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Original Article

MR Imaging of Renal Cell Carcinoma: Associations among Signal Intensity, Tumor Enhancement, and Pathologic Findings

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The purpose of this study was to compare the MR characteristics of renal cell carcinomas against histologic findings and to assess the correlations among signal intensity, tumor enhancement, and pathologic findings. Fifty-four patients (56 lesions) were examined by MR imaging and then underwent partial or radical nephrectomy. The pathologic diagnosis of all lesions was renal cell carcinoma. All MR examinations were performed as dynamic studies using the same 1.5-T scanner. MR characteristics were compared against pathologic findings after resection, and the correlations among signal intensity, tumor enhancement, and pathologic findings were then assessed. A significant correlation was observed between tumor grade and tumor enhancement, with G3 lesions tending to show little enhancement. Regardless of the histologic classification, G3 tumors were found to contain highly heterotypic cancer cells and very few vessels by histopathologic examination. No significant correlations were noted between the other MR characteristics and pathologic findings. Renal cell carcinomas showing little enhancement tend to be highly malignant lesions based on the pathologic findings. Special consideration is required for these tumors with regard to the selection of surgical intervention and follow-up observation.

Key words: kidney, kidney neoplasms, MR, diagnosis, grade

Over the past several decades, advances in various diagnostic imaging modalities have made it possible to detect small, asymptomatic renal cell carcinomas as well as large, symptomatic tumors. Most renal cell carcinomas are treated by surgical resection, and diagnostic imaging is very important for selecting the appropriate therapy and for assessing the patient's prognosis and complications [1-3].

Many studies have reported the usefulness of MR imaging for the evaluation of renal cell carcinoma [4-14]. Tumor size, perinephric extension, venous invasion, and metastasis can be evaluated for the staging of renal cell carcinoma. Some studies have demonstrated that even pathologic findings can be estimated by evaluating intratumor characteristics in MR images [6, 15]. Other studies have identified characteristic MRI findings and prognoses for certain pathologic classifications [16-22].

However, a systematic description of the correlations among tumor enhancement, the signal intensity of renal cell carcinomas on dynamic MRI, and pathologic findings in accordance with the present WHO classification has not, to our knowledge, been presented. Most renal cell carcinomas show a high degree of heterogeneity due to intratumor hemorrhage and necrosis and the presence of

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cystic components; moreover, the tumor component shows variable signal intensity and enhancement in MRI studies, and it is difficult to evaluate and systematically classify these characteristics.

The purpose of the present study was to compare the MR characteristics of renal cell carcinomas against histologic findings and to assess the correlations among tumor enhancement, signal intensity, and pathologic findings.

Materials and Methods

Patient selection. Fifty-four patients (43 men and 11 women; 25–85 years of age; mean age, 61 years; sequential cases) who had undergone MR examination between June 1996 and June 2000 were included in this study. All patients subsequently underwent partial or radical nephrectomy and were diagnosed as having renal cell carcinoma based on the findings of pathologic examination. Before 1998, pathologic findings were evaluated in accordance with former classification systems, but all findings were later reviewed in accordance with the current WHO classification. Patients who had not undergone surgical resection, but had undergone biopsy alone, were excluded from this study. The maximum time between MR imaging and nephrectomy was 30 days.

MR imaging technique. All MR examinations were performed using a 1.5-T scanner (Magnetom VISION; Siemens, Erlangen, Germany) with a phased-array coil. The sequences used included the following: T1-weighted breath-hold axial fast low-angle shot (TR range/TE range, 161/4.1; flip angle, 80) (the first 31 patients), T1-weighted breath-hold axial fast low-angle shot (TR/TE, 152/5.2; flip angle, 80) (the next 24 patients), and T2-weighted breath-hold axial turbo spin echo (TR/TE, 4900/138; echo train length, 29) (all patients). After dynamic studies were performed, T1-weighted images were obtained using the same parameters as before injection. All sequences were acquired using 16–18 sections and a slice thickness of 8 mm. The matrix was 128 × 256 and the field of view was 330 mm.

