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Original Article

Role of rCBV values derived from dynamic susceptibility contrast-enhanced magnetic resonance imaging in differentiating CNS lymphoma from high grade glioma: a meta-analysis

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Abstract: Background and purpose: In the preoperative period, discriminating CNS lymphoma from high grade glioma is important as treatment approaches differ significantly. Hence, this meta-analysis was to evaluate the sensitivity and specificity of the relative cerebral blood volume (rCBV) values derived from dynamic susceptibility contrast-enhanced magnetic resonance imaging (DSCE-MRI) in differentiating CNS lymphoma from high grade glioma. Materials and methods: The following databases were searched from January 2000 to July 2014: Medline, PubMed and Embase. No language restrictions were applied. Data analysis was conducted using Meta-Disc 1.4. Results: A total of 79 patients (n = 30 lymphoma, n = 49 high grade glioma) and 89 lesions (n = 40 lymphoma, n = 49 high grade glioma) were included in the rCBV analysis. The pooled sensitivity, specificity, negative likelihood ratio, positive likelihood ratio and diagnostic odds ratio for differentiating CNS lymphoma from high grade glioma were 0.90 (95% CI 0.76-0.97), 0.98 (95% CI 0.89-1.00), 0.13 (95% CI 0.06-0.29), 21.07 (95% CI 5.61-79.19), and 187.63 (95% CI 33.15-1061.86), respectively. And the value of I^2 of DOR was 0.0%, indicating that there was no statistically significant heterogeneity of DOR between the included studies. Conclusions: Our meta-analysis suggests that the rCBV values derived from DSCE-MRI could be useful in differentiating CNS lymphoma from high grade glioma in the preoperative. Further well-designed researches involving larger patient cohorts are needed to confirm this conclusion.

Keywords: CNS lymphoma, high grade glioma, rCBV values, meta-analysis

Introduction

Central nervous system (CNS) lymphoma consists of primary CNS lymphoma, CNS intravascular lymphomatosis, systemic lymphoma that metastasized to the CNS and primary ocular lymphoma [1]. In addition, primary CNS lymphomas account for about 4-6% of all extranodal lymphomas and 4% of all intracranial lesions [2]. High grade gliomas account for about 50% of primary malignant cerebral tumors [3]. In a patient with high grade glioma, tumor resection followed by postoperative chemotherapy and radiation therapy is recommended as the standard of care [4]. On the contrary, the strategy for the treatment of lymphoma is combined high-dose chemotherapy and radiotherapy without surgery [5]. Surgical intervention is often restricted to performing a biopsy to obtain the tumor tissue for a histopathologic diagnosis [6, 7]. So, it is crucial to distinguish CNS lymphoma from high grade glioma preoperatively. Various advanced magnetic resonance imaging (MRI) techniques have been searched for discriminating the type of intracranial lesion without histopathologic examination, such as (DWI) [8], diffusion tensor imaging (DTI) [9], and magnetic resonance spectroscopy (MRS) [10].

As an advanced imaging technique, dynamic susceptibility contrast-enhanced magnetic resonance imaging (DSCE-MRI) can be used to compute neovascularized regions through the measure of the relative cerebral blood volume (rCBV) values, which reflect the quantity of blood present within a specific tissue [11].

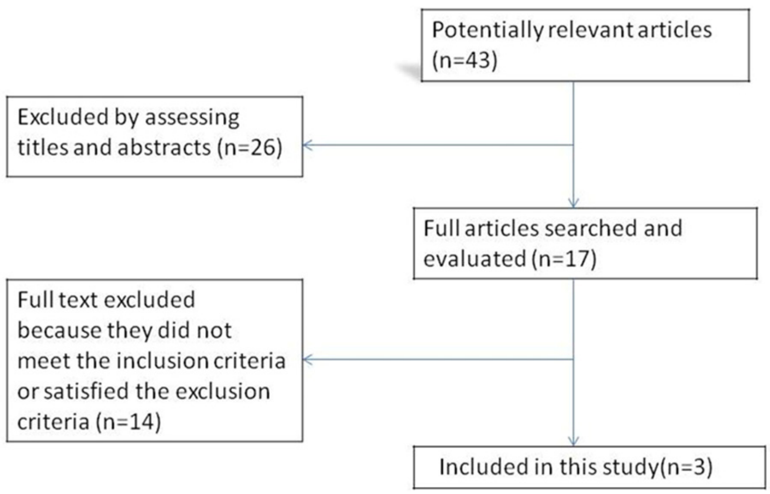

Figure 1. Flow chart of the study selection process.

