Original Article

Comparison of magnetic resonance spectroscopy and diffusion weighted imaging in the differentiation of glioma recurrence from radiation necrosis: meta-analysis

Wen-Fei Li, Yu-Chen Zhang, Chen Niu, Li-Ping Guo, Feng-Li Liang, Xiao Ling, Xuan Niu, Ming Zhang

Department of Radiology, First Affiliated Hospital, School of Medicine, Xi’an Jiao Tong University, Xi’an, Shaanxi, People’s Republic of China

Received November 13, 2015; Accepted April 8, 2016; Epub October 15, 2016; Published October 30, 2016

Abstract: Aim: The purpose of this study was to compare the diagnostic accuracy of diffusion-weighted magnetic resonance imaging (DWI) and magnetic resonance spectroscopy (MRS) for the diagnosis of differentiating glioma recurrence from radiation necrosis through a meta-analysis. Methods: We performed a meta-analysis of all available studies of the diagnostic performance of DWI and MRS for differentiating glioma recurrence from radiation necrosis. PubMed, Web of Science, and Chinese Biomedical databases (CBM) were searched for initial studies. Pooled sensitivity (SEN), specificity (SPE), negative likelihood ratio (NLR), positive likelihood ratio (PLR), and diagnostic odds ratio (DOR) were calculated. Results: 5 studies involving 112 patients (116 lesions) met all inclusion and exclusion criteria. For DWI, the pooled sensitivity of Apparent Diffusion Coefficient (ADC) was 0.80 and specificity was 0.81. Overall, PLR was 3.90, NLR was 0.28 and DOR was 17.53. For MRS, the pooled sensitivity of Cho/Cr was 0.86 and specificity was 0.79. PLR was 3.37, NLR was 0.22, and DOR was 21.04. The pooled sensitivity of Cho/NAA was 0.75 and specificity was 0.88, PLR was 4.57, NLR was 0.27, and DOR was 25.83. Without statistically significant differences except for the fact that the pooled sensitivity of Cho/NAA and Cho/Cr, and Cho/NAA also displayed higher area under the curve and Q *index compared with ADC (P<0.05). Conclusion: Both DWI and MRS were accurate tools for detecting glioma recurrence. Although MRS seemed to be superior to DWI, the latter could also be used to differentiate glioma recurrence from radiation necrosis when the former was unavailable. However, MRS and DWI could play different roles in differentiating glioma recurrence from radiation necrosis. Because of significant publication bias, pooled diagnostic measures might be overvalued. Large-sample randomized controlled studies were needed to establish its value for differentiating glioma recurrence from radiation necrosis.

Keywords: DWI, MRS, glioma recurrence, radiation necrosis

Introduction

Primary tumor of the central nervous system had an annual age-adjusted incidence rate of 28/100 000 in adults. Gliomas accounted 28% of intracranial tumors but 80% of malignant tumors [1]. So far, the current standard treatment was surgery followed by adjunctive radiotherapy and chemotherapy [2]. However, differentiating glioma recurrence from radiation necrosis remained a great challenge. To solve the problem, numerous innovative magnetic resonance imaging technologies were focusing on metabolic, structural and hemodynamic properties of tissues, like proton magnetic resonance spectroscopic imaging (1H-MRS), diffusion weighted imaging (DWI), perfusion-weighted imaging (PWI) and dynamic susceptibility contrast magnetic resonance imaging [3-8].

DWI was a magnetic resonance imaging (MRI) technique, which based on the imaging of the molecular mobility of water [9]. Apparent diffusion coefficient (ADC) was the most widely used parameter, it could be used to grading gliomas easily and quickly [10]. Previous studies had investigated the diagnostic value of ADC in distinguishing glioma recurrence from radiation necrosis, but the findings had been incongruent [11, 12].
MRS provided information about metabolic tissue composition, advanced spectroscopic methods had been used to quantify markers of brain tumor metabolism, (choline [Cho]), (creatinine [Cr]), (N-acetyl-aspartate [NAA]), (lactate [Lac] or lipids) were the most commonly used parameters [13]. Results were usually expressed as ratios between brain metabolites. There were some studies have evaluated the diagnostic role of MRS for distinguishing glioma recurrence from radiation necrosis [14-16], nevertheless, the sensitivity and specificity of each research were different. Although many studies compared the effect between the DWI and MRS, but there were no uniform results [3-8]. Matsusue [5] reported that DWI had equivalent diagnostic efficiency with MRS and perfusion MRI. In contrast, Fink [3] reported that a perfusion MR and multi-voxel MRS superior than DWI for distinguishing glioma recurrence from post-treatment effects. Thus, the aim of this meta-analysis was to compare the diagnostic value of DWI and MRS for differentiating glioma recurrence from radiation necrosis.