Using an MR-compatible power injector (Sonicshot50; Nemotokyorindo, Tokyo, Japan), 0.1 mmol/kg of gadopentetate dimeglumine (Magnevist; Schering, Berlin, Germany) was administered by bolus injection, followed by a saline flush of 12 ml. T1-weighted imaging was performed at 40 sec (early phase) and 120 sec (late phase).

Image evaluation and statistical analysis. All MR imaging sequences were evaluated by 2 radiologists (T.Y., T.K.) who were blinded to the pathological diagnosis, and individual opinions were recorded. During each examination, the number, size, and location of the renal cell carcinomas were determined and the intratumor characteristics were evaluated. In the assessment of intratumor characteristics, the following factors were evaluated: intensity of solid components of the tumor on T1-weighted images (T1WI) and T2-weighted images (T2WI), tumor enhancement in the early and late phases, and the presence of necrosis and hemorrhage in the tumor. In the present study, the solid component was defined as the part of the tumor containing no obvious necrosis or hemorrhage. For both T1- and T2-weighted sequences, the signal intensity of the renal cortex was used as a reference for determining the signal intensity of the solid component: "low intensity" when lower than that of the cortex, "isointensity" when similar, and "high intensity" when higher. The enhancement pattern was classified by comparison against cortical enhancement into the following 3 levels: (++), good enhancement; (+), mild enhancement; and (+/−), no or very little enhancement. If enhancement of the solid component was similar to that of the cortex, the tumor was classified as (++); if no or very little enhancement was observed, the tumor was classified as (+/−); and if enhancement was intermediate between (++) and (+/−), the tumor was classified as (+). In some lesions the solid component showed several patterns; in such cases the predominant pattern was used for classification.

The kappa statistic was applied to evaluate interobserver agreement in the MR findings. Tumor characteristics on MR images were compared against pathologic findings after resection. The pathologic findings included classification and nuclear grade. The pathologic classification was determined in accordance with the current WHO classification, and the nuclear grade was determined in accordance with the Japanese classification system [23]. When the tumor cell nucleus was smaller than a normal tubular cell nucleus, the tumor was classified as grade 1 (G1); when similar as grade 2 (G2); when larger as grade 3 (G3); and when evaluation of the tumor cell nucleus was impossible it classified as grade X (Gx). When the tumor cell nuclei were of more than one size, the predominant grade was chosen.

Histopathological diagnosis was performed in all cases using H.E. staining. Colloidal iron staining was added when chromophobe cell ca. was suspected. The final

diagnosis was based on the dominant cell type.

The correlations between MR characteristics and pathologic findings were evaluated. Data were tested for significance using the chi-square and Fisher's exact tests for individual and combined variables in order to identify the characteristics that might be useful for the evaluation of renal cell carcinomas.

Results

Fifty-six renal cell carcinomas of various types were identified in the 54 patients. Fifty-two patients had a solitary lesion. Two patients had 2 lesions, one with 2 renal cell carcinomas in the left kidney and the other with one in each kidney. Twenty-four lesions were in the right kidney and 32 were in the left kidney. The diameter of the lesions ranged from 15 to 200 mm (mean, 59 mm). The interobserver agreement for tumor intensity on MR images and tumor enhancement was good: $\kappa = 0.75$ for tumor intensity and $\kappa = 0.67$ for tumor enhancement.

MRI findings. The findings for the signal intensity of the 56 renal cell carcinomas were as follows: in T1WI, low intensity in 26, isointensity in 24, and high intensity in 6; and in T2WI, low intensity in 15, isointensity in 15, and high intensity in 26. The tumor enhancement findings were as follows: in the early phase, (++) in 23, (+) in 28, and (+/−) in 5; and in the late phase, (++) in 3, (+) in 48, and (+/−) in 5.

Pathologic findings and statistical significance. The pathologic tumor grades were as follows: G1 in 11, G2 in 41, G3 in 4, and Gx in 0. The correlation between grade and signal intensity in MR images was not significant ($P > 0.05$) (Table 1). A significant correlation was observed between G3 and "no or very little enhancement" in both dynamic early- and late-phase images ($P = 0.036$) (Table 2). G3 renal cell carcinomas showed a tendency toward little tumor enhancement.

