Apparent Diffusion Coefficient Characteristics of Various Adrenal Tumors

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Purpose: Using pathologically proven tumors and 3 methods of apparent diffusion coefficient (ADC) measurement, we examined the potential of diffusion-weighted imaging (DWI) to differentiate adrenal tumors.

Methods: We evaluated adrenal tumors of 52 patients who underwent magnetic resonance (MR) examination including DWI and adrenal resection or biopsy between July 2006 and August 2011. Tumors included 25 cortical adenomas, 14 pheochromocytomas, 6 adrenal metastases, and seven others. We defined the tumor’s “solid” region as an enhancing area on contrast-enhanced MR or computed tomography (CT) and measured the ADC of the tumor’s “entire” and “solid” regions within a region of interest (ROI) placed on an ADC map (“entire” and “solid” ADCs). We obtained a “minimum” ADC by placing an ROI in an area showing the lowest ADC within the “solid” region. We also calculated the ratio of “non-solid” area to “entire” tumor and compared the average “entire,” “solid,” and “minimum” ADCs and the ratio of “non-solid” area to “entire” tumor between benign and malignant groups.

Results: The average “entire” ADC was significantly higher for the benign (1.35 ± 0.38 × 10⁻³ mm²/s) than malignant group (1.01 ± 0.17 × 10⁻³ mm²/s), and the average “solid” and “minimum” ADC and the ratio of “non-solid” area to “entire” tumor did not differ significantly between the benign and malignant groups.

Conclusion: The higher “entire” ADC value of the benign group, which might be obtained incidentally, can be considered dependent on the condition of necrosis, hemorrhage, and degeneration. ADC measurement of a tumor’s “solid” region was not useful for differentiating pathologically proven adrenal tumors.

Keywords: adrenal gland, apparent diffusion coefficient, cortical adenoma, diffusion-weighted imaging, MRI

Introduction

The adrenal gland and other organs develop many kinds of tumor, and imaging is employed for their differentiation. Specific findings including fat, hemorrhage, calcification, and washout pattern after contrast injection help distinguish histological subtype but are not always detected, and we sometimes encounter “indeterminant” tumors in daily practice.¹⁻³

Diffusion-weighted imaging (DWI) is a magnetic resonance (MR) sequence that is sensitive to the random movement of water molecules. High cellular density, one of several abnormal conditions that show decreased apparent diffusion coefficient...
(ADC), results in shrinkage of the extracellular space and is considered the main cause of restricted diffusion for a malignant tumor. Recently, ADC has been reported useful for predicting the difference in histological subtype and grade of such malignant tumors as hepatocellular carcinoma, astrocytic tumors, and bladder cancer and for distinguishing between benign and malignant tumors. ADC is an imaging parameter that can potentially describe histological difference. Therefore, the provision of additional information for diagnosing adrenal tumors, especially “indeterminant” tumors, is of clinical value. Only 4 reports have discussed the relationship among benign or malignant adrenal tumors, histological type, and ADC, and no report has addressed the usefulness of DWI for differentiating adrenal tumors. In some cases, the methods of ADC measurement were obscure, and in most cases, final diagnosis of adrenal tumor was made clinically.

Therefore, we re-examined the potential of DWI for differentiating adrenal tumors using pathologically proven tumors and 3 methods of ADC measurement.

