TÜBİTAK

Original Article

Turk J Med Sci
2010; 40 (1): 31-38
© TÜBİTAK
E-mail: medsci@tubitak.gov.tr
doi:10.3906/sag-0904-53

Can dynamic multidetector computerized tomography detect renal cell carcinoma subtypes?

Ayhan DİRİM[1], Nihal TUTAR[2], Levent PEŞKİRCİOĞLU[1], Hüseyin ÇELİK[1], Mehmet İlteriş TEKİN[1], Hakan ÖZKARDEŞ[1]

Aim: To evaluate the efficacy of the biphasic and triphasic dynamic multidedector computerized tomography (MDCT) in the preoperative prediction of histological subtypes of renal cell carcinoma (RCC).

Materials and methods: The preoperative dynamic MDCT findings of 51 patients with renal mass who had undergone nephrectomy were reviewed retrospectively. Twenty-five of the patients had biphasic (portal and excretory) and 26 had triphasic (arterial, portal, and excretory) MDCT images. Tumor size, presence of calcification, tumor-aorta attenuation values in all phases and homogeneicity of the tumor were noted for every patient. In heterogeneous tumors, the minimum and maximum attenuation values were noted to determine the extent of heterogeneicity. These data were compared for histopathological subtypes of the tumors.

Results: In 8 patients, calcifications were detected in the mass although there were no significant differences among tumor subtypes with regard to the presence of calcification. In 33 patients the tumor was hypervascular with 24 clear type and clear type RCC showed more prominent contrast enhancement than papillary RCC. The enhancement degree showed no significant difference among other tumor subtypes. Moreover, when biphasic and triphasic computed tomography (CT) findings were compared, the positive predictive value of triphasic CT in detecting hypervascular clear tumors was greater (17/18; 94.4% versus 7/11; 63.6%).

Conclusion: The dynamic MDCT technique appears to be useful in preoperative evaluation of renal masses suspected of being malignant and may also provide information about the histopathological subtype of RCC.

Key words: Multidedector computerized tomography, renal cell carcinoma, renal cancer subtypes

Dinamik multidedektör komputerize tomografi renal hücreli kanser subtiplerini belirleyebilir mi?

Amaç: Renal hücreli kanser (RHK) histolojik subtiplerinin preoperatif tahmininde bifazik ve trifazik dinamik multidedektör komputerize (bilgisayarlı) tomografinin (DMKT) etkinliğini değerlendirmek.

Yöntem ve gereç: Renal kitle nedeniyle nefrektomi yapılan 51 hastanın preoperatif dinamik MDKT bulguları retrospektif olarak değerlendirildi. Yirmibeş olguda bifazik (portal ve ekskretuar), 26 olguda ise trifazik (arteryal, portal, ve ekskretuar) MDKT görüntüleri elde edildi. Her olgunun tümör çapı, kalsifikasyon varlığı, her fazdaki tümör-aorta atenüasyon değerleri ve tümör homojenitesi belirlendi. Heterojen tümörlerde heterojenite farkı/derecesini belirlemek için minimum ve maksimum atenüasyon değerleri not edildi. Bu veriler tümörün histopatolojik subtipleriyle karşılaştırıldı.

Bulgular: Sekiz olguda kitlede kalsifikasyon saptandı ancak kalsifikasyon varlığı ile tümör subtipleri arasında bir farklılık sözkonusu değildi. Otuzüç olguda tümör hipervaskülerdi. Bu olguların 24'ü şeffaf hücreli tipteydi ve şeffaf hücreli tip papiller tipe göre daha belirgin kontrastlanma göstermekteydi. Diğer tümör tipleri arasında kontrastlanma derecesi açısından farklılık izlenmedi. Yine bifazik ve trifazik tomografi bulguları karşılaştırıldığında trifazik tomografinin hipervasküler şeffaf hücreli tümörü saptamadaki pozitif prediktif değeri bifazikten yüksekti (17/18; % 94,4'e karşın 7/11; % 63,6).

Sonuç: Dinamik MDKT tekniği malignite şüphesi olan renal kitlelerin preoperatif değerlendirmesinde yararlı olması yanında RHK'in histopatolojik subtiplerinin belirlenebilmesi konusunda da bilgi verebilir.

