MULTIPHASE COMPUTED TOMOGRAPHY OF MALIGNANT KIDNEY TUMORS: RADIOLGIC-PATHOLOGIC COMPARISON

Ivan Žokalj¹, Miljenko Marotti², Hussein Saghir¹, Slavko Gašparov³, Branko Kolarić⁴,⁵ and Antonio Plešnar⁶

¹Department of Radiology and Ultrasound, Čakovec County Hospital, Čakovec; ²Department of Diagnostic and Interventional Radiology, Sestre milosrdnice University Hospital Center; ³Department of Pathology and Cytology, Merkur University Hospital, Zagreb; ⁴Department of Social Medicine and Epidemiology, School of Medicine, University of Rijeka, Rijeka; ⁵Service for Public Health, Social Medicine and Gerontology, Public Health Institute of Zagreb County, Zagreb; ⁶Department of Surgery, Division of Urology, Čakovec County Hospital, Čakovec, Croatia

SUMMARY – The aim of this retrospective study was to evaluate diagnostic test parameters of multiphase spiral computed tomography (CT) of the kidneys in the assessment of malignant renal tumors. Fifty-one patient records were reviewed. The imaging protocol included unenhanced and postcontrast scans during arterial and nephrographic phase. CT findings were compared with pathology findings to assess the value of spiral CT (sensitivity, specificity, negative predictive value, positive predictive value and accuracy) in the detection and characterization of tumors, and in the evaluation of local extension of malignant renal tumors. Spiral CT had a 96.08% sensitivity and accuracy in the detection of tumors. Characterization of renal tumors with CT had a sensitivity of 94.12% and accuracy of 96.08%. In the detection of fibrous capsule penetration, CT reached a sensitivity of 91.97% and specificity of 51.28%. In the evaluation of canal system propagation, the sensitivity was 100% and specificity 90.70%. CT had a sensitivity of 75%, specificity of 95.75% and positive predictive value of 60% in the evaluation of regional lymph node involvement. In the detection of the main renal vein invasion, CT showed 60% sensitivity and 100% specificity. Spearman’s rank correlation coefficient between the mean tumor size on CT images and renal specimen was 0.916. In conclusion, multiphase spiral CT has satisfactory diagnostic parameters in the detection, characterization and evaluation of local extension of renal tumors except for detection of the main renal vein invasion.

Key words: Kidney, Malignant tumor; Computed tomography

Introduction

Renal cell carcinoma (RCC) usually occurs at age 50-70 and accounts for 90% of malignant tumors of renal cortex. In the past, RCC was more common in men, however, a tendency of leveling the male/female patient ratio has been observed with time, which has been reduced to less than 3:1 and in recent years to only 1.6:1.¹,² The use of imaging techniques based on volume acquisition of data by computed tomography (CT) of kidneys has made it possible to diagnose the tumor and obtain all information necessary for planning treatment with one examination. Data that were previously obtained with the use of ultrasound (US), excretion urography, conventional CT and selective

Correspondence to: Ivan Žokalj, MD, Department of Radiology and Ultrasound, Čakovec County Hospital, Ivana Gorana Kovačica 1e, HR-40000 Čakovec, Croatia
E-mail: ivan.zokalj@ck.t-com.hr
Received February 6, 2012, accepted June 18, 2012
renal angiography are now united in one examination. The introduction of rapid spiral CT scanners has allowed dynamic recording of the kidneys during several phases of excretion of intravenously administered iodinated contrast material (or organ perfusion phases after intravenous administration of iodinated contrast material)\(^3,4\). Besides detection and characterization of renal tumors, CT has an important role in staging of the tumor\(^4,5\). At the time of writing of this article, US is the first diagnostic tool for suspected pathologic changes of the kidneys due to its relatively wide availability and patient safety. US detection of renal tumors has a sensitivity of 79%-83%. The wide use of US for evaluation of kidney diseases has resulted in a significant increase in early detection of malignant tumors of the kidney\(^6,7\). Magnetic resonance (MR) is a method that has almost all the benefits of CT in addition to the fact that it is not connected with the use of ionizing radiation. Unwanted side effects of the paramagnetic contrast materials are by far less common in relation the side effects associated with iodine contrast agents. Because of these facts, MR has been increasingly used in diagnostic evaluation of patients with kidney tumors\(^8,9\). Modern imaging methods allow for earlier detection and more detailed depiction of the tumor and vascular supply of the affected organs\(^3,10,11\). Better representation of tumor relationship to the surrounding structures has led to a higher rate of nephron-sparing surgery, which is especially important because of the population aging and the increasing number of people with impaired renal function\(^10-14\). The main goal of this study was to assess diagnostic value (sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and accuracy) of spiral CT of kidneys performed according to the imaging protocol that contains a combination of unenhanced and postcontrast scans obtained during the arterial phase and nephrographic phase in preoperative evaluation of malignant kidney tumors.