Table 1. Basic information of individual articles

Study	Year	No. of patients (n)	Study design	Field strength (T)	QUADAS score
Xing [16]	2013	38	R	3.0	12
Toh [17]	2013	35	C	3.0	12
Abul-Kasim [18]	2008	6	R	3.0	11

R, Retrospective; C, Consecutive; QUADAS score, The quality assessment of diagnostic accuracy studies score.

Table 2. The key information of individual articles

Study	TP	FP	FN	TN	+LR	-LR	SE	SP	DOR
Xing [16]	18	1	2	25	23.40	0.10	0.90	0.96	225.00
Toh [17]	13	0	2	20	35.44	0.16	0.87	1.00	221.40
Abul-Kasim [18]	5	0	0	3	7.33	0.10	1.00	1.00	77.00

TP, True positive; FP, False positive; FN, False negative; TN, True negative; +LR, Positive likelihood ratio; -LR, Negative likelihood ratio; SE, Sensitivity; SP, Specificity; DOR, Diagnostic odds ratio.

Hence, this meta-analysis was to evaluate the sensitivity and specificity of rCBV values derived from DSCE-MRI in differentiating CNS lymphoma from high grade glioma.

Materials and methods

Two independent authors searched (R.F.L. and M.L.) the Medline, PubMed and Embase databases from January 2000 to July 2014. The databases were searched using the following terms: dynamic susceptibility contrast-enhanced magnetic resonance imaging, relative cerebral blood volume, DSCE-MRI, rCBV; lymphoma; glioma, tumor, neoplasm, cancer. No language restrictions were applied.

The inclusion criteria were the following: (a) DSCE-MRI was performed in all included patients prior to surgical resection or biopsy; (b) the diagnosis of the tumor cases was confirmed through histopathology.

The exclusion criteria were the following: (a) the articles could not provide adequate data to calculate the total number of true negatives, false negatives, true positives and false positives; (b) the tumor cases were included in other articles; (c) the literature type was a comment, review, case report, animal study, editorial or letter. Disagreements were resolved through discussion and consensus.

Two authors (R.F.L. and M.L.) independently evaluated the quality of included articles according to the QUADAS tool [12, 13]. Disagreements were resolved through discussion and consensus. The QUADAS includes 14 items, and all items can be replied by "unclear", "no", or "yes". We weighted all the items equally, and scored each item 0.5 points for "unclear", 0 points for "no", and 1 point for "yes".

The same independent researchers (R.F.L. and M.L.) extracted data from each included article and disagreements were resolved by consensus. Extracted data comprised information about the QUADAS score, the study design, the authors, the number of patients, the publication year and the MRI field strength. For each study, the numbers of true-negative, false-negative, true-positive and false-positive were extracted.

For each included study, the sensitivity, specificity, negative likelihood ratio (-LR), positive likelihood ratio (+LR), diagnostic odds ratio (DOR) and their 95% confidence intervals (CI)

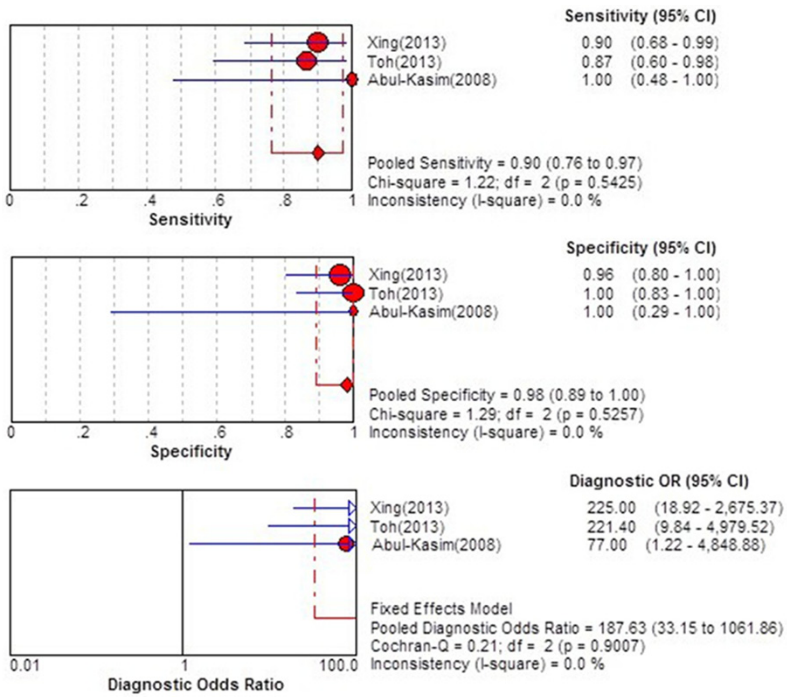

Figure 2. The pooled sensitivity, specificity, and DOR of rCBV for discriminating CNS lymphoma from high grade glioma.