Anahtar sözcükler: Multidedektör komputerize tomografi, renal hücreli karsinom, renal kanser subtipleri

Received: 30.04.2009 – Accepted: 15.10.2009

[1] Department of Urology, Faculty of Medicine, Başkent University, Ankara - TURKEY
[2] Department of Radiology, Faculty of Medicine, Başkent University, Ankara - TURKEY

Correspondence: *Ayhan DİRİM, Department of Urology, Faculty of Medicine, Başkent University, 5. Sokak, No: 48, 06490 Bahçelievler, Ankara - TURKEY*
E-mail: drayhan_dirim@yahoo.com

Introduction

Computed tomography (CT) remains to be the gold standard modality for diagnosing and staging renal neoplasms, and the wide use of CT for abdominal imaging has led to earlier detection of many small renal neoplasms (1-3). Preoperative estimation of the tumor subtype may help to choose the appropriate treatment modality and provide information for predicting postoperative prognosis. Papillary RCC are associated with a better prognosis than other cell types at a similar stage, but papillary renal cancers are more frequently multiple, bilateral, and can be hereditary (4, 5). These characteristics of papillary RCC may let the physician to plan a partial nephrectomy in selected patients if it can be detected preoperatively by MDCT.

Materials and methods

Patients

The dynamic MDCT findings of 51 patients who had undergone radical (n = 41) or partial (n = 10) nephrectomy between May 2005 and October 2007 because of renal mass were reviewed retrospectively. Twenty-five of the patients had biphasic (portal and excretory) and 26 had triphasic (arterial, portal, and excretory) MDCT images. Tumor size, presence of calcification and necrosis, and tumor–aorta attenuation values in all phases and homogeneicity of the tumor were recorded for every patient. In heterogeneous tumors the minimum and maximum attenuation values were recorded to determine the extent of heterogeneicity. These data were compared for histopathological subtypes of tumors.

CT examination

Triphasic renal CT was performed on either a Somatom Plus 4 (Siemens Medical Systems, Germany) or a Volume Zoom (Siemens Medical Systems, Germany) 16 detector scanner. Oral contrast agent was administered to all patients. Each patient was scanned before intravenous contrast administration for precontrast imaging. Then arterial, portal, and excretory phase images were obtained. Delay time was 20 seconds for the arterial phase, 60 seconds for the portal phase, and 5 min for the excretory phase images. Slice thickness was 5 mm for all phases. Nonionic contrast media (150 mL) was injected using a mechanical injector at a rate of 4.5 mL/sec. Axial CT images were reconstructed after the scanning had finished in axial and coronal planes using the multiplanar reconstruction (MPR) technique in each patient.

Statistical analysis

The Kruskal Wallis analysis of variance and chi-square tests were used as statistical methods. A P value of 0.05 was accepted as cut-off for statistical significance. The analyses were done using SPSS 11.0 for Windows.

Results

Patients

There were 22 female and 29 male patients with a mean age of 59.8 years (range: 34-80). The male-to-female ratio was 1.07/1 in clear cell RCC, 5.5/1 in papillary RCC, and 1/1 in chromophobe cell RCC. While 2 patients with oncocytoma and 2 patients with angiomyolipoma (AML) were females, the patient with leiomyosarcoma was male. Neither age nor sex significantly differed among tumor subtypes (P = 0.771, P = 0.131, respectively).

Pathological findings

The histopathologically detected tumor subtypes were noted as 29 clear cell RCC; 13 papillary RCC; 4 chromophobe cell RCC; 2 oncocytomas; 2 angiomyolipomas; and 1 leiomyosarcoma. There was no significant difference among tumor subtypes in terms of tumor grades (P = 0.952).

CT findings

The mean tumor size was 5.06 cm (range: 1-19). Distribution of tumor sizes according to histological subtypes is shown in Table 1. There was no significant difference between tumor subtypes with respect to tumor size (P = 0.341)

Table 1. The distribution of tumor size according to histological subtypes.

	n	Mean tumor size (range) (cm)
Clear cell RCC	29	4.9 (1.8-12)
Papillary RCC	13	4.9 (1.2-19)
Chromophobe cell RCC	4	8.6 (2-15)
Oncocytoma	2	3.1 (1.3-5)
Angiomyolipoma	2	5.9 (1.8-10)
Leiomyosarcoma	1	10

Tumor densities during precontrast, arterial, portal, and late phases (hypodense, isodense, and hyperdense) did not show any significant difference according to tumor subtypes (P = 0.560, P = 0.289, P = 0.459, and P = 0.157, respectively).

