Preoperative Grading of Presumptive Low-Grade Astrocytomas on MR Imaging: Diagnostic Value of Minimum Apparent Diffusion Coefficient


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**BACKGROUND AND PURPOSE:** Histopathologic grade of glial tumors is inversely correlated with the minimum apparent diffusion coefficient (ADC). We assessed the diagnostic values of minimum ADC for preoperative grading of supratentorial astrocytomas that were diagnosed as low-grade astrocytomas on conventional MR imaging.

**MATERIALS AND METHODS:** Among 118 patients with astrocytomas (WHO grades II–IV), 16 who showed typical MR imaging findings of low-grade supratentorial astrocytomas on conventional MR imaging were included. All 16 patients underwent preoperative MR imaging and diffusion-weighted imaging. The minimum ADC value of each tumor was determined from several regions of interest in the tumor on ADC maps. To assess the relationship between the minimum ADC and tumor grade, we performed the Mann-Whitney U test. A receiver operating characteristic (ROC) analysis was used to determine the cutoff value of the minimum ADC that had the best combination of sensitivity and specificity for distinguishing low- and high-grade astrocytomas.

**RESULTS:** Eight of the 16 patients (50%) were confirmed as having high-grade astrocytomas (WHO grades III and IV), and the other 8 patients were confirmed as having low-grade astrocytomas (WHO grade II). The median minimum ADC of the high-grade astrocytoma (1.035 × 10⁻³ mm²·sec⁻¹) group was significantly lower than that of the low-grade astrocytoma group (1.19 × 10⁻³ mm²·sec⁻¹) (P = 0.021). According to the ROC analysis, the cutoff value of 1.055 × 10⁻³ mm²·sec⁻¹ for the minimum ADC generated the best combination of sensitivity (87.5%) and specificity (79%) (P = 0.021).

**CONCLUSION:** Measuring minimum ADC can provide valuable diagnostic information for the preoperative grading of presumptive low-grade supratentorial astrocytomas.
major therapeutic intervention before MR imaging. In addition, patients who underwent surgery >1 month after the preoperative MR imaging examination were also excluded.

Sixteen patients met our inclusion criteria (8 men and 8 women). Their ages ranged from 21 to 77 years (median age, 42 years). In all except 1 patient, MR imaging was performed on the day of surgery; 1 patient underwent MR imaging 1 day before surgery. The preoperative MR imaging diagnosis of all the included patients was low-grade glioma (WHO grade II astrocytoma).

**MR Imaging and Image Processing**

All MR imaging examinations were performed with a 1.5T MR imaging system (Signa EchoSpeed, Version 8.2.3 software; GE Healthcare, Milwaukee, Wis) with a standard head coil. Conventional MR images included fluid-attenuated inversion recovery imaging (TR/TE/TI, 9000/165/2200 ms; number of signals acquired, 1; section thickness, 5 mm; intersection gap, 2 mm; matrix size, 256 × 192; FOV, 22.0 × 22.0 cm), T1-weighted (TR/TE 450/20 ms; number of signals acquired, 1; section thickness, 5 mm; intersection gap, 2 mm; matrix size, 256 × 224; FOV, 21.9 × 21.9 cm), T2-weighted (TR/TE, 11,000/59 ms; number of signals acquired, 1; section thickness, 5 mm; intersection gap, 2 mm; matrix size, 256 × 256; FOV, 21.9 × 21.9 cm), and contrast-enhanced T1-weighted images as well as DWIs. The DWIs were acquired in the transverse plane by using a spin-echo echoplanar sequence with diffusion gradient encoding in 3 orthogonal directions (TR/TE,11,000/59 ms; number of signals acquired, 1; section thickness, 5 mm; intersection gap, 2 mm; matrix size, 256 × 256; FOV, 21.9 × 21.9 cm) with a b-value of 1000 s/mm², followed by the automatic generation of isotropic DWI. Images without motion-probing gradients (b = 0 s/mm²) were obtained simultaneously.

