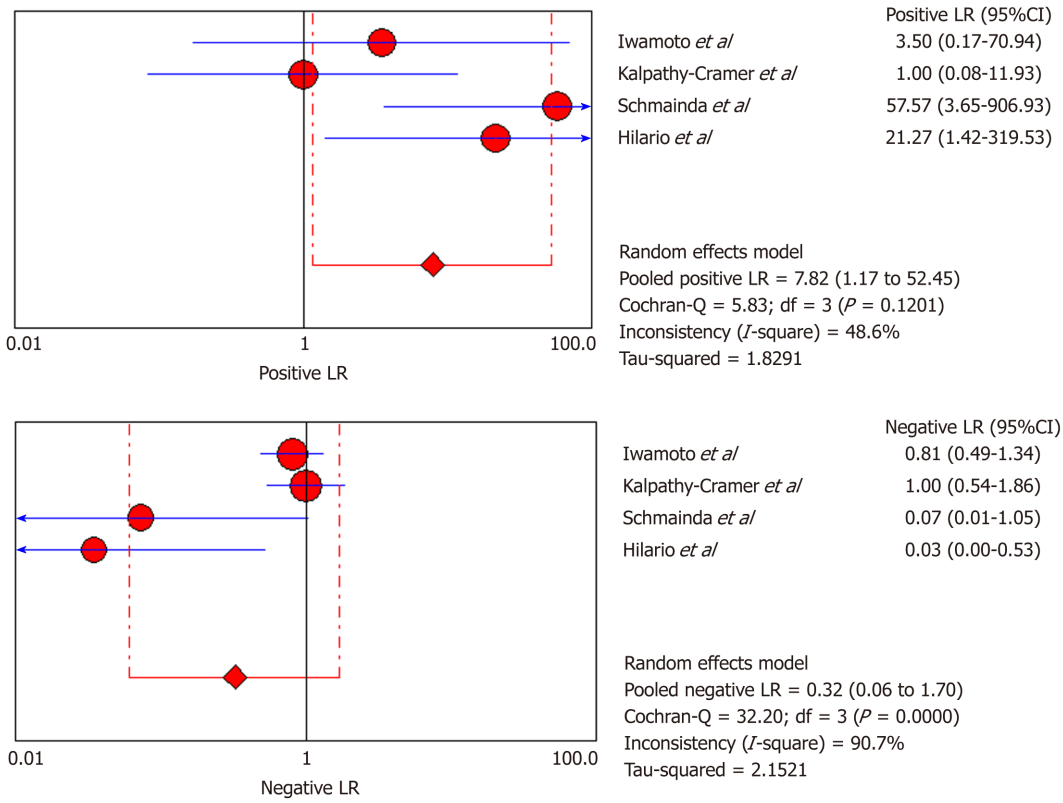


Figure 7 Likelihood ratio + and likelihood ratio - of dynamic susceptibility contrast magnetic resonance imaging in the evaluation of response to antiangiogenic therapy in recurrent gliomas.

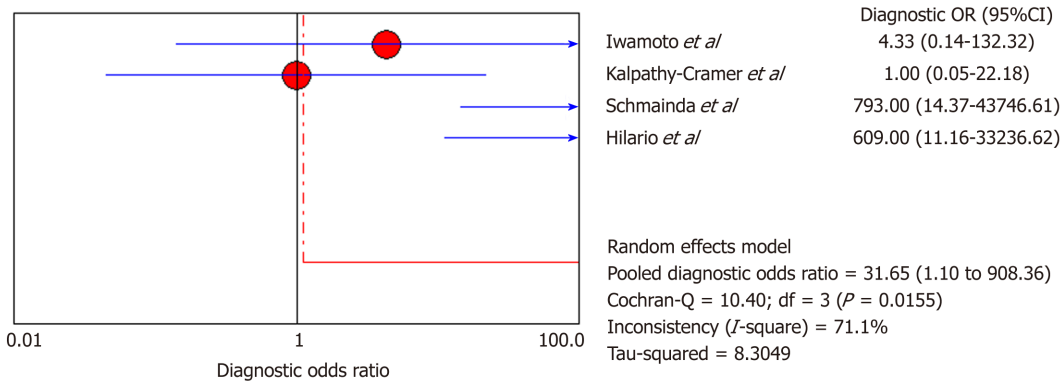


Figure 8 Diagnostic odds ratio of dynamic susceptibility contrast magnetic resonance imaging in the evaluation of response to antiangiogenic therapy in recurrent gliomas.

