Original Investigation

Diagnostic Values of DCE-MRI and DSC-MRI for Differentiation Between High-grade and Low-grade Gliomas: A Comprehensive Meta-analysis

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Rationale and Objectives: This study aimed to collect the studies on the role of dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) and dynamic susceptibility contrast MRI (DSC-MRI) in differentiating the grades of gliomas, and evaluate the diagnostic performances of relevant quantitative parameters in glioma grading.

Materials and Methods: We systematically searched studies on the diagnosis of gliomas with DCE-MRI or DSC-MRI in Medline, PubMed, China National Knowledge Infrastructure database, Cochrane Library, and Embase published between January 2005 and December 2016. Standardized mean differences and 95% confidence intervals were calculated for volume transfer coefficient (K^{trans}), volume fraction of extravascular extracellular space (V_e), rate constant of backflux (K_{ep}), relative cerebral blood volume (rCBV), and relative cerebral blood flow (rCBF) using Review Manager 5.2 software. Sensitivity, specificity, area under the curve (AUC), and Begg test were calculated by Stata 12.0.

Results: Twenty-two studies with available outcome data were included in the analysis. The standardized mean difference of K^{trans} values between high-grade glioma and low-grade glioma were 1.18 (0.91, 1.45); V_e values were 1.43 (1.06, 1.80); K_{ep} values were 0.65 (–0.05, 1.36); rCBV values were 1.44 (1.08, 1.81); and rCBF values were 1.17 (0.68, 1.67), respectively. The results were all significant statistically ($P < .05$) except K_{ep} values ($P = .07$), and high-grade glioma had higher K^{trans}, V_e, rCBV, and rCBF values than low-grade glioma. AUC values of K^{trans}, V_e, rCBV, and rCBF were 0.90, 0.88, 0.93, and 0.73, respectively; rCBV had the largest AUC among the four parameters ($P < .05$).

Conclusion: Both DCE-MRI and DSC-MRI are reliable techniques in differentiating the grades of gliomas, and rCBV was found to be the most sensitive one.

Key Words: Gliomas; grading; DCE-MRI; DSC-MRI; meta-analysis.

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INTRODUCTION

Gliomas are the most common primary malignant tumors of the central nervous system. According to the 2016 World Health Organization (WHO) classification of tumors of the central nervous system (1), gliomas are divided into four grades based on their histology and molecular features. Accurate grading of gliomas is critical to the determination of surgery scheme, treatment response, and prognostic evaluation. On pathology, low-grade gliomas (LGGs) are slowly proliferating tumors that display cytological atypia but no signs of anaplasia, endothelial cell proliferation, or brisk mitotic activity (2). However, in high-grade gliomas (HGGs), substantial hyperplasia of anomalous cells can be observed, resulting in neovascularization and incomplete basement membrane of tumor neovasculature, which in turns leads to augmentation of microvascular permeability, a histologic marker of HGG (3). Furthermore, the abnormal vessels of tumors are usually tortuous and disorganized. The resultant disordered cerebral hemodynamics alter blood volume and blood flow directly.

Conventional morphologic magnetic resonance imaging (MRI) can estimate benign and malignant tumors based grossly on the range of cytotoxic edema, hemorrhage, necrosis, signal intensity heterogeneity, and degree of enhancement. However, it has been reported that 9.5% HGG showed no enhancement, whereas 22.72% of LGG enhanced after contrast administration (4). Therefore, quantitative and reliable imaging

Acad Radiol 2017; ■:■■–■■

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https://doi.org/10.1016/j.acra.2017.10.001

methods are needed. Dynamic contrast-enhanced MRI (DCE-MRI) is a noninvasive technology that provides information about the microcirculation of tumors. It assesses several valuable parameters including volume transfer coefficient (K^{trans}), volume fraction of extravascular extracellular space (V_e), and rate constant of backflux (K_{ep}), all of which can reflect the permeability of new vessels and are indicative of malignant grade of tumors (3). Dynamic susceptibility contrast MRI (DSC-MRI) is another advanced technique that provides perfusion information with parameters such as cerebral blood volume (CBV) and cerebral blood flow (CBF). Increased tumor vascularity and tumor grade correlate credibly with relative CBV (rCBV) and relative CBF (rCBF) (5).