The ADC maps were calculated from isotropic DWI, and images were obtained with a b-value of 0 s/mm². The minimum ADC of each tumor was determined by placing regions of interest on conventional MR imaging: histopathologic diagnosis and minimum ADC Table 1 summarizes the histopathology of a given brain astrocytoma.

**Table 1: Sixteen patients with presumptive low-grade astrocytomas on conventional MR imaging: histopathologic diagnosis and minimum ADC**

<table>
<thead>
<tr>
<th>Patients/Sex/Age (yr)</th>
<th>Histologic Diagnosis*</th>
<th>Minimum ADC†</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/M/47</td>
<td>Grade II astrocytoma</td>
<td>1.185</td>
</tr>
<tr>
<td>2/F/48</td>
<td>Grade II astrocytoma</td>
<td>1.229</td>
</tr>
<tr>
<td>3/F/40</td>
<td>Grade II astrocytoma</td>
<td>1.725</td>
</tr>
<tr>
<td>4/M/43</td>
<td>Grade II astrocytoma</td>
<td>1.166</td>
</tr>
<tr>
<td>5/M/41</td>
<td>Grade II astrocytoma</td>
<td>1.03</td>
</tr>
<tr>
<td>6/F/25</td>
<td>Grade II astrocytoma</td>
<td>1.196</td>
</tr>
<tr>
<td>7/M/21</td>
<td>Grade II astrocytoma</td>
<td>1.518</td>
</tr>
<tr>
<td>8/M/55</td>
<td>Grade II astrocytoma</td>
<td>1.057</td>
</tr>
<tr>
<td>9/F/36</td>
<td>Grade III astrocytoma</td>
<td>0.982</td>
</tr>
<tr>
<td>10/F/77</td>
<td>Grade III astrocytoma</td>
<td>1.104</td>
</tr>
<tr>
<td>11/F/70</td>
<td>Grade III astrocytoma</td>
<td>0.902</td>
</tr>
<tr>
<td>12/F/38</td>
<td>Grade III astrocytoma</td>
<td>1.053</td>
</tr>
<tr>
<td>13/M/39</td>
<td>Grade III astrocytoma</td>
<td>1.025</td>
</tr>
<tr>
<td>14/M/23</td>
<td>Grade III astrocytoma</td>
<td>1.046</td>
</tr>
<tr>
<td>15/M/49</td>
<td>Grade IV astrocytoma</td>
<td>0.90</td>
</tr>
<tr>
<td>16/M/60</td>
<td>Grade IV astrocytoma</td>
<td>1.24</td>
</tr>
</tbody>
</table>

* WHO criteria. † 10⁻³ mm²·sec⁻¹.

**Results**

Among 118 patients with pathologically confirmed astrocytomas, 107 (107/118, 90.7%) were diagnosed as having high-grade astrocytomas (WHO grades III and IV) and 11 (11/118, 9.3%) with low-grade astrocytomas (WHO grade II).

Sixteen patients who had the preoperative MR imaging diagnosis of low-grade astrocytoma were included in this study. Among those 16 patients, the histopathologic diagnosis of 8 patients was low-grade astrocytoma (group A, 8/11, 77%) and that of the other 8 patients was high-grade astrocytoma (group B, 8/107, 7.5%). There were 6 patients (6/8, 75%) with anaplastic astrocytomas (WHO grade III) and 2 (2/8, 25%) with glioblastoma multiforme (WHO grade IV) in the group A patients. All group B patients had diffuse astrocytomas (WHO grade II).

The median minimum ADC (1.035 × 10⁻³ mm²·sec⁻¹) for group B was significantly lower than that for group A (1.19 × 10⁻³ mm²·sec⁻¹) (P = .021), though some overlap of distribution was shown between the values of the 2 groups (Table 2 and Figs 1–3). There was no statistically significant age difference between the 2 patient groups (Table 2) (P = .529).

According to the ROC analysis, the cutoff value of 1.055 × 10⁻³ mm²·sec⁻¹ for the minimum ADC generated the best combination of sensitivity (87.5%) and specificity (79%). The difference in the grading between the 2 groups classified by using this cutoff value of the minimum ADC was significant (P = .021).