**Materials and methods**

**Search strategy**

A systematic literature search was performed to identify studies assessing the diagnostic value of DWI and MRS for differentiating glioma recurrence from radiation necrosis. We system-
Table 1. Characteristics of studies included in the meta-analysis

<table>
<thead>
<tr>
<th>Study name</th>
<th>Year</th>
<th>Country</th>
<th>Study design</th>
<th>Language</th>
<th>No. of patient</th>
<th>No. of lesion</th>
<th>Mean age (yr) (range)</th>
<th>M/F</th>
<th>Histology</th>
<th>Reference standard</th>
<th>Imaging field strength</th>
<th>MRS metabolite ratio</th>
<th>ADC ratio</th>
<th>QUADAS scores</th>
</tr>
</thead>
<tbody>
<tr>
<td>DiCostanzo et al.</td>
<td>2014</td>
<td>Italy</td>
<td>R</td>
<td>English</td>
<td>29</td>
<td>29</td>
<td>63 (38-74)</td>
<td>18/11</td>
<td>HGG (29)</td>
<td>His + Cli</td>
<td>3T</td>
<td>Cho/Cr and Cho/NAA</td>
<td>NA</td>
<td>23</td>
</tr>
<tr>
<td>Fink et al.</td>
<td>2012</td>
<td>USA</td>
<td>R</td>
<td>English</td>
<td>38</td>
<td>39</td>
<td>48 (28-70)</td>
<td>20/18</td>
<td>NA</td>
<td>His + Cli</td>
<td>3T</td>
<td>Cho/Cr and Cho/NAA</td>
<td>&lt;1.28</td>
<td>23</td>
</tr>
<tr>
<td>Meng et al.</td>
<td>2011</td>
<td>China</td>
<td>R</td>
<td>Chinese</td>
<td>22</td>
<td>22</td>
<td>45 (13-73)</td>
<td>10/12</td>
<td>NA</td>
<td>His + Cli</td>
<td>3T</td>
<td>Cho/Cr and Cho/NAA</td>
<td>&lt;1.66</td>
<td>17</td>
</tr>
<tr>
<td>Matsusue et al.</td>
<td>2010</td>
<td>USA</td>
<td>R</td>
<td>English</td>
<td>15</td>
<td>15</td>
<td>47 (30-64)</td>
<td>9/6</td>
<td>LGG (7), HGG (6)</td>
<td>His + Cli</td>
<td>1.5T/3T</td>
<td>Cho/Cr and Cho/NAA</td>
<td>&lt;1.30</td>
<td>24</td>
</tr>
<tr>
<td>BobekBillewicz et al.</td>
<td>2010</td>
<td>Poland</td>
<td>R</td>
<td>English</td>
<td>8</td>
<td>11</td>
<td>23-68</td>
<td>3/5</td>
<td>HGG (8)</td>
<td>His + Cli</td>
<td>3T</td>
<td>Cho/Cr</td>
<td>&lt;1.59</td>
<td>25</td>
</tr>
</tbody>
</table>

ADC, Apparent diffusion coefficient; Cho, Choline; Cli, Clinical; Cr, Creatine; M, Male; F, Female; HGG, High grade glioma; His, Histology; LGG, Low grade glioma; MRS, Magnetic resonance spectroscopy; NA, Not available; NAA, N-acetyl-aspartate; R, Retrospective.
Literature selection

Two investigators, who were blinded to the journal, author, institution and date of publication, independently evaluated all eligible studies. The inclusion criteria were: (1) patients were histopathologically diagnosed as glioma, and has a history of treatment with surgery or radiotherapy or chemotherapy; (2) DWI and MRS was used to differentiate glioma recurrence from radiation necrosis; (3) The values of true positive (TP), false positive (FP), false negative (FN), true negative (TN) should be calculated from the data reported; (4) the effective case number was greater than 8 in selected studies; (5) only publications in English and Chinese were included. Abstracts presented at conferences, letters, unpublished data, reviews, case reports, editorials and comments were excluded. Initial searches identified 619 articles. According to the inclusion and exclusion criteria mentioned above, Only 5 (1 Chinese article and 4 English articles) of these articles were included this analysis which contained the appropriated data.