With the advent of the high-field MR scanner and the development of advanced imaging technologies, increasingly more studies have concentrated on grading of gliomas with DCE-MRI and DSC-MRI in recent years. Law et al. (6) found rCBV was the best parameter in discriminating glioma grade, followed by CBF, CBV, and K^{trans}. However, Patankar et al. (7) reported that K^{trans} had a higher area under the curve (AUC) value than CBV for glioma discrimination (0.979 and 0.966, respectively). Furthermore, Zhang et al. (3) and Sun et al. (8) found that K_{ep} had no significant difference in glioma grading ($P > .05$), whereas Wang et al. (9) reported that HGG had a lower K_{ep} than LGG in pediatric gliomas ($P < .01$), which contradicted with the results of Awasthi et al. (10) and Roy et al. (11) The large variations in different studies may be because of various types of scanners, field strength, contrast agents, imaging protocols, parameters, and post-processing methods, etc. In some instances, because of small sample sizes and incomplete parameters of individual studies, the reliability and reproducibility of these two technologies remains unclear. Therefore, we propose a comprehensive meta-analysis with a large sample size to address contradictory findings from different studies and to evaluate the diagnostic performance of relevant parameters in the grading of gliomas, the results of which would provide more reliable information to clinicians.

MATERIALS AND METHODS

Data Sources

Two reviewers searched for any literature concerned with grading gliomas with DCE-MRI or DSC-MRI in Medline, PubMed, China National Knowledge Infrastructure database, Cochrane Library, and Embase published between January 2005 and December 2016. Medical subject headings or search keywords were combined into a formula of (astrocytoma or glioblastoma or glial tumor or astrocytic tumor or glioma or oligodendroglioma or oligodendroglial tumor) and (DCE-MRI or DSC-MRI or K_{ep} or K^{trans} or V_e or rCBV or rCBF), with the searching limitations in the title or abstract of the article. Only studies written in English or Chinese were reviewed. We also scrutinized references in the included studies and searched for newly published studies every 2 months. Manual retrieval was performed if necessary.

Studies Selection

The following inclusion criteria were established: (1) DCE-MRI or DSC-MRI was applied in differentiating different grades of gliomas; (2) at least one of the quantitative indices for K^{trans}, V_e, K_{ep}, rCBV, and rCBF could be extracted or calculated from the study; (3) all the cases had been diagnosed pathologically; (4) neither surgery nor chemotherapy was conducted before magnetic resonance examination; (5) the scores of quality assessment of included studies were at least 9 because the high quality of included studies is the foundation of a credible meta-analysis; the standards for evaluation were stated in the quality assessment section (12); (6) any histologic subtypes of gliomas were included; and (7) the following exclusion criteria were established: (1) animal experiments, such as those using rats; (2) any graduation thesis, meeting records, reviews, duplications, or studies that have not been published; (3) similar studies that were written by the same first authors. Those performing the analysis were blinded to the institution. (4) Lack of key data (eg, standard deviation); and (5) other imaging modalities (eg, computed tomography, positron emission tomography) were used.

Data Abstraction and Quality Assessment

In accordance with 2007 WHO criteria, gliomas of grades I and II were classified into LGG, and grades III and IV into HGG (13), taking the average of grades I and II, and grades III and IV as the mean value if the data had not been merged. Two reviewers extracted the data independently from each study including the author, year of publication, type of MR machine, country, age of patients, types of gliomas, publication journal, DCE and DSC sequences, kinetic models, leakage correction, contrast type, flow rate, dose, numbers of oligoastrocytomas and oligodendrogliomas, post-processing software, mean value, and standard deviation of the related parameters according to the inclusion and exclusion criteria. True positive, false positive, false negative, and true negative data were also necessary to calculate diagnosis values. The revised Quality Assessment of Diagnostic Accuracy Studies checklist was used to assess the quality of each study with 14 criteria in terms of the risk of bias (14). Each criterion was judged as "Yes (low risk of bias)," "No (high risk of bias)," or "Unclear." When a criterion was judged as Yes, the score increased by one. If the results contradicted each other, especially in terms of quality assessment, another senior clinician or statistician was invited to discuss the results to achieve a consensus.

Data Synthesis

Review Manager software version 5.2 (Cochrane Collaboration, Oxford, UK) was applied to calculate the effect size and the 95% confidence interval (CI). Stata version 12.0

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