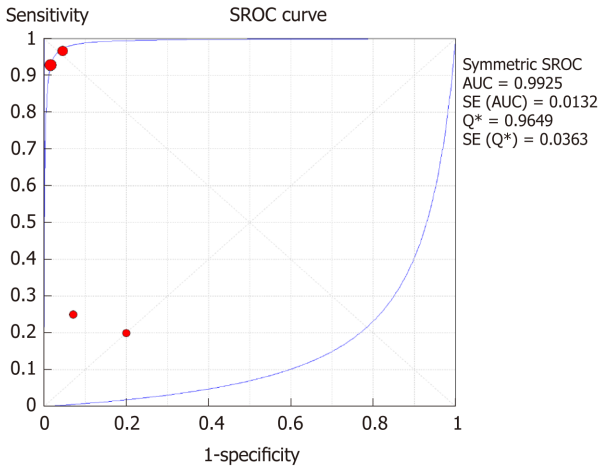
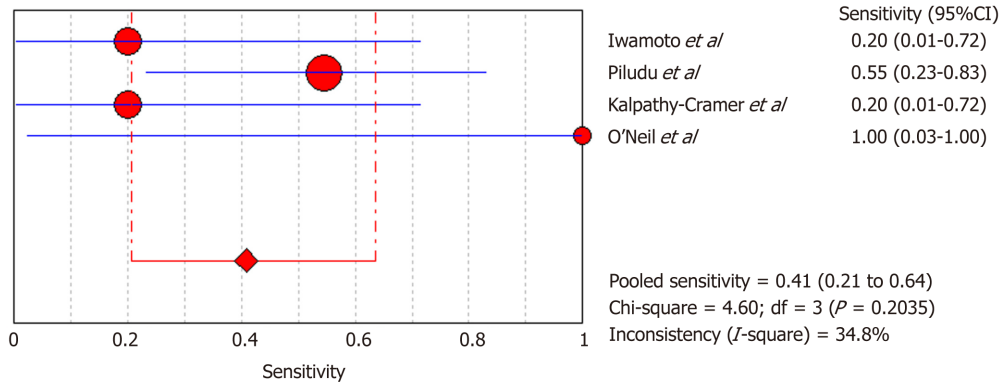


Figure 9 Summary receiver operating characteristic curve for dynamic susceptibility contrast magnetic resonance imaging. SROC: Summary receiver operating characteristic.



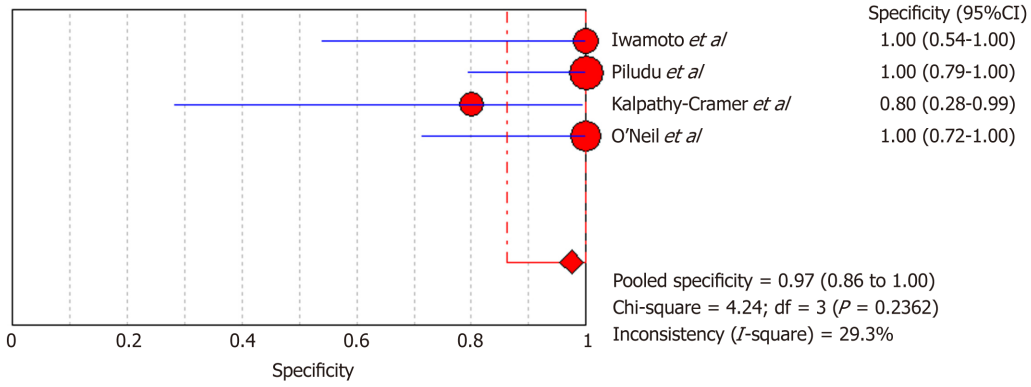


Figure 10 Sensitivity and specificity of dynamic contrast-enhanced magnetic resonance imaging in the evaluation of response to antiangiogenic therapy in gliomas.