Materials and Methods

Study population

Our hospital’s institutional review board approved this retrospective study and waived the requirement for informed consent. We identified 90 consecutive patients from our hospital’s medical records who underwent preoperative MR examination and adrenal resection or biopsy for adrenal tumors between July 2006 and August 2011. We excluded 38 patients who underwent MR imaging with a 3-tesla scanner or a different 1.5T scanner from the hospital’s main 1.5T scanner and 4 patients whose images showed poor quality or a tiny adrenal lesion that precluded precise ADC measurement. Finally, we included 52 patients (25 men, 27 women; aged 23 to 84 years, mean age 54.6 years) with 52 pathologically proven adrenal tumors. In 7 patients with bilateral adrenal tumors, we analyzed only unilateral tumors diagnosed by biopsy or resection. Histologically, the tumors (size range one to 14 cm, average size 3.55 ± 2.61 cm) comprised 25 cortical adenomas, 14 pheochromocytomas, 6 adrenal metastases, 2 adrenal cortical adenocarcinomas, and one each, myelolipoma, hemangioma, malignant lymphoma, cryptococcosis, and ganglioneuroma. The primary tumors of adrenal metastases were lung cancer in 2 patients and renal cell carcinoma, endometrial carcinoma, urethral carcinoma and colon cancer in one patient each. Two of the 14 pheochromocytomas recurred 2 and 5 years after surgery and were considered malignant; the other 12 did not recur in the 2.5 to 5 years after surgery and were considered benign. Table 1 shows the division of tumors into benign and malignant groups.

MR imaging

Patients underwent MR examinations within 3 months before surgery or biopsy using a whole-body 1.5T scanner (Intera Achieva Nova Dual; Philips Medical Systems, Best, The Netherlands) equipped with a 4-element sensitivity encoding (SENSE) body coil. Imaging included axial fat-suppressed T2-weighted fast spin-echo (FSE), axial dual-echo T1-weighted fast field-echo (FFE), and axial DWI. All sequences covered the whole adrenal gland.

Detailed imaging parameters of axial DWI were: respiratory trigger, single-shot echo-planar imaging; repetition time (TR)/echo time (TE), 1190 ms/71 ms; 128 × 73 matrix, 36 × 30.4-cm field of vision (FOV); 6-mm section thickness; 1.5-mm intersection gap; 0.7 half scan factor; one signal average; spectral presaturation inversion recovery; SENSE factor, 2; b-factors, 0, 500, and 1000; diffusion gradients applied in 3 axes; 20 sections acquired; and 2- to 3-min acquisition time. ADC maps were automatically generated on the operat-

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Number of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cortical adenoma</td>
<td>25</td>
</tr>
<tr>
<td>Pheochromocytoma</td>
<td>12</td>
</tr>
<tr>
<td>Myelolipoma</td>
<td>1</td>
</tr>
<tr>
<td>Hemangioma</td>
<td>1</td>
</tr>
<tr>
<td>Cryptococcosis</td>
<td>1</td>
</tr>
<tr>
<td>Ganglioneuroma</td>
<td>1</td>
</tr>
<tr>
<td>Adrenal metastasis</td>
<td>6</td>
</tr>
<tr>
<td>Pheochromocytoma</td>
<td>2</td>
</tr>
<tr>
<td>Adrenocortical carcinoma</td>
<td>2</td>
</tr>
<tr>
<td>Malignant lymphoma</td>
<td>1</td>
</tr>
</tbody>
</table>

Table 1. Tumor profile of benign and malignant groups
ing console using all 3 images, with b-factors of 0, 500, and 1000, and ADC values were obtained by measuring intensities on the map.

Basically, dynamic contrast-enhanced MR study was optionally performed in patients who did not undergo contrast-enhanced multi-phase helical computed tomography (CT) with a 64-MDCT scanner (Aquilion 64, Toshiba Medical, Tokyo, Japan). A few patients with renal dysfunction did not undergo contrast-enhanced MR or CT study.

Image analysis

In consensus, 2 experienced radiologists measured the ADC of each tumor in a region of interest (ROI) placed on the ADC map. They selected the slice on which the tumor appeared largest and placed the largest possible round or oval ROI with an area of at least 0.7 cm² on the “entire” tumor or on its “solid” region, and they placed an ROI in an area showing the lowest ADC within the “solid” region to obtain the “minimum” ADC. The area of “minimum ADC” is considered the most cellular part of a tumor, and its use allows the complete exclusion of influence by partially necrotic or degenerative components on the measurement of “solid” ADC. Furthermore, this measurement technique may allow detection of tumors with the worst histological grade.6,7 Basically, we defined the tumor’s “solid” region as an area of enhancement on contrast-enhanced MR or CT imaging. For ADC measurement of “solid” regions of tumor in patients who did not undergo contrast-enhanced study, areas of hemorrhage, degeneration, or necrosis were avoided by referring to fat-suppressed T2-weighted FSE and T1-weighted FFE. Furthermore, we calculated the ratio of “non-solid” area to “entire” tumor as a percentage by surrounding each area freehand.