Quality assessment

The same two investigators who performed the database searches also performed the related data extraction independently. Relevant studies were further examined with QUADAS criteria [17]. Basal characteristics (authors, year of publication), and patients’ demographic characteristics (mean age, sex, and number) and technical aspects (imaging field strength, b value, quantitative parameter, cut-off value, reference standard, TP, FP, FN and TN value) were extracted.

Statistical analysis

Meta-disc software (Version 1.4) and Stata 11.0 software (Stata, College Station, TX) was performed to analysis our result. The sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR), diagnostic odds ratio (DOR) and their 95% confidence intervals (CIs) were calculated from the original data. We also obtained the summary receiver operating characteristic (SROC) curve and the area under the curve (AUC). We used I² tests to test heterogeneity. An I² value ranges from 0% to 40% was regarded as “mild heterogeneity”, value ranges

<table>
<thead>
<tr>
<th>Study name</th>
<th>Year</th>
<th>Metabolite ratio</th>
<th>Cut-off</th>
<th>TP</th>
<th>FP</th>
<th>FN</th>
<th>TN</th>
</tr>
</thead>
<tbody>
<tr>
<td>DiCostanzo et al.</td>
<td>2014</td>
<td>Cho/Cr</td>
<td>NA</td>
<td>17</td>
<td>2</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cho/NAA</td>
<td>NA</td>
<td>10</td>
<td>0</td>
<td>11</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ADC ratio</td>
<td>NA</td>
<td>17</td>
<td>1</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>MRS and DWI</td>
<td>NA</td>
<td>18</td>
<td>1</td>
<td>3</td>
<td>7</td>
</tr>
<tr>
<td>Fink et al.</td>
<td>2012</td>
<td>Cho/Cr</td>
<td>≥1.54</td>
<td>22</td>
<td>1</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cho/NAA</td>
<td>≥1.05</td>
<td>21</td>
<td>1</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ADC ratio</td>
<td>&lt;1.28</td>
<td>21</td>
<td>2</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Meng et al.</td>
<td>2011</td>
<td>Cho/Cr</td>
<td>≥1.51</td>
<td>10</td>
<td>1</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cho/NAA</td>
<td>≥1.42</td>
<td>12</td>
<td>1</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ADC ratio</td>
<td>&lt;1.66</td>
<td>14</td>
<td>2</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Matsusue et al.</td>
<td>2010</td>
<td>Cho/Cr</td>
<td>≥1.29</td>
<td>10</td>
<td>1</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cho/NAA</td>
<td>≥1.06</td>
<td>9</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>MRS</td>
<td>Cho/Cr≥1.29, Cho/NAA≥1.06</td>
<td>9</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>BobekBiliewicz et al.</td>
<td>2010</td>
<td>ADC ratio</td>
<td>&lt;1.30</td>
<td>9</td>
<td>1</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cho/Cr</td>
<td>≥1.35</td>
<td>4</td>
<td>1</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cho/NAA</td>
<td>≥2.11</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ADC ratio</td>
<td>&lt;1.59</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td>5</td>
</tr>
</tbody>
</table>

NA, Not available; Cho, Choline; Cli, Clinical; Cr, Creatine; NAA, N-acetyl-aspartate.
Differentiating glioma recurrence from radiation necrosis

Table 3. Parameters and patterns of MRS in all studies

<table>
<thead>
<tr>
<th>Study name</th>
<th>Pattern</th>
<th>Slice thickness (mm)</th>
<th>TR (ms)</th>
<th>TE (ms)</th>
<th>FOV</th>
<th>Acquisition time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Di Costanzo et al.</td>
<td>NA</td>
<td>10</td>
<td>1,500</td>
<td>144</td>
<td>24 cm</td>
<td>6 min 53 s</td>
</tr>
<tr>
<td>Fink et al.</td>
<td>SVS/MVS</td>
<td>NA</td>
<td>2,000</td>
<td>144/288</td>
<td>24 cm</td>
<td>NA</td>
</tr>
<tr>
<td>Meng et al.</td>
<td>SVS</td>
<td>NA</td>
<td>2,000</td>
<td>144</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Matsusue et al.</td>
<td>MVS</td>
<td>NA</td>
<td>2,000</td>
<td>144/288</td>
<td>24 cm</td>
<td>5-7 min</td>
</tr>
<tr>
<td>BobekBillewicz et al.</td>
<td>SVS (1.5T)</td>
<td>NA</td>
<td>1,300/1500</td>
<td>135/30</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>SVS (3T)</td>
<td>NA</td>
<td>1,083</td>
<td>288/35s</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

MVS, Multi-voxel spectroscopic; SVS, Signal-voxel spectroscopic; NA, Not available.