The pathologic findings with regard to tumor classification were as follows: 43 clear cell carcinomas, 6 granular cell carcinomas, 0 chromophobe cell carcinomas, 1 spindle cell carcinoma, 0 renal cell carcinomas originating in a cyst, 3 cystic renal cell carcinomas, and 3 papillary renal cell carcinomas. Only one case of spindle cell carcinoma was seen in our series: a pT3b tumor that showed low intensity in T1WI and isointensity in T2WI, exhibited little enhancement, and was judged to be grade 3 (Fig. 1). Three cases had papillary renal cell carcinomas: two that exhibited little enhancement, one judged to be grade 3, and none that showed high intensity in T2WI (Fig. 2). Forty-three cases (77%) had clear cell carcinomas (Figs. 3, 4). Many clear cell carcinomas showed high intensity in T2WI (58%) and exhibited tumor enhancement (98%) (Table 3). However, no significant correlations were seen between pathologic classification and grade (Table 4). Statistical analysis was insufficient to evaluate the correlations between MR characteristics and pathologic classification, because some pathologic classifications had few cases (Table 3).

Table 1 Correlation between grade and tumor intensity

	Tumor intensity					
	T1WI			T2WI		
	Low	Iso	High	Low	Iso	High
G1	8	3	0	3	1	7
G2	16	20	5	11	12	18
G3	2	1	1	1	2	1

Table 2 Correlation between grade and tumor enhancement

	Tumor enhancement					
	Early phase			Late phase		
	(++)	(+)	(+/−)	(++)	(+)	(+/−)
G1	6	4	1	0	10	1
G2	16	23	2	2	37	2
G3	1	1	2	1	1	2

Histopathologic examination. Microscopically, the 4 cases classified as G3 and the 5 cases classified as (+/−) were evaluated in detail. Two cases classified as G3 were (+/−), one with spindle cell carcinoma and the other with papillary renal cell carcinoma. The spindle cell ca. was solid and showed congestion with fusiform tumor cells, poor vascularity in an irregular distribution, and no evidence of sinusoidal vessels. The other 2 cases classified as G3 had clear cell carcinomas: one with a heterotypic lesion with large nuclei, stroma, and rare vessels and the other with a spindle cell component (Fig. 5). These were "atypical" clear cell carcinomas. Two cases classified as (+/−) were G2: one with an "atypical" clear cell carcinoma and the other with a granular cell carcinoma. The granular cell ca. showed a predominantly solid pattern with poor vascular growth and occasional mitoses. The remaining