Statistical analysis

We compared the average “entire,” “solid,” and “minimum” ADCs and the ratio of “non-solid” area to “entire” tumor between the benign and malignant groups. First, we performed the F-test to examine the equality of variance and then Student’s t-test or Welch test based on the F-test result. In addition, we used Tukey’s test to compare the average “entire,” “solid,” and “minimum” ADCs and the ratios of “non-solid” area to “entire” tumor of cortical adenoma, pheochromocytoma, and adrenal metastasis. These 3 tumors are frequently encountered in daily practice and should be differentiated for their appropriate clinical management. For all tests, P < 0.05 indicated a statistically significant difference.

Results

Tables 2 to 4 summarize results.

“Entire” ADC and ratio of “non-solid” area to “entire” tumor

Because the P value of the F-test was 0.0073, we performed the Welch test. The average “entire” ADC was significantly higher for the benign group (1.35 ± 0.38 × 10⁻³ mm²/s) than the malignant group (1.01 ± 0.17 × 10⁻³ mm²/s) (P = 0.0001) and for pheochromocytomas (1.43 ± 0.44 × 10⁻³ mm²/s) than adrenal metastases (1.01 ± 0.16 × 10⁻³ mm²/s) (P = 0.038) but did not differ significantly between cortical adenomas and pheochromocytomas or adrenal metastases. Although the average ratio of “non-solid” area to “entire” tumor was significantly higher in pheochromocytomas than cortical adenomas (P = 0.009), it did not differ significantly between the benign and malignant groups, using the Student t-test (the P value of the F-test was 0.69.).

“Solid” ADC

Because the P value of the F-test was 0.064, we performed the Student t-test. There was no signifi-
Table 3. Average “entire,” “solid,” and “minimum” apparent diffusion coefficients (ADCs) and ratios of “non-solid” area to “entire” tumor in cortical adenomas, pheochromocytomas, and adrenal metastases

<table>
<thead>
<tr>
<th>Tumor</th>
<th>Entire</th>
<th>Solid</th>
<th>Minimum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cortical adenoma</td>
<td>1.28 ± 0.30 (0.76 to 2.17)</td>
<td>1.43 ± 0.44* (0.61 to 2.28)</td>
<td>1.01 ± 0.16 (0.81 to 1.14)</td>
</tr>
<tr>
<td>Pheochromocytoma</td>
<td>1.17 ± 0.30 (0.55 to 1.98)</td>
<td>1.09 ± 0.30 (0.53 to 1.62)</td>
<td>0.97 ± 0.18 (0.78 to 1.16)</td>
</tr>
<tr>
<td>Adrenal metastasis</td>
<td>0.94 ± 0.33 (0.14 to 1.98)</td>
<td>0.76 ± 0.32 (0.21 to 1.25)</td>
<td>0.72 ± 0.23 (0.47 to 0.98)</td>
</tr>
</tbody>
</table>

Data are average ± standard deviation. Numbers in parentheses represent the range of ADCs or ratios of “non-solid” area to “entire” tumor. The unit of ADC is ×10⁻³ mm²/s. *The average “entire” ADC was significantly higher in pheochromocytomas than adrenal metastases (P = 0.038). **The average “non-solid” area was significantly higher in pheochromocytomas than cortical adenomas (P = 0.009). The sizes of cortical adenomas were 2.36 ± 1.39 cm, of pheochromocytomas, 3.86 ± 1.39 cm, and of adrenal metastases, 2.93 ± 0.67 cm.