Table 4. Parameters and patterns of DWI in all studies

<table>
<thead>
<tr>
<th>Study name</th>
<th>Slice thickness (mm)</th>
<th>Gap (mm)</th>
<th>TR (ms)</th>
<th>TE (ms)</th>
<th>Slice number</th>
<th>Matrix</th>
<th>Acquisition time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Di Costanzo et al.</td>
<td>5</td>
<td>1</td>
<td>11,000</td>
<td>66.6</td>
<td>NA</td>
<td>164×192</td>
<td>44 s</td>
</tr>
<tr>
<td>Fink et al.</td>
<td>4</td>
<td>1</td>
<td>5,210</td>
<td>53</td>
<td>30</td>
<td>112×89</td>
<td>NA</td>
</tr>
<tr>
<td>Meng et al.</td>
<td>6</td>
<td>1</td>
<td>5,000</td>
<td>65</td>
<td>NA</td>
<td>NA</td>
<td>18 s</td>
</tr>
<tr>
<td>Matsusue et al.</td>
<td>4</td>
<td>1</td>
<td>5,210</td>
<td>53</td>
<td>28</td>
<td>112×89</td>
<td>32 s</td>
</tr>
<tr>
<td>BobekBillewicz et al.</td>
<td>1.5T</td>
<td>5</td>
<td>3,100</td>
<td>99</td>
<td>NA</td>
<td>192×192</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>3T</td>
<td>4</td>
<td>3,080</td>
<td>70</td>
<td>NA</td>
<td>112×256</td>
<td>NA</td>
</tr>
</tbody>
</table>

NA, Not available.

from 30% to 60% was treated as “moderate heterogeneity”, value ranges from 50% to 90% was regarded as “substantial heterogeneity”, and I² ranges from 75% to 100% was considered as “considerable heterogeneity” [18]. A random effects model was used when P<0.05, if not, a fixed effects model was used when P>0.05.

Ethical approval

The ethical approval was not necessary for the reason that our study type was systematic review and meta-analysis.

Results

Literature selected

A total of 619 potentially relevant studies were initially selected. Five eligible studies were identified [3-7]. A flowchart summarizing the selection process of the finally included studies was shown in Figure 1. Study design was described as retrospective in all studies. The characteristics of the included studies were presented in Tables 1 and 2. QUADAS scores were shown in Table 1.

Spectroscopy and diffusion weighted imaging: acquisition technique

In the majority (n = 5) of the eligible studies, spectroscopic data were acquired with 3T magnets except one study examined MR spectroscopy at 1.5T and 3T. Single-voxel spectroscopy was used in 3 studies and two applying the multi-voxel spectroscopy. Water saturation was applied in all studies. Four studies provided information on spectroscopic voxel size (Table 3).

Demographic data

In these 5 included studies, a total of 112 patients and 116 lesions, of which 60 were men and 52 were women, were included. Age distribution was heterogeneously reported in Table 1, while mean age was reported in all studies (38-74, 28-70, 13-73, 30-64, 23-68). Final determination between tumor recurrence and radiation necrosis was decided either histologically or through combined clinical and imaging follow-up in all include articles, however, clinical follow-up criteria were imparity. MR protocols also different from each other, scan parameter and pattern of DWI and MRS were shown in Tables 3 and 4, respectively.
Differentiating glioma recurrence from radiation necrosis

Figure 2. Forest plot of the sensitivity and specificity of the meta-analysis. The pooled sensitivity and specificity of ADC in differentiation of recurrent glioma from radiation necrosis (A); The pooled sensitivity and specificity of Cho/Cr in differentiation of recurrent glioma from radiation necrosis (B); The pooled sensitivity and specificity of Cho/NAA in differentiation of recurrent glioma from radiation necrosis (C).
Differentiating glioma recurrence from radiation necrosis