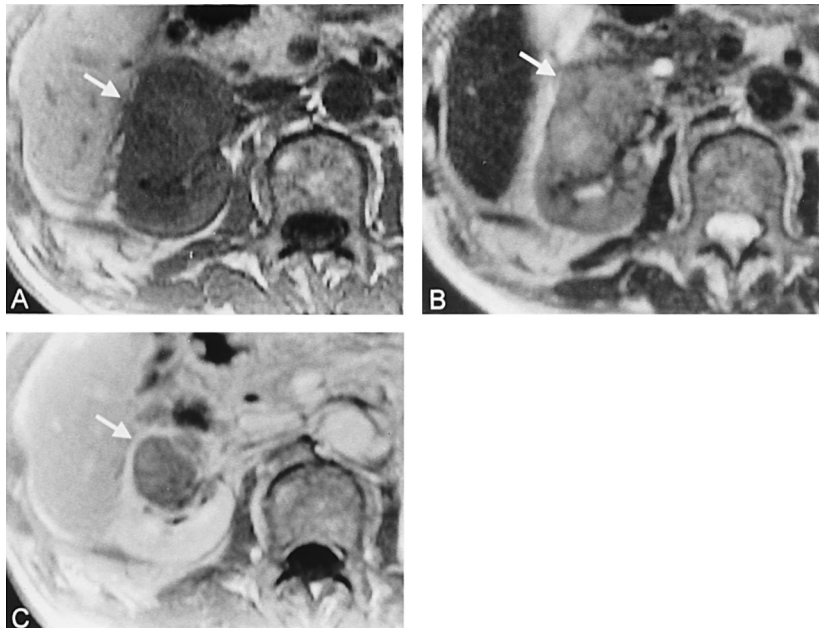

Fig. 1 A 77-year-old man with spindle cell carcinoma in the right kidney (pT3b, G3). This was the only case of spindle cell carcinoma in the present study. (**A**) In a T1-weighted image, the tumor shows low intensity (arrow). (**B**) In a T2-weighted image, the tumor shows isointensity (arrow). (**C**) In a dynamic study early-phase image, the tumor shows very little enhancement (arrow).

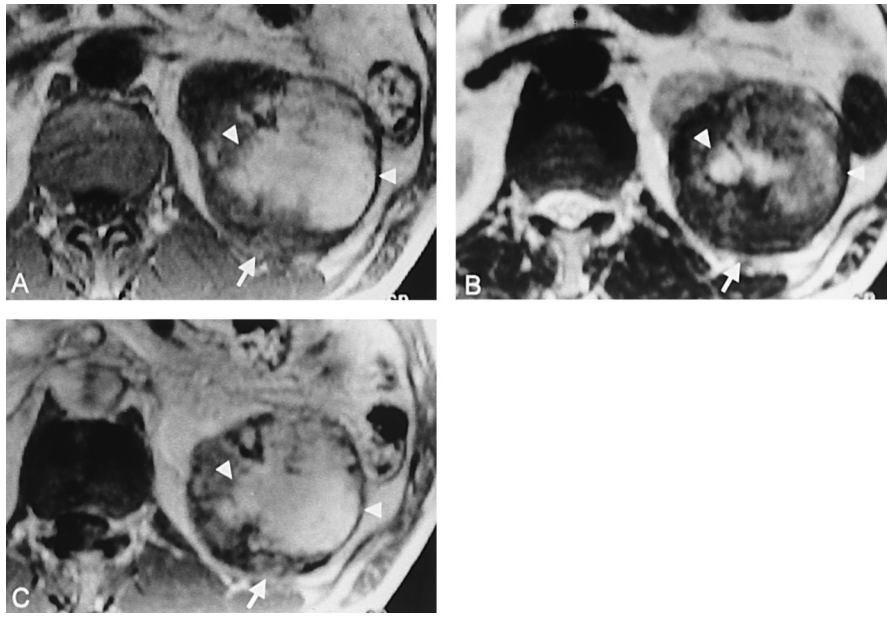

Fig. 2 A 66-year-old man with papillary cell carcinoma. (**A**) In a T1-weighted image, the tumor component shows high intensity (arrow). Bleeding is seen in the center of the tumor (this component shows high intensity in both T1-weighted and T2-weighted images, and no enhancement) (arrowhead). (**B**) In a T2-weighted image, the tumor component shows low intensity (arrow). (**C**) In a dynamic study early-phase image, the tumor component shows little enhancement (arrow).