**Discussion**

Conventional MR imaging alone may not always be reliable for predicting the histopathologic grading of a given brain astrocytoma. In our series, 50% of the patients (8/16) who were preoperatively diagnosed as having low-grade astrocyto-
ably according to tumor grade. A diffuse WHO grade II astro-
cause the therapeutic approach and prognosis differ consider-
on MR imaging. Scott et al16 demonstrated that nonenhancing
approximately 4% of glioblastomas are reported to be nonenhancing
anaplastic gliomas. They also demonstrated that approxi-
bral lesions on initial MR imaging and reported that 32% had
enhancing tumor biopsies. These are due to astrocytomas of-
ment, vascular hyperplasia, and necrosis.1 Of these his-
grades (I–IV) based on specific histologic features of the tu-
secutive MR imaging in characterizing cerebral tumors.9,13,14,19
is not always reliable for distinguishing high- from low-grade
tumor enhancement results mainly from disruption
of the blood-brain barrier, rather than from tumor vascular
proliferation; and these 2 entities are usually independent.2,10
Approximately 20% of low-grade gliomas enhance after the
administration of a gadolinium-based MR imaging contrast
agent, whereas approximately one third of nonenhancing gli-
omas are malignant.18 Moreover, large cerebral gliomas are
often histopathologically heterogeneous and may contain
components with varying grades of malignancy. In our series,
27% of the low-grade astrocytomas showed significant en-
hancess on gadolinium-based contrast agent administra-
tion. Hence, accurate preoperative grading of gliomas for ad-
equate treatment planning is often difficult on the basis of
conventional MR imaging alone.15

Traditionally, the extent of contrast enhancement has been
used as a mark of malignancy: Most high-grade gliomas show
moderate-to-strong enhancement on postcontrast T1-
weighted images, whereas low-grade gliomas show minimal or
no enhancement. However, the enhancing pattern of a tumor
is not always reliable for distinguishing high- from low-grade
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of the blood-brain barrier, rather than from tumor vascular
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The revised WHO classification subdivides gliomas into 4
grades (I–IV) based on specific histologic features of the tu-
mor, such as cellularity, nuclear atypia, mitotic activity, pleo-
formism, vascular hyperplasia, and necrosis.1 Of these his-
tologic features, tumor cellularity has been the target of
quantitative assessment with DWI,1,12 though many factors
determine the ADC of biologic tissue. DWI reflects the mol-
ecular translational motion (Brownian motion) of water within
the section of the brain studied, and quantitative information
on the restriction of water molecule movement can be ob-
tained by calculating the ADC. Several studies have shown that
the ADC is well correlated with tumor cellularity on histologic
examination and the calculation of the ADC may aid conven-
tional MR imaging in characterizing cerebral tumors.9,13,14,19

High ADC values in intracranial tumors are attributed to
low tumor cellularity, necrosis, or cysts, and lower values are
attributed to attenuated highly cellular tumors.3 Indeed, sev-
eral studies have found higher ADC values in low-grade glio-
mas than in high-grade gliomas.2,3,9,13,14,19,20 These higher
ADC values in lower grade gliomas may reflect an increase in

Table 2: Comparison of patient age and median minimum ADC value for low-grade and high-grade astrocytoma groups

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Low-Grade Group</th>
<th>High-Grade Group</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>42 (21–55)†</td>
<td>44 (23–77)†</td>
<td>.529</td>
</tr>
<tr>
<td>Median minimum ADC (10(^{-3}) mm(^2) · sec(^{-1}))</td>
<td>1.190 (1.030–1.725)†</td>
<td>1.035 (0.900–1.240)†</td>
<td>.021</td>
</tr>
</tbody>
</table>

* Median (minimal-maximal).
† Mann-Whitney U test.
the water content of the interstitial spaces. Therefore, brain neoplasms with higher cellularity or of higher grade show a significant reduction in their ADC values and markedly increased signal intensity on DWI. Yamasaki et al\textsuperscript{13} suggested an inverse relationship between the mean ADC and astrocytic tumors of WHO grades II–IV.