were counted. In addition, an I^2 value > 50% indicated inconsistency [14]. If the inconsistency was statistically significant, we pooled the sensitivities and specificities, +LR, -LR, and DOR by the random-effect model (DerSimonian-Laird). If the inconsistency was not statistically significant, the fix-effect model (Mantel-Haenszel) was performed. Meta-analysis was conducted using Meta-Disc 1.4 software [15].

Results

A total of 43 potentially relevant studies were initially selected, 26 articles were considered as irrelevant for our purposes and not included in this meta-analysis after reviewing their titles, abstracts and keywords. For the remaining 17 relevant articles, full text was obtained and evaluated. Only 3 articles met the inclusion criteria of this analysis which contained the enough information [16-18]. In the two studies [16, 18], some of the patients had more than one lesion. The article [17] did not clearly mention the number of the lesions, in order to make it convenient for the statistical analysis, we regard that these patients had only one lesion. Flow chart of the study selection process is showed in **Figure 1**. The information of the 3 studies is demonstrated in **Tables 1** and **2**.

A total of 79 patients (n = 30 lymphoma, n = 49 high grade glioma) and 89 lesions (n = 40 lymphoma, n = 49 high grade glioma) were included in the rCBV analysis. The pooled sensitivity, specificity, -LR, +LR and DOR for differentiating CNS lymphoma from high grade glioma were 0.90 (95% CI 0.76-0.97), 0.98 (95% CI 0.89-1.00), 0.13 (95% CI 0.06-0.29), 21.07 (95% CI 5.61-79.19), and 187.63 (95% CI 33.15-1061.86), respectively (**Figure 2**). And the value of I^2 of DOR was 0.0%, indicating that there was no statistically significant heterogeneity of DOR between the 3 included studies. Due to the relative limited number of studies in this present meta-analysis, the funnel plot and the summary receiver operating characteristic curve was not draw, and the publication bias was not assessed.

Discussion

The results of our meta-analysis demonstrate that the rCBV values derived from DSCE-MRI, which had a pooled sensitivity of 0.90 (95% CI 0.76-97), a pooled specificity of 0.98 (95% CI 0.89-1.00), and a pooled DOR 187.63 (95% CI 33.15-1061.86) for differentiating CNS lymphoma from high grade glioma. These results suggest that DSCE-MRI may play an important role in the differential diagnosis of CNS lymphoma from high grade glioma.

Conventional MRI is very limited in making the differentiation CNS lymphoma from high grade glioma [19, 20]. However, discriminating CNS lymphoma from high grade glioma is very important as treatment approaches differ significantly. With the advent of advanced imaging techniques, the ability to distinguish CNS lymphoma from high grade glioma has long been a subject of interest. And among them, DSCE-MRI has been recognized as a promising and noninvasive advanced imaging technique in the evaluation of intracranial mass lesions [21, 22]. The rCBV as an important parameter which is widely used in the assessment of brain DSCE-MRI, the increase of neovascularization and microvascularization in the malignant cerebral tumors results in an increase of rCBV [16]. Contrary to high grade glioma, CNS lymphoma does not usually show a prominent histopathological feature of neovascularization, despite vascular abnormalities such as tumor infiltration of endothelial cells and even invasion into the vessel lumen could often be seen [21]. Hence, rCBV can be used to differentiate CNS lymphoma from high grade glioma; specifically, the parameter has been found to be significantly lower for CNS lymphoma than for high grade glioma [16, 17].

No language restrictions were applied in this analysis, thus to some extent has avoided the inclusion bias. And the QUADAS tool was used to evaluate the quality of the included studies this analysis. However, as CNS lymphomas are rare brain tumors, the number of cases in each included study is relatively small. We did not evaluate the level of publication bias and not draw a funnel plot and a summary receiver operating characteristic curve because of the relatively small number of studies included in our meta-analysis.

In conclusion, our meta-analysis suggests that the rCBV values derived from DSCE-MRI could be useful in differentiating CNS lymphoma from high grade glioma in the preoperative. Further well-designed researches involving larger patient cohorts are needed to confirm this conclusion.

Disclosure of conflict of interest

None.

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