Calcification was detected in 8 cases. These calcifications were located centrally in 4, peripherally in 2, and both centrally and peripherally in 2 patients. Presence of calcification did not show any significant difference in terms of tumor subtypes (P = 0.263).

Necrosis was observed in 22 patients (centrally in 17, peripherally in 1, and both centrally and peripherally in 4 patients). Presence of necrosis did not differ in terms of tumor subtypes (P = 0.369).

On MDCT scanning, homogeneus contrast enhancement was detected in 19 cases but there was no difference between subtypes according to the contrast enhancement pattern (P = 0.093) (Table 2). In heterogeneous tumors, the degree of heterogeneicity did not differ between tumor subtypes in each phase (Table 3).

In 33 patients, the tumor was hypervascular and clear type RCC (Figure 1) showed more prominent contrast enhancement than papillary RCC (Figure 2). The mean maximum enhancement was 104.6 ± 48.5 Hounsfield Units [HU] (30-210 HU) in clear cell tumors whereas it remained at 64.6 ± 40.8 HU (25-183 HU) in papillary RCC (P = 0.014). The enhancement degree showed no significant difference among other tumor subtypes (P > 0.05). The histological subtypes of 33 hypervascular masses on CT were clear cell RCC in 24 patients; chromophobe in 3, papillary in 2, oncocytoma in 2, AML in 1, and leiomyosarcoma in 1 case.

When the biphasic and triphasic CT findings were compared, the positive predictive value of triphasic CT in detecting hypervascular clear tumors was greater (17/18; 94.4% versus 7/11; 63.6%). The attenuation and enhancement values of each mass are shown in Table 4.

Table 2. The enhancement patterns according to histopathological subtypes.*

Enhancement Pattern	Tumor size (cm)	Histopathological Subtypes				
		Clear (n = 29)	Papillary (n =13)	Chromophobe (n = 4)	Oncocytoma (n = 2)	AML (n = 2)
Homogeneous		7	6	1	1	0
Heterogeneous	≤5	11	2	0	1	1
Total		18	8	1	2	1
Homogeneous		2	1	0	0	1
Heterogeneous	>5	9	4	3	0	0
Total		11	5	3	0	1

*The only case of leiomyosarcoma (heterogeneous) is not shown. AML = Angiomyolipoma

Table 3. The degree of heterogeneicity of RCC subtypes according to CT phases.

	Degree of Heterogeneicity					
	Clear cell RCC		Papillary RCC		Chromophobe RCC	
	biphasic (n = 6)	triphasic (n = 14)	biphasic (n = 4)	triphasic (n = 2)	biphasic (n = 1)	triphasic (n = 2)
Precontrast	19.1 ± 18.5	16.4 ± 7.9	22.5 ± 12	11.5 ± 4.9	7	18.9 ± 12.7
Arterial		65.7 ± 37.8		25.5 ± 19		24.7 ± 14.1
Portal	99.8 ± 38.5	90.3 ± 42	46.2 ± 24.5	110 ± 70.7	70	76.4 ± 45.2
Excretory	44.6 ± 5	50 ± 22.9	34 ± 22.6	32.6 ± 4.9	37	56.5 ± 31.6