Most of the published studies to date evaluated the diffusion properties in various pathologic types of tumors, rather than in a single type of tumor. We compared the ADC of diffuse astrocytic tumors (WHO grades II–IV), which have little mass effect, vasogenic edema, heterogeneity, hemorrhage/necrosis, or contrast enhancement on conventional MR imaging. We found a significant difference in the median minimum value for differentiating the low- and high-grade astrocytomas, though the minimum ADC of each group overlapped ($P = .021$). These results agree with those of previous reports. The cutoff value of $1.055 \times 10^{-3}$ mm$^2$ $\cdot$ sec$^{-1}$ for the minimum ADC provided the best combination of sensitivity (87.5\%) and specificity (79\%) for differentiating tumor grades ($P = .021$).

Fan et al\textsuperscript{12} evaluated the utility of DWI in patients with nonenhancing supratentorial brain gliomas. They also found that ADC values calculated from the tumor core were helpful in differentiating and grading nonenhancing gliomas, but their subjects included patients having tumors with heterogeneous signal intensity and clear evidence of central necrosis on conventional MR imaging. Therefore, their subjects differed from those in our study. Studies by Rollin et al\textsuperscript{10} and Lam et al\textsuperscript{21} failed to find a significant difference between the ADC values of high-grade and low-grade gliomas, and some studies have shown that tumor minimum ADC values have preoperative prognostic importance in patients with malignant supratentorial astrocytomas.\textsuperscript{4,22,23} In addition, Barker et al\textsuperscript{15} and Scott et al\textsuperscript{16} demonstrated that the risk of anaplasia in nonenhancing cerebral tumors increases with age, whereas we did not find any difference between the ages of the patients with high- and low-grade astrocytomas.

Other advanced imaging techniques such as MR spectroscopy and MR perfusion imaging, in addition to ADC measurement, have been suggested for prediction of preoperative glioma grading.\textsuperscript{1,3,10,12,20,24,27} Measurement of regional cerebral blood volume (rCBV) was reported as showing close correlation with histopathologic grade in gliomas.\textsuperscript{11,12,24} Because the rCBV measurement by using an MR perfusion study can reflect tumoral physiologic information such as the degree of neovascularity and angiogenesis, it might be very helpful to
grade gliomas correctly preoperatively. Therefore, further studies focusing on the lowest ADC areas with MR perfusion study parameters including rCBV may improve correct preoperative glioma grading. However, we believe the ADC measurement also has many practical advantages. For example, the DWI sequence and ADC measurement are readily available in most institutions and are the easiest to use and the least time-consuming. In addition, the postprocessing of the data is simple, and the variation in the analyzed results is minimal.4

Furthermore, measuring the lowest ADC within a tumor might aid in selecting an appropriate site for a stereotactic biopsy. Because gliomas are typically heterogeneous and can have different histopathologic grades within a single tumor, choosing a biopsy site on the basis of conventional MR imaging findings may not lead to an accurate estimation of tumor grade or appropriate establishment of the optimum treatment strategy. On the basis of our results, we believe that performing stereotactic biopsy at the lowest ADC area of the glioma might be helpful to establish a correct grading of patients with intracranial glioma.

One limitation of this study is that the histologic specimens did not necessarily come from the sites where the minimum ADC was measured. A given individual glioma, usually of high grade, often contains a continuum of histologic features of grades II–IV. Therefore, the range of ADC values within a given glioma can vary markedly.1,3 Thus, ideally, gliomas should be graded by using specimens from their most malignant portion.3 Although we included only the minimum ADC value measurements to sample the highest tumor cell attenuation or the most proliferative portion of the tumor, there still is potential mismatch between ADC measurements and histopathologic specimens. Another limitation of this study is that our sample size was small. The size was inherent to our inclusion criteria and restricted the study to only 7.5% of all patients with high-grade gliomas.

**Conclusion**

Conventional MR imaging findings of typical low-grade glioma may not always be reliable for grading brain astrocytomas. In this study, we have demonstrated an inverse correla-
tion between the minimum ADC value and histopathologic grade of astrocytic tumors. We believe that the lowest ADC measurement can provide valuable additional information for accurate preoperative grading of astrocytomas.

References