**Patients and Methods**

The study was approved by the institutional review board, Ethics Committee of the Čakovec County Hospital. Medical records of 51 patients, evaluated during the period from May 2001 to May 2007 with the diagnosis of malignant kidney tumors based on CT findings, confirmed by histopathologic findings of removed tumors, were included in the study. Demographic characteristics of the study group were as follows: 31 (60.8%) women and 20 (39.2%) men (±SD) patient age 60.61±13.63, age range 23-83 years; mean age of women 58.27, range 23-80 years; and mean age of men 68.30, range 44–83 years.

The method employed in the study was comparison (comparative analysis) of radiologic and pathologic reports in an attempt to assess diagnostic value of spiral CT in the detection of kidney tumors and characterization of renal tumors as malignant or benign, assessment of local extension of tumors and mean tumor size estimation. The following parameters were studied during assessment of the extension of renal tumors: tumor penetration through renal capsule, lymph node status according to their size, penetration into the collecting system, and the spread of tumors in the main renal vein. Preoperative CT images were taken from the Department picture archiving and communication system and re-evaluated by a radiologist (I.Ž.), who was aware of the fact that the patient had been operated on for a malignant tumor. The radiologist was unaware of pathologic reports.

CT procedures were performed on a single slice spiral (helical) CT scanner (High Speed Lxi, General Electric Medical Systems, Wisconsin, USA) with a maximum speed of x-ray tube rotation of 360 degrees 0.8 seconds and maximum length of the recorded volume of 120 cm. Collimation of x-ray beam on unenhanced scans was 5 to 10 mm with image reconstruction interval of 5 to 10 mm, and on postcontrast scans collimation of x-ray beam was 3-5 mm with reconstruction interval of 1.5 to 5 mm. Exposition values during scanning were 120-140 kV and 250-300 mA. The examination procedure began with scouts, anteroposterior and laterolateral. CT procedure contained a combination of the unenhanced and two series of postcontrast scans obtained during the arterial phase and nephrographic phase. Unenhanced scans of the abdomen and pelvis were done with collimation of x-ray beam of 5-10 mm and reconstruction interval of 5-10 mm. The scan delay period for the arterial phase was 15-25 seconds and for nephrographic phase 90-100 seconds from the beginning of intravenous administration of contrast material. Scans during the
Excretory phase were obtained only in patients with suspicion of tumor penetration in the renal collecting system based on previous cross-section imaging procedures. The excretory phase scans were performed with scan delay of 5 minutes. The intravenous iodine contrast material was administered using an automatic injector through 18-gauge intravenous cannula placed in the antecubital fossa at an average flow rate of 3–4 mL/s.

Urotropic water-soluble nonionic iodinated contrast materials were used, with iodine concentration of 300 mg I/mL in iopromide (Ultravist Schering AG, Berlin, Germany), iohexol (Omnipaque, Nycomed Amersham, Oslo, Norway), and 270 mg I/mL in iodixanol (Visipaque, Nycomed Amersham, Oslo, Norway). Patients were asked to drink 0.5 L of water 30 minutes before the examination and 0.5 L just before positioning on the CT scanner for better differentiation of the kidney from the surrounding bowel loops. Axial scans were obtained by reconstructing the data recorded in the computer management console and then were transferred to a workstation for the analysis and development of cross-sectional two-dimensional and three-dimensional reconstructions (Advantage Windows, GE Medical Systems, USA).

Analysis of data obtained by scanning began with the study of axial sections and then sections in different planes (multiplanar reconstructions/reformations), after which the preparation of the other types of reconstructions followed, such as multiple intensity projections (MIP) and volume rendering (VR), depending on the pathological changes studied. Perinephric stranding was chosen as a sign of possible perirenal propagation of the tumor. Lymph nodes were assessed on the basis of size. Lymph node involvement with metastasis was considered if the maximum node diameter was equal to or greater than 10 mm. Venous spread of the tumor was diagnosed if the postcontrast scans obtained during nephrographic phase depicted intraluminal filling defects in renal and/or inferior vena cava. A sign of tumoral thrombus was direct continuity of intraluminal contrast filling defect in renal vein with primary tumor in the kidney.