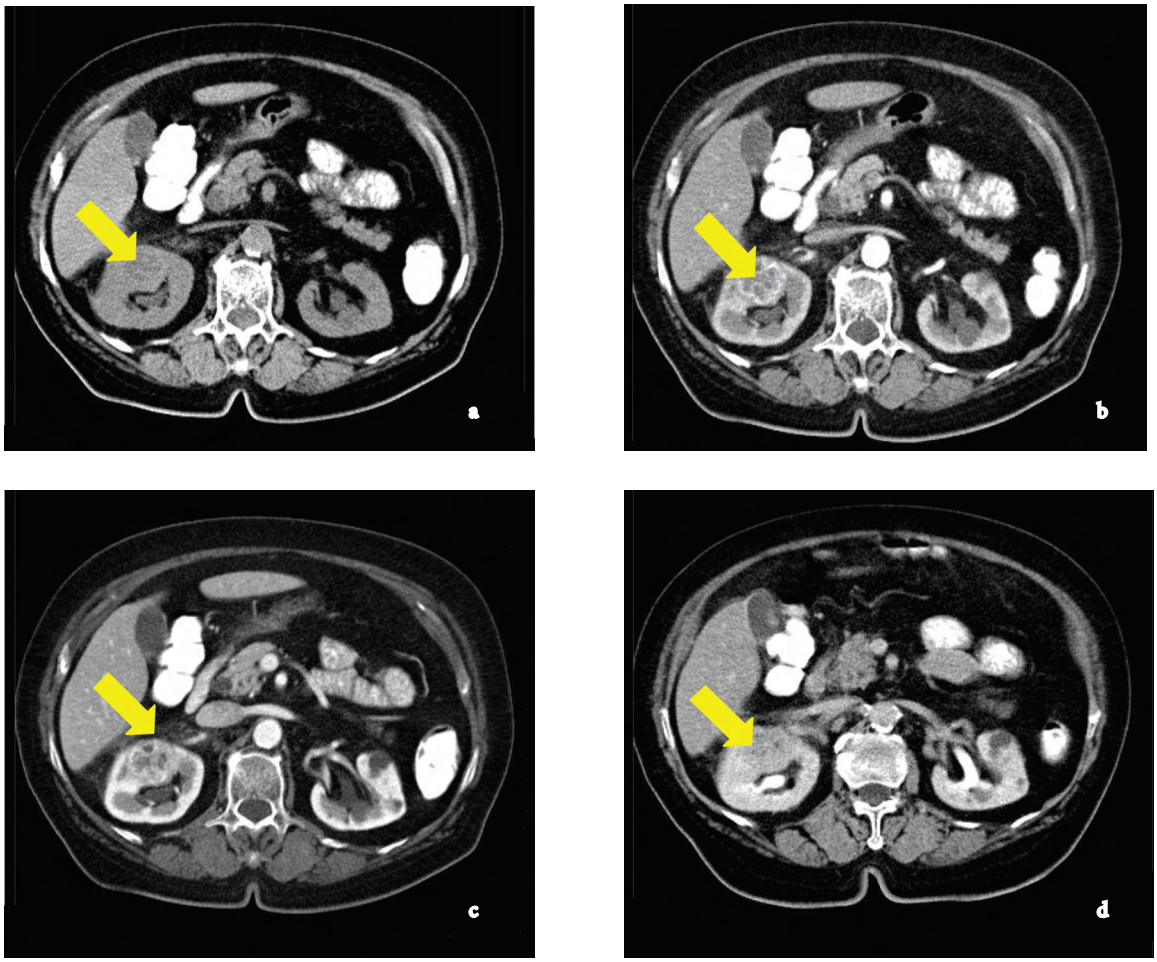

Figure 1. The preoperative triphasic MDCT images of a renal mass located anteriorly at the middle portion of the right kidney. Minimally hypodense region compared to parenchyma during precontrast scan (*a*); heterogenous contrast enhancement more prominent peripherally during arterial phase (*b*); contrast material wash-out causing difficulty in differring the mass from normal renal parenchyma during portal (*c*), and excretory (*d*) phases. Histopathological examination revealed clear cell carcinoma.

Discussion

Classification of RCC subtypes has become popular recently since the subtypes have a clear impact on prognosis (6,7). The histological subtypes of renal cell carcinoma can be classified as clear cell, papillary, chromophobe, collecting duct, and unclassified carcinomas (8,9). The conventional clear cell RCC is the most common subtype, accounting for approximately 70% of renal cell carcinomas. The overall 5-year survival rate of patients with RCC ranges from 55% to 60% (8,10,11). Clear cell RCC has lower overall 5-year survival rate compared to papillary and chromophobe tumors at the same stage (7,10).