Table 4. “Entire,” “solid,” and “minimum” apparent diffusion coefficients (ADCs) in other adrenal tumors

<table>
<thead>
<tr>
<th>Tumor</th>
<th>Entire</th>
<th>Solid</th>
<th>Minimum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myelolipoma</td>
<td>1.36</td>
<td>0.74</td>
<td>0.53</td>
</tr>
<tr>
<td>Hemangioma</td>
<td>2.10</td>
<td>2.10</td>
<td>1.01</td>
</tr>
<tr>
<td>Cryptococcosis</td>
<td>0.75</td>
<td>0.69</td>
<td>0.40</td>
</tr>
<tr>
<td>Ganglioneuroma</td>
<td>1.74</td>
<td>1.42</td>
<td>0.91</td>
</tr>
<tr>
<td>Adrenocortical</td>
<td>0.91, 1.07</td>
<td>0.75, 1.07</td>
<td>0.59, 0.69</td>
</tr>
<tr>
<td>carcinoma*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malignant lymphoma</td>
<td>0.75</td>
<td>0.70</td>
<td>0.55</td>
</tr>
</tbody>
</table>

The unit of ADC is ×10⁻³ mm²/s. *The data of 2 tumors are listed side by side.

to be a cortical adenoma. This finding represents abundant intracytoplasmic lipid in clear cells, one constituent of a cortical adenoma. Because chemical shift MR imaging is more sensitive than unenhanced CT in detecting small amounts of fat, it may be more useful for diagnosing a cortical adenoma. However, lipid-poor adenomas cannot be diagnosed using these 2 methods. In such cases, the rate of washout after contrast enhancement can be used. On dynamic contrast-enhanced study, most cortical adenomas show strong enhancement in the early phase and less enhancement in the delayed phase. Pheochromocytomas and adrenocortical adenocarcinomas also enhance strongly in the early phase but are continuously enhanced until the delayed phase. Depending on the kind of primary tumor, many adrenal metastases may show delayed enhancement, which is termed low washout rate. However, there can be some overlap in washout rate between cortical adenomas and other adrenal tumors. In addition, because adrenal metastases from hepatocellular carcinoma and renal cell carcinoma may contain scant fat, it is not always easy to differentiate adrenal tumors using only the previously described diagnostic methods. A new diagnostic aid, such as a complimentary imaging parameter, is desirable.

Differentiation between benign and malignant tumors and prediction of histological subtype are very important in adrenal tumors as well as other tumors.

Although several studies have compared ADCs of adrenal tumors, most have found the ADC of little value in differentiating adrenal tumors because there is no significant difference between benign and malignant tumors or among the histological subtypes. However, we considered 2 problems with the previous studies—that the methods of ADC measurement were obscure and that most cases of adrenal tumor were finally diagnosed clin-
**Fig. 1.** A 39-year-old woman with left adrenal pheochromocytoma (benign).\[A\] The tumor was described as a marginally enhanced mass on gadolinium-enhanced fat-suppressed T1-weighted image (arrow). The central hypointense area of the tumor represents hemorrhage, degeneration, or necrosis (arrowhead). \[B\] On diffusion-weighted image with a b-factor of 1,000, the tumor’s margin was hyperintense (arrow), whereas the central region was hypointense (arrowhead). \[C\] A large oval region of interest (ROI) (large circle) was placed at the “entire” region, and the measured apparent diffusion coefficient (ADC) was $2.28 \times 10^{-3}$ mm$^2$/s (“entire” ADC). Furthermore, a small oval ROI (small circle) was placed at the “solid” region, which was consistent with an enhancing area at the margin of the tumor. The measured ADC was $1.34 \times 10^{-3}$ mm$^2$/s (“solid” ADC). Because the ADC of the “solid” region was homogenous, the “minimum” ADC was also decided as $1.34 \times 10^{-3}$ mm$^2$/s.