Measures of the value of diagnostic test (sensitivity, specificity, PPV, NPV, accuracy, and kappa test) were calculated with confidence interval with 95% probability (95%CI) for renal spiral CT (with unenhanced and postcontrast scans in the arterial and nephrographic phase) for the following parameters: tumor penetration through renal capsule estimated on the blur of perirenal adipose tissue (perinephric stranding), penetration of kidney tumor into the collecting system, penetration of kidney tumor into the main renal vein, and involvement of local lymph nodes. The 95%CI was calculated by Wald’s method. Correlation between the mean renal tumor size measured on CT scans and in renal specimens (surgically removed kidney or part of the kidney affected with the tumor) was calculated using the following method: nonparametric equivalent of Pearson’s correlation coefficient, the Spearman’s rank correlation coefficient calculated by Bland-Altman method and regression analysis, done by Passing and Bablock method.

**Results**

Renal cell carcinoma was diagnosed with pathologic methods in 49 of 51 patients and other types of renal malignant tumors in two patients. Solid forms of RCC were diagnosed in 47 patients and cystic form of RCC in 2 patients (Fig. 1). Collecting duct cell carcinoma (Bellini duct carcinoma)

![Fig. 1. Spearman’s rank correlation coefficient calculated by the Bland-Altman method during evaluation of correlation between the mean tumor size measured on computed tomography scans and the mean size of kidney tumor measured on surgically removed kidney.](image-url)
Multiphase computed tomography of malignant kidney tumors: radiologic-pathologic comparison

was diagnosed in one patient. The following types of other renal malignant tumors were represented with one case each: transitional cell cancer of renal pelvis (Fig. 2) and primitive neuroectodermal tumor. The sensitivity of multiphase spiral CT in the detection of renal tumors achieved a value of 0.96 with 95%CI of 0.74 to 0.99. PPV reached a value of 1.00 with 95%CI of 1.00 to 1.00, and accuracy was 0.96 with 95%CI of 0.91 to 0.99. The value of specificity, NPV and kappa could not be calculated because there were no false-positive and true negative findings. Spiral CT characterization of the tumor as malignant or benign reached a sensitivity of 0.94 with 95%CI of 0.88 to 0.99. The PPV was 1.00 with 95%CI of 1.00 to 1.00, and accuracy was 0.96 with 95%CI of 0.91 to 0.99. The value of specificity, NPV and kappa could not be calculated because there were no false-positive and true negative findings. The PPV value of 100% should be considered taking into account the number of the observed group members (n=51). The value of spiral CT staging of renal malignant tumors was evaluated by observing the following parameters: tumor penetration through the connective capsule of the kidney, kidney tumor penetration in the collecting system, tumor propagation into the main renal vein, and lymph node status (Table 1). The penetration of the kidney tumor in the collecting system was correctly diagnosed with CT and histologically confirmed in 8 patients. In 4 patients, the tumor penetration into the collecting system was suspected because the tumor compressed the collecting system but it was not confirmed by histopathologic analysis. There were no false-negative cases. The 100% sensitivity should be considered as a consequence of the small number of patients with CT diagnosis of tumor penetration into the collecting system (n=12), which was histologically confirmed in 8 cases. CT assessment of local lymph nodes showed 75% sensitivity, 95.74% specificity, 94.12% accuracy and 0.6349 kappa, which should be analyzed considering the fact that in 88% of study patients (45 of 51 patients) the finding was true negative. Spread of the renal tumor in the main renal

Table 1. Diagnostic value measurements (sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), accuracy, and kappa test) of computed tomography evaluation of kidney tumor extension. Values were calculated with confidence interval with 95% probability (95%CI)