The enhancement patterns of renal masses are important and provide invaluable data about tumor vascularity. Dynamic thin-section CT with administration of contrast medium by bolus peripheral injection has been reported to be superior to conventional enhanced CT in evaluating tumor vascularity (12,13). The enhancement property is the mainstay of predictions about tumor histology. Preoperative estimation of histology may also provide advantages besides prediction of prognosis as to decide a survey for metastases, planning the operative approach, and also discriminating benign lesions as oncocytoma, angiomyolipoma, complicated cysts, or benign mesenchymal tumors (6, 14). The prediction

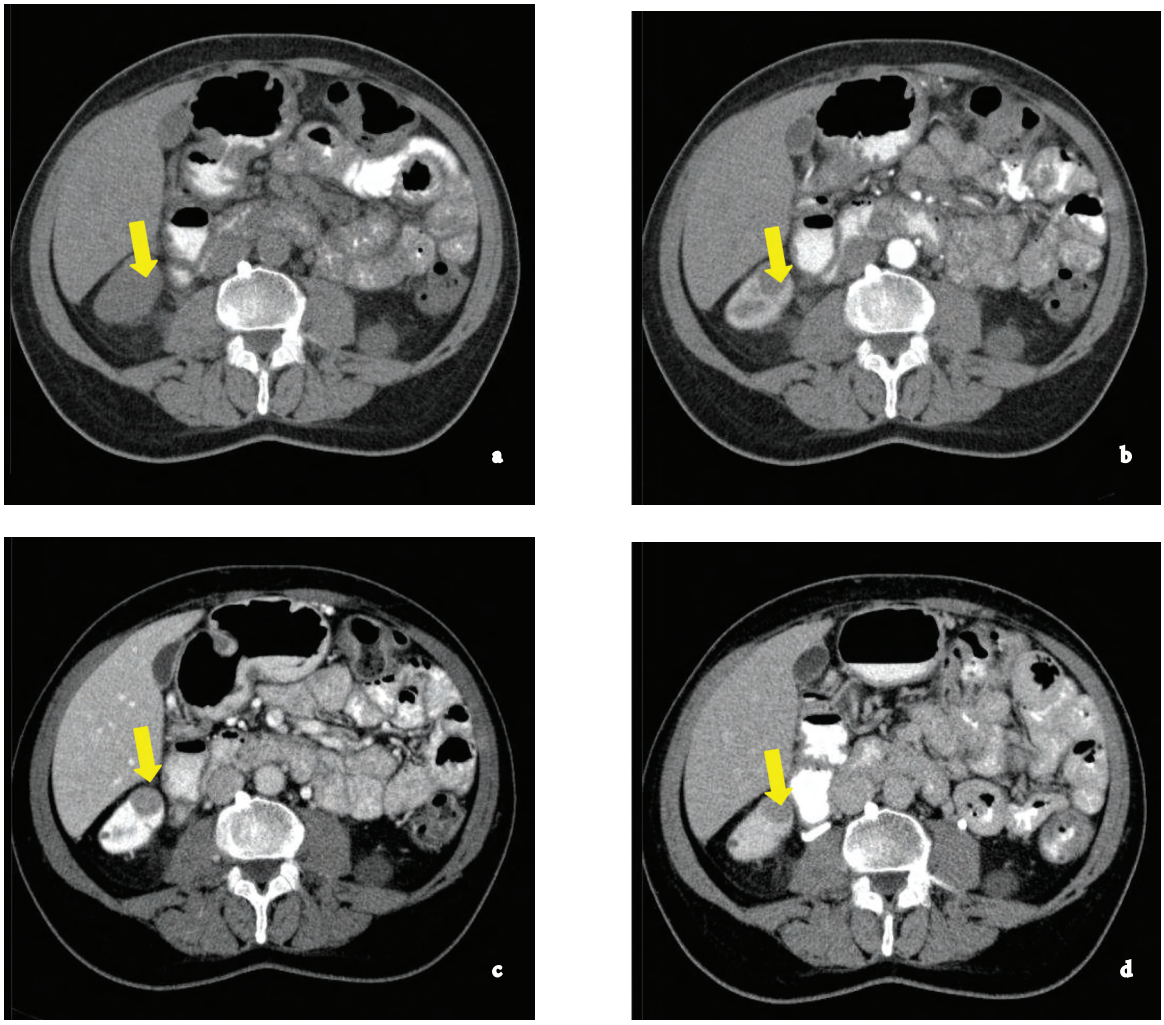

Figure 2. The preoperative triphasic MDCT images of a renal mass located anteriorly at the lower pole of right kidney. Isodence appearance during precontrast scan (*a*); a hypodense mass with a poor contrast enhancement during arterial (*b*); portal (*c*); and excretory (*d*) phases. Histopathological examination revealed papillary RCC.