Diagnostic accuracy of MRS and DWI

The diagnostic data of DWI and MRS were performed pooled analysis, respectively. The pooled sensitivities and specificities of these methods were shown in Figure 2. The pooled of ADC sensitivity was 0.80 (95% CI: 0.70, 0.88) and specificity was 0.81 (95% CI: 0.64, 0.92). Overall, PLR was 3.90 (95% CI: 2.00, 7.61) and NLR was 0.28 (95% CI: 0.18, 0.45) (see in Figure 2A). With MR spectroscopic data, two variables (Cho/NAA and Cho/Cr ratios) were shown to differentiate recurrent glioma from radiation necrosis. The pooled sensitivity of Cho/Cr was 0.86 (95% CI: 0.76, 0.93) and specificity was 0.79 (95% CI: 0.59, 0.92), PLR was 3.37 (95% CI: 1.77, 6.40) and NLR was 0.22 (95% CI: 0.11, 0.46) (see in Figure 2B). The pooled sensitivity of Cho/NAA was 0.75 (95% CI: 0.64, 0.85) and specificity was 0.88 (95% CI: 0.68, 0.97), PLR was 4.57 (95% CI: 1.78, 11.72) and NLR was 0.27 (95% CI: 0.09, 0.67) (see in Figure 2C). Three variables (Cho/NAA, Cho/Cr, and ADC ratio) diagnostic odds ratio (DOR) were 25.83 (95% CI: 6.51, 102.5), 21.04 (95% CI: 6.5, 68.13), 17.3 (95% CI: 6.08, 50.56), respectively. The SROC curves with Q *index for DWI and MRS were shown in Figure 3A and 3B respectively. The AUC and Q *index of MRS were significantly higher than those of ADC (P<0.01).

Assessment of publication bias

The presence of publication bias was confirmed by the Egger test (P<0.001). Because the small sample size, our conclusion was adopted cautiously. Multimodal imaging trials and multicenter trials should be implemented in the future.

Discussion

With the advanced of the glioma therapy, radiotherapy had become an indispensable ways of intracranial malignant tumor treatment [19]. However, clinical and imaging manifestations of radiation necrosis liked tumor recurrence. Accurate diagnosis of these post-treatment lesions, either radiation necrosis or tumor recurrence, was vital to the patient’s prognosis. Whether a mass was a recurred glioma was usually determined by histopathology. Nevertheless, histopathological examination could not be applied to every patient due to ethical reasons; it was unreasonable to perform a biopsy or surgical resection in patients who showed absence of clinical or radiological progression. Therefore, the current study used histopathological results and/or clinical and/or radiological follow-up as the reference standard. Conventional MRI with gadolinium contrast couldn’t distinguish between tumor recur-
Differentiating glioma recurrence from radiation necrosis accurately, owing to their similar imaging manifestations in gadolinium-enhanced MRI [20]. Modern advancements with PET scans, DWI and MRS had shown prospect for differentiating tumor recurrence from radiation necrosis [21]. Previous studies demonstrated that PET methods appeared relatively specific instrument as to evaluation of the response to treatment and differentiation between recurrent tumor tissue and radiation necrosis [22, 23]. FDG uptake suggested the presence of glioma recurrence, whereas absence of FDG uptake suggested the presence of necrosis [24]. Voges et al [25] reported 11C-methionine superior to FDG in illustrating residual of recurrent tumor tissue. While 11C-methionine uptake may be increased when disruption of the blood brain barrier, such as cerebral hematoma or even necrotic areas resulted from radiotherapy [26]. PET scan was an expensive examination, and had certain radiation effect to human body as well. MRI was a noninvasive and economic methods, the most important advantage was no radiation to human. Besides, only a few studies with small patient populations reported comparison of DWI and MRS in differentiating glioma recurrence from radiation necrosis in humans directly.

For decades, MRS had been used as a value imaging tool to reveal the metabolism of brain tumor. The metabolic profiles of tumor recurrence and radiation necrosis had been widely studied, but there was still no consensus about which spectroscopic parameter(s) and/or which threshold level(s) ensure the better distinction accuracy [3, 4, 8]. “Nonnormalized” ratios had been largely used and several studies have reported that recurrent tumours had higher Cho/NAA and Cho/Cr than radiation necrosis [3, 4, 8]. Taking into account the threshold values that maximized the discriminative power, the reported diagnostic accuracy of Cho/NAA and/or Cho/Cr ranged between 86 and 91% [3-6, 8]. This study had demonstrated that MRS exhibited a high diagnostic accuracy for the detection of glioma recurrence, with the high sensitivity of the Cho/Cr (0.86) and specificity of the Cho/NAA (0.88).