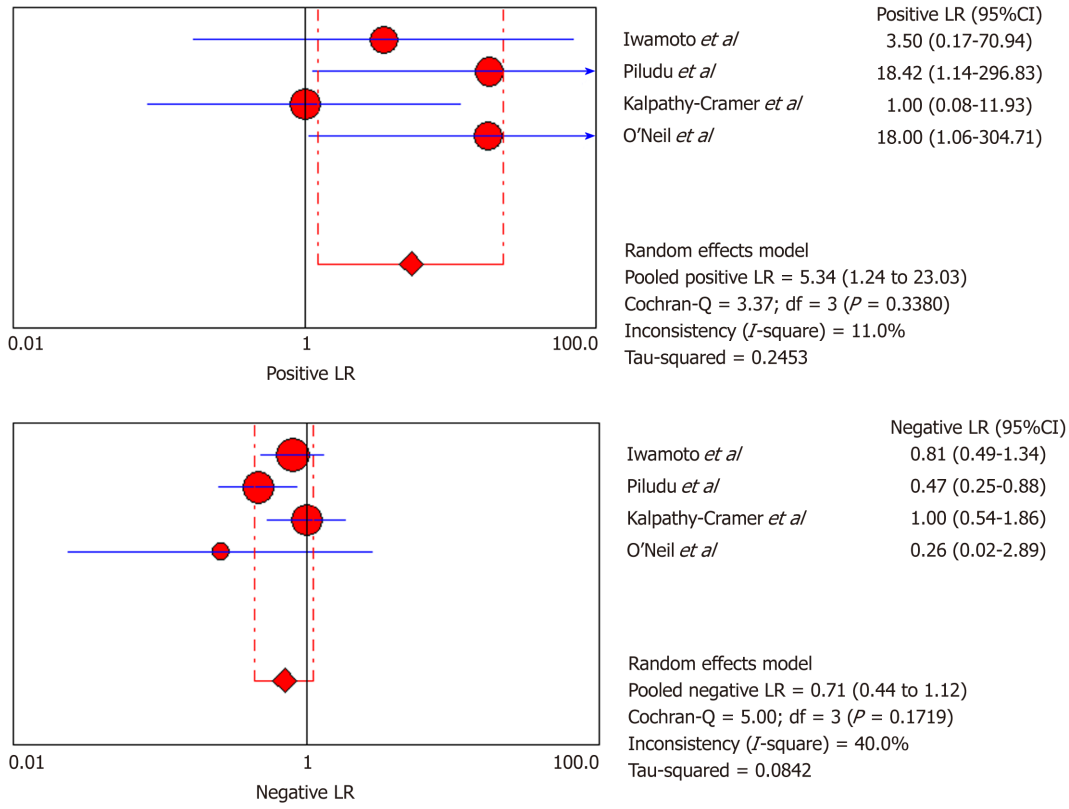


Figure 11 Likelihood ratio + and likelihood ratio - of dynamic contrast-enhanced magnetic resonance imaging in the evaluation of response to antiangiogenic therapy in recurrent gliomas.

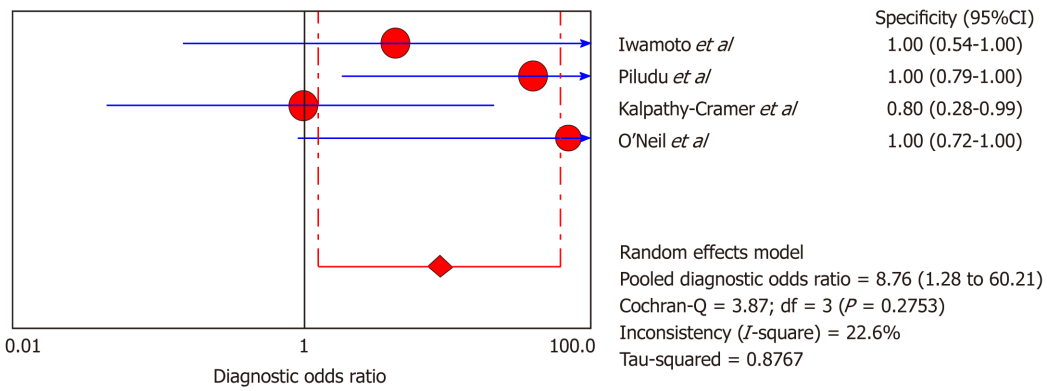


Figure 12 Diagnostic odds ratio of dynamic contrast-enhanced magnetic resonance imaging in the evaluation of response to antiangiogenic therapy in recurrent gliomas.