of the subtype of RCC may influence the degree of preoperative evaluation. For example, a patient with a subtype of RCC that tends to not metastasize, such as chromophobe renal carcinoma, may not need to undergo a complex matastasis survey (6). For patients with surgically treatable RCC, radical nephrectomy has been indicated as the standard treatment. In spite of improved surgical techniques, postoperative mortality and morbidity remain high. With this point of view, precise preoperative identification of the subtype of RCC may be helpful in determining the appropriate extent of surgery. For example, an unnecessarily wide resection may be avoided in patients with a subtype that is likely to recur or metastasize, thereby reducing postoperative morbidity and mortality (6). Furthermore, a papillary RCC may be preferentially treated with nephron sparing surgery because the propensity of the disease is bilateral and diagnosed at an earlier stage. In addition, because of the possibility of synchronous or metachronous lesions, patients with papillary RCC should be followed up more closely after undergoing partial nephrectomy (15).

In terms of CT findings, clear cell RCC is often a hypervascular tumor, which tends to be heteregeneous when larger (14). It is demonstrated

Table 4. The attenuation and enhancement levels in biphasic* and triphasic CT phases in terms of histopathological subtypes.

		Histopathological Subtypes				
		Clear cell RCC (n = 11)	Papillary RCC (n = 10)	Chromophobe cell RCC (n = 1)	Oncocytoma (n = 1)	AML (n = 1)
Biphasic Dynamic CT Phase	Precontrast					
	Attenuation	36 ± 15	28.4 ± 15.4	31	44	25
	Portal					
	Attenuation	136.4 ± 63.2	71.4 ± 29.6	95	205	113
	Enhancement	100.7 ± 62.9	43.3 ± 22.5	64	106	90
	Excretory					
	Attenuation	68.8 ± 28.6	60.5 ± 20.5	68	113	57
	Enhancement	37.6 ± 28.2	42.8 ± 27.9	57	55	32
		Clear cell RCC (n = 18)	Papillary RCC (n = 3)	Chromophobe cell RCC (n = 3)	Oncocytoma (n = 1)	AML (n = 1)
Triphasic Dynamic CT Phase	Precontrast					
	Attenuation	34.2 ± 14	48.5 ± 37	32.8 ± 21.2	24	31
	Arterial					
	Attenuation	97.5 ± 43.8	68.2 ± 43.9	44.1 ± 10.5	25	33
	Enhancement	64.8 ± 40.4	19.8 ± 7.5	25.5 ± 25	1	2
	Portal					
	Attenuation	130.9 ± 33.5	128.8 ± 56.2	85.8 ± 20.5	210	68
	Enhancement	98.7 ± 37.2	94.2 ± 73.7	70 ± 45.3	185	37
	Excretory					
	Attenuation	87.5 ± 25.9	86.7 ± 25.1	57.8 ± 21.1	63	114
	Enhancement	55.7 ± 25.6	44.7 ± 14.1	33.1 ± 11.6	40	83

*The only case of leiomyosarcoma (heterogeneous) is not shown. AML = Angiomyolipoma

that conventional RCC exhibits stronger enhancement than nonconventional RCC (6, 14, 16), which is attributed to its rich vascular network and alveolar architecture (7, 14). Twenty four of our 29 patients with clear cell carcinoma showed hypervascular CT images (P = 0.000). In our series clear cell RCC showed stronger enchancement than only papillary RCC among other subtypes. It was remarkable that the positive predictive value of triphasic CT in detecting hypervascular clear tumors was greater than that of biphasic CT. The lesions of clear cell RCC were predominantly heterogeneous (20/29 cases, P = 0.041). The lesions over 5 cm tended to be more heterogeneous but this correlation was not statistically significant. When the degree of heterogeneicity is evaluated in heterogeneous tumors, no statistically significant difference was observed according to the CT technique (biphasic vs. triphasic) and phases (precontrast, arterial, portal, and excretory) or tumor subtypes.

