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Noninvasive evaluation of cerebral glioma grade by using multivoxel 3D proton MR spectroscopy

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Abstract

Objective: To determine whether metabolite ratios in multivoxel 3D proton MR spectroscopy (^{1}H MRS) is different between low-grade and high-grade gliomas and may be useful for glioma grading.
Materials and Methods: Thirty-nine patients (23 male and 16 female; 22–75 years old; mean age, 44.92±12.65 years) suspected of having gliomas underwent 3D ^{1}H MRS examinations. Metabolite ratios [choline (Cho)/creatine (Cr), *N*-acetylaspartate (NAA)/Cr and Cho/NAA] were measured. Tumor grade was determined by using the histopathologic grading. Receiver operating characteristic analysis of metabolite ratios was performed, and optimum thresholds for tumor grading were determined. The resulting sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) for identifying high-grade gliomas were calculated.
Results: Diagnostic-quality 3D ^{1}H MRS with readily quantifiable Cho, Cr and NAA peaks was obtained in 94.87% of the cases. The Cho/Cr and Cho/NAA ratios were significantly higher in high-grade than in low-grade glioma (P<.001), whereas the NAA/Cr ratios were significantly lower in high-grade than in low-grade glioma (P<.001). Receiver operating characteristic analysis demonstrated a threshold value of 2.04 for Cho/Cr ratio to provide sensitivity, specificity, PPV and NPV of 84.00%, 83.33%, 91.30% and 71.43%, respectively. Threshold value of 2.20 for Cho/NAA ratio resulted in sensitivity, specificity, PPV and NPV of 88.00%, 66.67%, 84.62% and 72.73%, respectively. Overall diagnostic accuracy was not statistically significantly different between Cho/Cr and Cho/NAA ratios (χ^2=0.093, P=.76).
Conclusion: Metabolite ratios of low-grade gliomas were significantly different from high-grade gliomas. Cho/Cr and Cho/NAA ratios could have the superior diagnostic performance in predicting the glioma grade.

Keywords: Brain; Glioma; Magnetic resonance (MR); Proton MR spectroscopy; Tumor grade

1. Introduction

In a patient suspected of having cerebral glioma, noninvasive preoperative evaluation of brain tumor grade is important for treatment planning and prediction of prognosis [1]. Conventional MRI is considered to be an established and useful tool in brain tumor grading, but MRI-based tumor grading may lead to low-grade or high-grade misclassification in some cases [1–7]. Proton MR spectroscopy (^{1}H MRS), which is a noninvasive functional imaging method providing complementary information to anatomical imaging, has been proposed as an alternative modality for grading cerebral glioma [2–4].

Previous studies on this topic mostly employed single-voxel or 2D multivoxel ^{1}H MRS techniques. The data of these studies have proved that the ^{1}H MRS technique has the potential to more accurately predict cerebral glioma grade than conventional MRI [2–4,8]. However, these studies only assess metabolite concentrations of a single voxel for the single-voxel ^{1}H MRS technique [2,8] or of a multivoxel at a single slice for the 2D multivoxel ^{1}H MRS method [3,4]. The 3D chemical shift imaging (CSI) ^{1}H MRS technique enables coverage of a relatively larger volume of interest (VOI) and allows evaluation of multiple regions of the lesion [9,10].

To noninvasively identify gliomas grade, 3D ^{1}H MRS technique was performed on 39 patients with cerebral gliomas in our study. The purpose of this study was to determine whether metabolite concentrations at 3D ^{1}H MRS are different between low-grade and high-grade gliomas and may be useful for predicting the grade of cerebral glioma.

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2. Methods

2.1. Subjects

Thirty-nine patients (23 male and 16 female; 22–75 years old; mean age, 44.92±12.65 years) with supratentorial gliomas were enrolled in this study. These patients underwent MR imaging/3D ^{1}H MRS examinations and subsequent surgery for tumor removal. Histopathologic specimen obtained via surgical resection was graded by the WHO II criteria: 26 high grade (Grade III, *n*=10; Grade IV, *n*=16) and 13 low grade (Grade I, *n*=5; Grade II, *n*=8). Written informed consent was obtained from all patients after the nature of the examination had been fully explained, and the study was approved by the institutional review board.