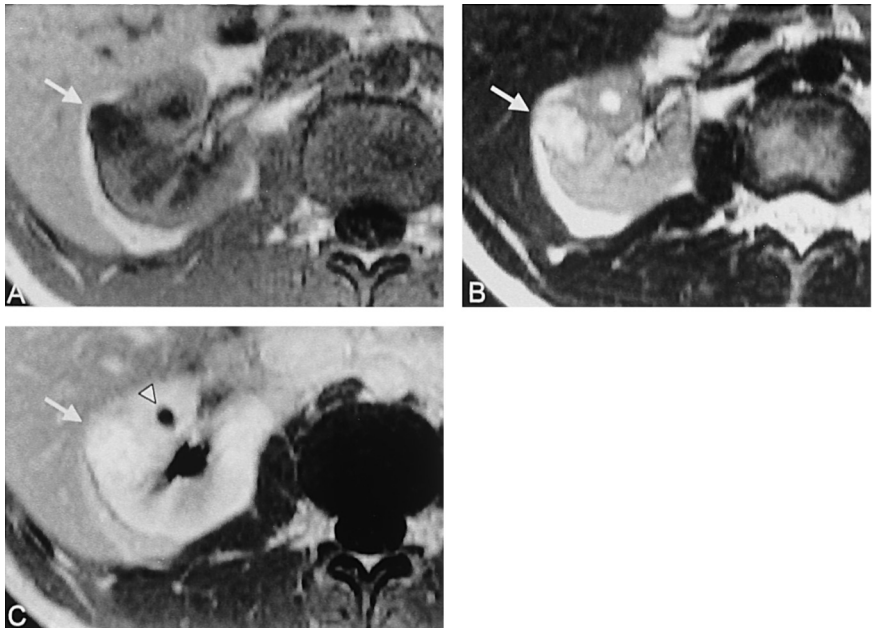

Fig. 3 A 30-year-old man with clear cell carcinoma in the right kidney. This is a "typical" renal cell carcinoma. (**A**) In a T1-weighted image, the tumor shows low intensity (arrow). (**B**) In a T2-weighted image, the tumor shows high intensity (arrow). (**C**) In a dynamic study early-phase image, the tumor shows good enhancement (arrow). A renal cyst is seen (arrowhead).

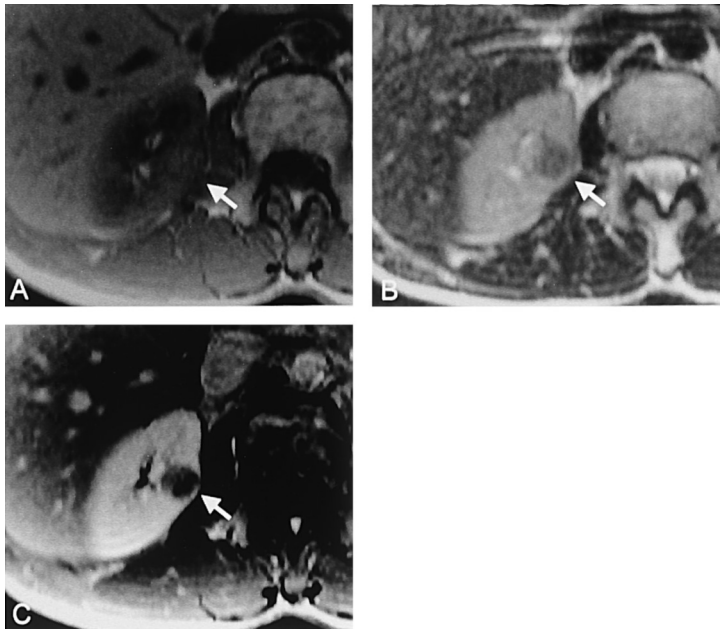

Fig. 4 A 59-year-old man with clear cell carcinoma. This is a case of clear cell carcinoma showing low intensity in T2-weighted images and very little enhancement. (**A**) In a T1-weighted image, the tumor shows isointensity (arrow). (**B**) In a T2-weighted image, the tumor shows low intensity (arrow). (**C**) In a dynamic study early-phase image, the tumor shows very little enhancement (arrow).

Table 3 Correlation between classification and tumor intensity, enhancement

	Tumor intensity						Tumor enhancement					
	T1WI			T2WI			Early phase			Late phase		
	Low	Iso	High	Low	Iso	High	(++)	(+)	(+/−)	(++)	(+)	(+/−)
Clear	22	18	3	9	9	25	23	19	1	2	40	1
Granular	0	4	2	4	2	0	0	5	1	0	5	1
Chromophobe	0	0	0	0	0	0	0	0	0	0	0	0
Spindle	1	0	0	0	1	0	0	0	1	0	0	1
Origin in cyst	0	0	0	0	0	0	0	0	0	0	0	0
Cystic RCC	2	1	0	0	2	1	0	3	0	1	2	0
Papillary	1	1	1	2	1	0	0	1	2	0	1	2