Papillary renal cell carcinoma is typically a hypovascular and homogeneous tumor on CT. It usually appears in low stage and grade at presentation and tends to be multifocal or bilateral (1,4,15,17-20). In our cases 11 of 13 papillary RCC were hypovascular (P = 0.013) and 7 of them were homogeneous (P = 0.782). No significant correlation was observed with the tumor grade. It has been reported that calcifications are more frequently observed in papillary renal cell carcinoma (6,16). Our findings supported this finding since 4 of the 8 calcific lesions were in the papillary group.

Kondo et al. reported 2 distinct patterns of chromophobe cell RCC**.** Pattern 1 was characterized by a tumor enhancement with low density to isodensity compared to the renal medulla in the corticomedullary phase during dynamic CT scan (21). The tumors of this group were isodense on unenhanced CT scans with a lobulated appearance and a spoke wheel-like enhancement in some cases. Pattern 2 was characterized by a hyperdense enhancement in the corticomedullary phase. The tumors of this group were iso- to high-density without homogeneicity on unenhanced CT scans with a lobulated appearance in selected cases and no spoke wheel-like enhancement. None of our 4 chromophobe patients showed a spoke wheel-like enhancement. Only 1 patient out of 3 with lobulated appearance who were in concordance with pattern 1 had homogeneicity. The remaining one patient had a hyperdense appearance in precontrast and arterial sections without having the homogeneicity described in pattern 2. All patients, except one with the characteristics of pattern 1, were hypervascular.

It is well known that oncocytomas are phenotypically closely related to chromophobe cell RCC, which makes it difficult to differentiate from RCC (22-24). Both oncocytoma cases in our group were hypervascular, without having calcifications and lobulations. These lesions were isodense in precontrast sections whereas hyperdense in portal phases. Only 1 of these 2 oncocytoma lesions was homogeneous.

Two of our cases were angiomyolipomas. Both of these lesions were isodense in precontrast and portal sections. These lesions also had no calcifications and lobulations. One of these lesions was homogeneous and the other one was hypervascular.

Fujimoto et al. and Wildberger et al. proposed that stronger enhancement is an important finding to differentiate conventional RCC from other subtypes (14, 16). Our findings support this statement only for papillary RCCs. Besides, we conclude that combination of other diagnostic parameters should be used in order to estimate the tumor subtypes just as suggested by Kim JK et al. (6). For example, a hypervascular heterogeneous lesion without any calcification may be estimated as a clear cell RCC. On the other hand, a hypovascular lesion with calcification more prominently may suggest papillary RCC.

Conclusion

CT scanning appears as a very helpful imaging modality in the diagnosis of renal cell carcinoma and discrimination of histological subtypes. Dynamic workup with triphasic imaging emphasizes the importance of a meticulous technique in CT scanning. Although hypervascularity and calcifications seem to be important parameters in suggesting histological RCC subtypes, the low incidences of certain types of tumors hinder the explanation of the real predictive power of CT findings.

References

1. Yamashita Y, Takahashi M, Watanabe O, Yoshimatsu S, Ueno S, Ishimaru S et al. Small renal cell carcinoma: pathologic and radiologic correlation. Radiology 1992; 184: 493-8.
2. Bosniak MA. The small (< 3.0 cm) renal parenchymal tumor: detection, diagnosis and controversies. Radiology 1991; 179: 307-17.
3. Curry NS, Bissada NK. Radiologic evaluation of small and indeterminant renal masses. Urol Clin North Am 1997; 24: 493-505. Review.
4. Mancilla-Jimenez R, Stanley RJ, Blath RA. Papillary renal cell carcinoma: a clinical, radiologic, and pathologic study of 34 cases. Cancer 1976; 38: 2469-2480.
5. Mydlo JH, Bard RH. Analysis of papillary renal adenocarcinoma. Urology 1987; 30: 529-534.
6. Kim JK, Kim TK, Ahn HJ, Kim CS, Kim KR, Cho KS. Differentiation of subtypes of renal cell carcinoma on helical CT scans. AJR Am J Roentgenol 2002; 178: 1499-1506.
7. Reuter VE, Presti JC Jr. Contemporary approach to the classification of renal epithelial tumors. Semin Oncol 2000; 27: 124-137.
8. Bostwick DG, Eble JN. Diagnosis and classification of renal cell carcinoma. Urol Clin North Am 1999; 26: 627-35.
9. Bostwick DG, Eble JN, Murphy GP. Conference summary: diagnosis and prognosis of renal cell carcinoma-1997 workshop. Cancer 1997; 80: 975-76.