**Fig. 2.** A 72-year-old woman with left adrenal metastasis from lung cancer.\[A\] The tumor was described as a mildly enhanced mass on gadolinium-enhanced fat-suppressed T1-weighted image (arrows). \[B\] On diffusion-weighted image with a b-factor of 1,000, the tumor was entirely hyperintense (arrow). \[C\] An oval region of interest (ROI) (large circle) was placed at the “entire” region, and the measured apparent diffusion coefficient (ADC) was $1.16 \times 10^{-3}$ mm$^2$/s (“entire” ADC). Because this tumor was composed of only solid components, the ADC of the “solid” region was considered to be the same as that of the “entire” region (“solid” ADC). On the other hand, a small oval ROI (small circle) was placed in an area showing the lowest ADC within the “solid” region (“minimum” ADC). The “minimum” ADC was $0.98 \times 10^{-3}$ mm$^2$/s.
ically. In this study, we re-examined the diagnostic potential of the ADC for differentiating pathologically proven adrenal tumors and employed 3 methods of ADC measurement—placing an ROI in the “entire” area of a tumor, in its “solid” region, and in an area showing the lowest ADC within the “solid” region. As a result, the average ADC in the “entire” tumor area was significantly higher for the benign than malignant group, but the average ADC of the “solid” area did not differ significantly between the 2 groups. Considering that the average ADC in the “entire” tumorous regions in pheochromocytomas was significantly higher than in adrenal metastases, we speculated that the higher ADC of the benign group might be principally due to remarkable necrosis, hemorrhage, and degeneration in pheochromocytomas. In fact, 12 of 14 pheochromocytomas were classified as benign in this study. However, because the average “non-solid” area did not differ significantly between the benign and malignant groups, higher “entire” ADC of benign group can be considered dependent on the condition of necrosis, hemorrhage, and degeneration. This result might be obtained incidentally in this population. The absence of difference in “solid” and “minimum” ADCs between benign and malignant groups or among 3 popular histological subtypes (cortical adenoma, pheochromocytoma and adrenal metastasis) suggests that it is difficult to describe difference in tumor cell and histological architecture of adrenal tumors using the ADC. In daily practice, radiologists are especially asked to differentiate between cortical adenoma and adrenal metastasis. The ADC may be of less clinical value in such a situation, as several reports have concluded.9–12

Adrenal tumors, except cortical adenoma, pheochromocytoma, and adrenal metastasis, may show characteristic ADC values. Unfortunately, we did not analyze statistics because of our small number of cases of each tumor. As described in the Results, the ADC values can be high for hemangiomas as a result of abundant fluid in dilated vascular space and for ganglioneuromas because of remarkable myxomatous change. On the other hand, the ADCs of malignant lymphoma and cryptococcosis representative of granulomatous lesion should be low because of high cellular density and fibrosis. The ADC of myelolipoma may depend on the amount of myeloid cells included; a mass formation composed of myeloid cells probably shows low ADC due to high cellular density. It seemed that the ADC of adrenocortical carcinoma was close to that of adrenal metastasis. In such cases, the ADC may give additional information for differential diagnosis of adrenal tumors.

This study has several limitations. First, we had a relatively small number of cases of each tumor because we evaluated only pathologically proven tumors scanned on 1.5T MR imaging. Second, most cortical adenomas were functionally active, and it is unclear if the ADC differs between non-functional and functional adenomas. Third, the primary lesions of adrenal metastases were diverse. Radiological findings of metastatic tumors should be similar to those of primary lesions. Although we speculated that the ADCs of adrenal metastasis would be diverse, we observed no gross difference among the 6 tumor types in this study.

Conclusion

The higher “entire” ADC value of the benign group, which might be obtained incidentally, can be considered dependent on the condition of necrosis, hemorrhage, and degeneration. ADC measurement of the “solid” region of tumors was not useful for differentiating in pathologically proven adrenal tumors.

Acknowledgments

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References