Table 4 Correlation between classification and grade

	Grade		
	G1	G2	G3
Clear	9	32	2
Granular	0	6	0
Chromophobe	0	0	0
Spindle	0	0	1
Origin in cyst	0	0	0
Cystic RCC	1	2	0
Papillary	1	1	1

Fig. 5 (A) A 75-year-old man with clear cell carcinoma (G1). The microscopic findings for the tumor component are shown (bar indicates 100 μm, H.E. stain). The clear cell carcinoma shows similar cellular sizes, similar nuclear sizes, and a large amount of clear cytoplasm. This was called the alveolar type in the former classification system. Sinusoidal capillaries are abundant, which is why the tumor shows good enhancement. This case can be considered a typical clear cell carcinoma. (B) A 57-year-old woman with clear cell carcinoma (G3). The microscopic findings for the clear cell component are shown (bar indicates 100 μm, H.E. stain). The clear cell carcinoma shows various cellular sizes, various nuclear sizes, and varying amounts of clear cytoplasm. Capillaries and connective tissue are seen, but no sinusoidal capillaries are observed, which means that blood flow is poorer than in the case described in (A). This case is an atypical clear cell carcinoma compared with the case described in (A).

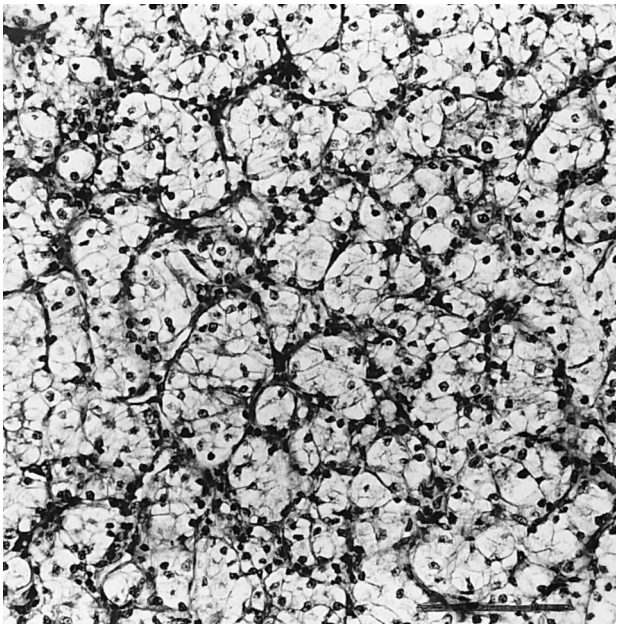

Fig. 5A

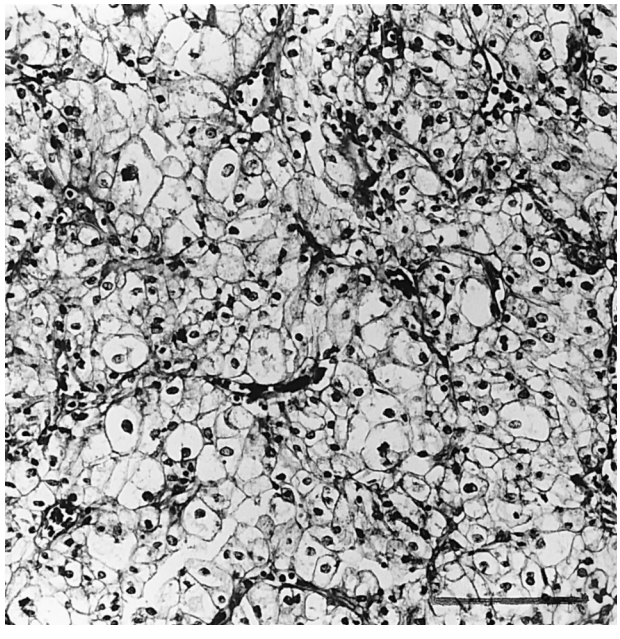

Fig. 5B

(+/−) case was G1, and consisted of a papillary renal cell carcinoma. The histopathological findings indicated that higher-grade tumors were likely to have poor vascularity.