10. Bonsib SM. Risk and prognosis in renal neoplasms. A pathologist's prospective. Urol Clin North Am 1999; 26: 643-60.

11. Soyer P, Dufresne A, Klein I, Barbagelatta M, Herve JM, Scherrer A. Renal cell carcinoma of clear type: correlation of CT features with tumor size, architectural patterns, and pathologic staging. Eur Radiol 1997; 7: 224-29.

12. Foley WD, Berland LL, Lawson TL, Smith DF, Thorsen MK. Contrast enhancement technique for dynamic hepatic computed tomographic scanning. Radiology 1983; 147: 797-803.

13. Zeman RK, Fox SH, Silverman PM, Davros W, Carter LM, Griego D, et al. Helical (spiral) CT of the abdomen. AJR Am J Roentgenol 1993; 160: 719-25.

14. Fujimoto H, Wakao F, Moriyama N, Tobisu K, Sakamoto M, Kakizoe T. Alveolar architecture of clear cell renal carcinomas (< or = 5.0 cm) show high attenuation on dynamic CT scanning. Jpn J Clin Oncol 1999; 29: 198-203.

15. Herts BR, Coll DM, Novick AC, Obuchowski N, Linnell G, Wirth SL, et al. Enhancement characteristics of papillary renal neoplasms revealed on triphasic helical CT of the kidneys. AJR Am J Roentgenol 2002; 178: 367-72.

16. Wildberger JE, Adam G, Boeckmann W, Münchau A, Brauers A, Günther RW, et al. Computed tomography characterization of renal cell tumors in correlation with histopathology. Invest Radiol 1997; 32: 596-601.

17. Kletscher BA, Qian J, Bostwick DG, Andrews PE, Zincke H. Prospective analysis of multifocality in renal cell carcinoma: influence of histological pattern, grade, number, size, volume and deoxyribonucleic acid ploidy. J Urol 1995; 153: 904-6.

18. Zbar B, Glenn G, Lubensky I, Choyke P, Walther MM, Magnusson G, et al. Hereditary papillary renal cell carcinoma: clinical studies in 10 families. J Urol 1995; 153: 907-12.

19. Blath RA, Mancilla-Jimenez R, Stanley RJ. Clinical comparison between vascular and avascular renal cell carcinoma. J Urol 1976; 115: 514-19.

20. Bard RH, Lord B, Fromowitz F. Papillary adenocarcinoma of kidney: Radiographic and biologic characteristics. Urology 1982; 19: 16-20.

21. Kondo T, Nakazawa H, Sakai F, Kuwata T, Onitsuka S, Hashimoto Y, et al. Spoke-wheel-like enhancement as an important imaging finding of chromophobe cell renal carcinoma: a retrospective analysis on computed tomography and magnetic resonance imaging studies. Int J Urol 2004; 11: 817-24.

22. Noguchi S, Nagashima Y, Shuin T, Kubota Y, Kitamura H, Yao M, et al. Renal oncocytoma containing "chromophobe" cells. Int J Urol 1995; 2: 279–80.

23. Amin MB, Crotty TB, Tickoo SK, Farrow GM. Renal oncocytoma: a reappraisal of morphologic features with clinicopathologic findings in 80 cases. Am J Surg Pathol 1997; 21: 1–12.

24. Cochand-Priollet B, Molinié V, Bougaran J, Bouvier R, Dauge-Geffroy MC, Deslignières S, et al. Renal chromophobe cell carcinoma and oncocytoma. A comparative morphologic, histochemical, and immunohistochemical study of 124 cases. Arch Pathol Lab Med 1997; 121: 1081–6.