2.2. MR imaging and proton MR spectroscopic imaging

All examinations including MR imaging and proton MR spectroscopic imaging were performed on a 3.0-T MR scanner (Signa EXCITE II; GE Medical Systems, Milwaukee, WI, USA). The conventional MR images consisted of axial T1-weighted spin-echo (SE), T2-weighted fast SE and fluid-attenuated inversion-recovery (FLAIR) images obtained by using a section thickness of 6 mm, field of view (FOV) of 240 mm and a matrix of 320×224. Then, contrast-enhanced T1-weighted SE images were obtained in axial, coronal and sagittal planes after intravenous administration of gadopentetate dimeglumine (Magnevist; Schering, Germany) at a dose of 0.1 mmol/kg body weight.

Proton MR spectroscopy was performed as the last sequence in the present study. Three-dimensional multivoxel ^{1}H MRS was performed with a 3D CSI technique. The following parameters were used for 3D ^{1}H MRS: a point-resolved spectroscopy sequence (PRESS), which included six presaturation bands placed around the VOI to minimize contamination by the air-filled sinuses and osseous; TR/TE=1000/144; FOV=120 mm; matrix=8×8; voxel thickness=20–60 mm, depending on the location and size of lesions; spacing=10 mm; locs per slab=8; acquisition=1 average; scanning time=8 min 36 s. The VOI was placed on a contrast-enhanced axial T1-weighted image to ensure that voxels were placed over the contrast-enhancing area of lesion and over the normal-appearing contralateral brain parenchyma on T2 and FLAIR images. Automatic prescanning was performed before each spectroscopic scan to yield consistent 20±5 Hz full width-at-half-maximum and 95–99% water saturation (if necessary, higher-order shim was performed).

2.3. Proton MR spectroscopic image analysis

The 3D ^{1}H MRS data were processed off-line by using a software on a workstation (FuncTool 3.1 software package; Sun, GE Healthcare). Spectra and metabolite maps for each "slice" along the third dimension were extracted from the individual CSI images with the CSI FuncTool Display tool. Within the obtained VOI, separate voxels (voxel size, 15×15×10 mm) were individually placed in the area of enhancement and in normal-appearing contralateral brain parenchyma [9]. Metabolite peaks used were as follows: *N*-acetylaspartate (NAA) at 2.02 ppm, choline-containing compounds (Cho) at 3.22 ppm and (phospho-) creatine (Cr) at 3.01 ppm. According to metabolite maps, metabolite ratios (maximal Cho/Cr and Cho/NAA ratios, and minimal NAA/Cr ratios) were calculated by the software. To ensure spectral quality and acceptable spectroscopic data, the normal metabolite ratios were obtained from the normal-appearing contralateral brain parenchyma and were compared with the ratios obtained from the tumor area.

2.4. Statistical analysis

Statistical analysis was performed using the commercial software SPSS for Windows release 11.5 (SPSS, Inc., Chicago, IL, USA). *P* values of less than .05 were considered statistically significant. The metabolite ratios of Cho/Cr, Cho/NAA and NAA/Cr were calculated (mean±S.D.). Comparisons of median metabolite ratios between low-grade and high-grade tumors were analyzed by using the Mann–Whitney *U* test.

Receiver operating characteristic (ROC) curves were used to describe and compare the performance of the diagnostic values of the metabolite ratios. The area under the ROC curve gave an estimate of the overall accuracy of each metabolite ratio. High-grade tumors were considered as true positive, and low-grade tumors were regarded as true negative. The optimal cutoff value of the metabolite ratios was obtained from the ROC analysis. The resulting sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of different metabolite ratios were calculated.

3. Results

In all 39 patients, the quality of spectroscopic image was good–excellent in 27 cases, satisfactory in 10 cases and poor in two cases. Accordingly, 3D proton MR spectroscopic imaging data analysis with readily quantifiable Cho, Cr and NAA peaks was successfully performed in 37 (94.87%, 37/39) cases. In the remaining patients (a Grade I patient with a lesion adjacent to fossa orbitalis and the other, a Grade IV one, with a hemorrhagic lesion), significant susceptibility artifact could not be overcome despite attempts at the use of multiple presaturation bands and higher-order shim. Magnetic resonance and MR spectroscopic images are shown in Figs. 1 and 2.

3.1. Comparison of metabolite ratios between tumor regions and normal-appearing contralateral brain parenchyma

The metabolite ratios of cerebral gliomas and normal-appearing contralateral brain parenchyma are summarized in Table 1. Both the Cho/Cr and Cho/NAA ratios of tumors were significantly higher than those of the normal-appearing