Discussion

Seventy-seven percent of the renal cell carcinomas in the present study were clear cell carcinomas. Some studies have reported that the detection of intratumor lipid in a renal cell carcinoma suggests that it is a clear cell carcinoma [16, 17]. However, clear cell carcinomas have shown variable signal intensity in MRI studies, as well as various stages and grades, and there are no characteristic patterns of these features. Therefore, even if a tumor is suspected to be a clear cell carcinoma, its malignant potential and grade cannot be accuraPhoney estimated. Previous studies have reported that spindle cell carcinomas are highly malignant [18, 19]. There was only one spindle cell carcinoma in the present study, and it was a highly malignant tumor (pT3b, G3). This tumor showed low- to isointensity and exhibited little enhancement in MR images (Fig. 1). Papillary renal cell carcinomas tended to show low intensity in T2WI and to exhibit little enhancement in our series. These results are in agreement with the literature [20, 21]. However, it is not uncommon for clear cell carcinomas to show low- to isointensity in MRI studies, and tumors with little enhancement are occasionally encountered (2% of cases our series) (Fig. 4). In addition, previous studies have reported that chromophobe cell carcinomas tend to exhibit little tumor enhancement, although there were no cases of such tumors in our series [22]. These findings indicate that it is impossible to identify the tumor as a spindle cell carcinoma, a papillary renal cell carcinoma, or a chromophobe cell carcinoma when the tumor shows low intensity or exhibits little enhancement in MRI studies.

Based on the above, previous studies have shown that MRI findings can be suggestive of clear cell carcinoma but do not permit the malignant potential of the lesion to be determined. On the other hand, MRI findings cannot suggest other classifications for which the malignant potential is known, such as spindle cell carcinoma. This indicates that the malignant potential of renal cell carcinomas cannot be evaluated by MRI. However, we were able to establish a correlation between grade and tumor enhancement of renal cell carcinomas, with tumors exhibiting little enhancement tending to be high-grade lesions. Previous studies have reported that high-grade renal cell carcinomas are highly malignant and have a poor prognosis [24, 25]. We think that tumors showing little enhancement should be given special consideration with regard to the selection of surgical intervention and follow-up observation, because they tend to be highly malignant and to have poor prognosis. Regardless of the histologic classification, G3 tumors were found to contain highly heterotypic cancer cells and very few vessels by histopathologic examination. Tumors exhibiting no to very little enhancement showed the same tendency. Presumably, tumor growth is too rapid to permit sufficient vessels to develop, and as a result, highly malignant renal cell carcinomas may tend to show little enhancement. No other significant correlations were observed between MRI characteristics and histopathologic findings in the present study.

The present study suffers from a number of limitations. A definitive pathological diagnosis cannot be established based on MR imaging findings. This can only be conclusively determined by performing surgical resection. Nevertheless, we feel that attempting to predict the characteristics of a tumor as accurately as possible by performing non-invasive imaging diagnosis, before undertaking invasive procedures, is of significant value. It so happened that there were no cases of chromophobe cell carcinoma in our series. This may be one reason for our results. Statistical analysis was insufficient to evaluate the correlations between MR characteristics and pathologic classification, because some pathologic classifications had few cases. Some highly malignant renal cell carcinomas were excluded-*e.g.*, lesions in patients who did not undergo surgery due to metastases or poor general condition. A pathologic diagnosis could not be obtained in these cases, and even if autopsy were performed, it would be impossible to compare MR imaging and pathologic findings due to the delay between the 2 examinations in most of these cases.

In conclusion, renal cell carcinomas showing little enhancement tend to be high-grade lesions. These tumors should be given special consideration with regard to the selection of surgical intervention and follow-up observation, because they tend to be highly malignant and to have a poor prognosis. The histopathological findings indicated that higher-grade tumors were likely to have poor vascularity. No other significant correlations were seen between MRI and histopathologic findings.

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