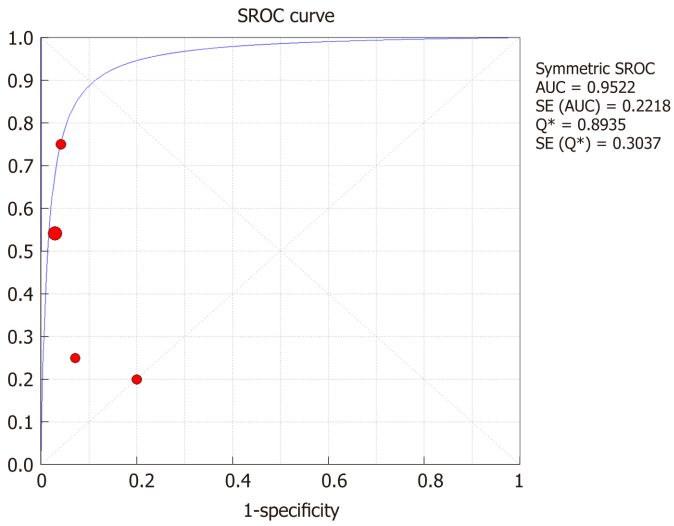


Figure 13 Summary receiver operating characteristic curve for dynamic contrast-enhanced magnetic resonance imaging. SROC: Summary receiver operating characteristic.

ARTICLE HIGHLIGHTS

Research background

The perfusion-weighted imaging is an advanced magnetic resonance (MR) technique capable of giving a detailed hemodynamic status of the tumors; this has prompted a surge of studies both *in vitro* and *in vivo* with some of these studies done on humans. The current meta-analysis is exploring the clinical application of this method in recurrent glioma patients after antiangiogenic therapy.

Research motivation

So far, biopsy, which is too invasive, is the gold standard for diagnosing brain tumors; perfusion-weighted magnetic resonance imaging (PW-MRI) offers a non-invasive way for diagnosing, grading, and assessing progression of brain tumors. Therefore, scientifically proving that this method works is of paramount importance in the spirit of encouraging its incorporation to the daily clinical practices.

Research objectives

The primary objective of this study was to assess the use of PW-MRI in evaluating the response of recurrent gliomas to antiangiogenic treatment based on the already available literature, and the finding of this study showed that both dynamic contrast-enhanced MRI and dynamic susceptibility contrast MRI could be used for this purpose. These findings would warrant further human-based studies on this MR technique to achieve its universal acceptability for clinical use.

Research methods

Studies related to this topic were searched in PubMed, Google Scholar, and other scientific search engines. The selected studies were sorted according to the Preferred Reporting Items for Systematic Reviews guidelines, and only six studies meeting the inclusion criteria were included in the current meta-analysis. Meta-Disc 1.4 software and Microsoft Excel were used to analyze the data.

Research results

The sensitivity and specificity of this study proved that PW-MR techniques are capable of evaluating treatment response in patients with brain tumors, *i.e.*, recurrent gliomas, and these findings, together with other related studies, mean that we are getting a step closer to its complete adaption for clinical use. The only concern is what should be done to improve and perfect this technique.

Research conclusions

This meta-analysis showed that PW-MRI could be used to assess brain tumor therapeutic response. However, more studies must be conducted because that is the only way we will be sure of its clinical efficacy in diagnosing, follow-up, and treatment of brain tumors.

Research perspectives

While searching for studies, we realized that very few studies had been carried out on human subjects; this tells us that there is more to be done until it is adopted universally for clinical use. There are many studies carried on animals, which mean the technique is being perfected and improved with each passing day. We need more studies assessing its application on human subjects.

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