The diagnostic value of DWI in differentiating tumor recurrence from radiation necrosis had not been fully reported, nor had a threshold of ADC been established that provided the best diagnostic accuracy [27, 28]. In fact, comparing diffusion features between recurrent tumor and radiation necrosis groups, some authors [11, 12] measured significantly higher ADC values in radiation necrosis group, while others [29] found significantly higher ADC values in the recurrent tumor and others [30] still did not find any significant differences in mean ADC values. In the current study, DWI showed a high diagnostic accuracy in detecting glioma recurrence, with an overall sensitivity was 0.80 (95% CI: 0.70, 0.88) and specificity was 0.81 (95% CI: 0.64, 0.92). The AUC and Q *index of MRS were higher than those of DWI (P<0.05).

In the presented meta-analysis, we demonstrated the slightly advantage of MRS over DWI for differentiating glioma recurrence from radiation necrosis. Various studies had reported on the broad range of the diagnosis accuracy of this imaging technique. The current study showed that the pooled sensitivity of DWI was 82%. Because ADC influenced by many factors, such as the field strength, sequence, b value, previous studies though a higher b-value provided better contrast and higher ADC value theoretically [31]. Hein et al showed that ADC ratios (1.43 vs. 1.82*10⁻³ mm²/s) and mean ADC values (1.18 vs. 1.4*10⁻³ mm²/s) in the recurrence group was significantly lower than those of the radiation necrosis group [32]. Similar results presented by these studies [8, 11, 33]. MRS reflected the information of brain metabolism more than the ADC, not only could reflect the cell intensity, and also could reflect the damage of neurons. Previous studies suggested that tumor recurrence might be characterized by high Cho and low NAA levels [3, 4, 16, 34]. In this meta-analysis, the pooled sensitivity of Cho/NAA was higher than DWI, and the pooled specificity was closer to DWI (79-81%). Substantial data in the literature also demonstrated Cho/NAA diagnosis accuracy was better than the ADC, this results was consistent with previous articles [4, 35]. Moreover, in SROC analyses, the AUC of Cho/NAA was higher than that of ADC (see Figure 3). Some studies considered combining 3T DWI and MRS diagnostic results using multiparametric scoring system had potential to improve overall diagnostic accuracy in distinguishing glioma progression from post-radiation change beyond that of each technique alone [5, 7].
Our systematic review found only included 5 studies that directly compared DWI and MRS in differentiating glioma recurrence from radiation necrosis. Therefore, our conclusion should be interpreted cautiously because of some reasons. The five limited included papers varied a lot in several aspects. As we known, different field strength (1.5T and 3T) and different MRI equipments with different methodology and post-processing could result in unfavorable results. Firstly, most included articles paid attention to diagnostic accuracy of single metabolite ratio, it is unknown if combined metabolite ratios could improve diagnostic efficiency. Secondly, although the absence of heterogeneity in this meta-analysis, designs of the included studies varied a lot, such as glioma grades, sample size and cut off values. Thirdly, this meta-analysis only included papers published in the English and Chinese language, which may miss some eligible unpublished studies or reported in other languages. Besides, some inevitable publication bias existed in the results as Egger's regression test indicated in the meta-analysis.

Conclusions

Our meta-analysis demonstrated that MRS superiority over glioma recurrence from radiation necrosis than DWI. So far, this was the first meta-analysis to compare the overall diagnostic value of MRS and DWI in detecting recurrent glioma from radiation necrosis. Although MRS had an advantage over DWI in detecting the recurrence of glioma, DWI as an alternative tool when MRS is unavailable. Based on the above results, we tentatively indicated that MRS was a favorable imaging method in the detection of tumor recurrence in glioma owing to high sensitivity. Cho/Cr was highly specific but had low sensitivity in recurrence diagnosis. However, the results of the meta-analysis were concluded from 5 limited studies. Multimodal imaging trials and multicenter trials should be required in the future. Using prospective designs and large-sample randomized controlled studies are needed to establish its value for differentiating glioma recurrence from radiation necrosis.

Disclosure of conflict of interest

None.

Abbreviations

DWI, diffusion-weighted magnetic resonance imaging; MRS, Magnetic Resonance Spectroscopy; ADC, Apparent Diffusion Coefficient; CBM, Chinese Biomedical databases; SEN, sensitivity; SPE, specificity; NLR, negative likelihood ratio; PLR, positive likelihood ratio; DOR, diagnostic odds ratio.

Address correspondence to: Ming Zhang, Department of Radiology, First Affiliated Hospital, School of Medicine, Xi'an Jiao Tong University, 277 Yanta West Road, Xi'an 710061, Shaanxi, People's Republic of China. E-mail: zmmri@163.com

References

Differentiating glioma recurrence from radiation necrosis


Differentiating glioma recurrence from radiation necrosis