<table>
<thead>
<tr>
<th>Spread through capsule</th>
<th>Propagation into urinary collecting system</th>
<th>Lymph node involvement</th>
<th>Main renal vein spread</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>0.92</td>
<td>1.00</td>
<td>0.75</td>
</tr>
<tr>
<td>Specificity</td>
<td>0.51</td>
<td>0.91</td>
<td>0.96</td>
</tr>
<tr>
<td>PPV</td>
<td>1.00</td>
<td>0.67</td>
<td>0.60</td>
</tr>
<tr>
<td>NPV</td>
<td>0.95</td>
<td>1.00</td>
<td>0.98</td>
</tr>
<tr>
<td>Accuracy</td>
<td>0.61</td>
<td>0.92</td>
<td>0.94</td>
</tr>
<tr>
<td>Kappa</td>
<td>0.45</td>
<td>0.75</td>
<td>0.64</td>
</tr>
</tbody>
</table>
vein was diagnosed after histologic analysis in a small group of five patients. According to macroscopic tumor size measurements made by the pathologist, the mean tumor size in the study group was 62.96 mm, range 16-120 mm. The mean tumor size median in male patients was 59.77 mm, range 18-120 mm, and in female patients 72 mm, range 40-110 mm. Spearman’s rank correlation coefficient calculated using the Bland-Altman method during evaluation of correlation between the mean tumor size measured on CT scans and the mean tumor size measured in surgically removed kidneys was 0.916 with 95%CI of 0.854 to 0.952 and P<0.001 (Fig. 3). The measurements on CT scans significantly deviated from the measurements on surgical specimens in only 4 patients. The intercept A in the regression equation derived by Passing and Bablock method was 5.3333 with 95%CI 0.0000 to 11.3000, i.e. 95%CI included zero. The calculated values confirmed the hypothesis that the mean tumor size on CT scans did not differ significantly from the largest diameter measured on surgical specimens. Slope B was 0.9333 with 95%CI of 0.8600 to 1.0000. The fact that the confidence interval contained the value 1 was in favor of the above hypothesis (Fig. 4 and Table 2). Cusum test for linearity did not result in statistically significant deviation from the linear distribution of data (P>0.10) (Table 2).

Discussion

In the present study, spiral CT of kidney was performed according to the multiphase protocol consisting of unenhanced and two series of postcontrast scans (during arterial and nephrographic phases of contrast enhancement). Unenhanced scans were the basis for measuring attenuation coefficient increase on postcontrast scans and indirect assessment of tumor structure as well as to depict calcifications. CT angiography (CTA) was performed in order to get a detailed view of the arterial supply of the kidney and the tumor, which was important for better planning and selecting the most appropriate form of surgical treatment. CTA is a minimally invasive radiological diagnostic method like MR angiography, which can easily be incorporated into the protocol of CT examination performed with the purpose of detection
and characterization of expansive processes in the kidneys. The importance of arterial phase scans should not be neglected for the possibility of erroneous characterization of vascular changes, such as renal artery aneurysms, arteriovenous malformations and arteriovenous fistulas as solid occupying kidney lesions on scans taken during later perfusion phases such as nephrographic and excretory phases.

In previous studies, spiral CT reached 100% accuracy in the detection of renal tumors located mainly in the renal parenchyma and lower part of the pelvis. In these studies, CT imaging protocol usually consisted of unenhanced and postcontrast scans done during corticomedullary and nephrographic perfusion phases. Renal collecting system tumors were then identified and properly characterized despite the absence of postcontrast scans in excretory phase. In the present study, there were two false-negative cases of kidney tumors undiagnosed with CT (histologically dedifferentiated renal cell carcinoma). In both cases, there was a coincidence of inflammatory changes of the collecting system, which masked renal tumor. In one case, the tumor was found intraoperatively, and in another one during pathologic analysis of renal specimen (Fig. 5). In 48 of 51 patients, malignant tumors of the kidney were correctly diagnosed and characterized with CT. In one case, renal malignant tumor was incorrectly characterized as an atypical cyst without clear indications of the possible cancer in radiologic finding, and in two cases there was a coincidence of inflammatory changes and malignant tumor but changes in the kidney were characterized only as inflammatory changes. Previous studies achieved a sensitivity of 98%, specificity of 95%, PPV of 96% and accuracy of 96% in characterization of renal lesions detected by CT. Renal abscess is a special diagnostic problem that may lead to misinterpretation in CT diagnostics of kidney tumors. In our study, misdiagnosed patients had a history of recurrent urinary tract infections in both cases. Similar cases have been published previously and discussed as a specific problem in uroradiology.

In a study published in 1999, Macari and Bosniak applied a scanning protocol quite opposite to that used by other groups of authors to evaluate CT detection of expansive lesions of the kidneys, their characterization and assessment of vascularization. In a study conducted in small sample of 25 patients, the imaging protocol contained scans taken during nephrographic and excretory phases of kidney perfusion with contrast material. Excretory phase scans were performed 15 minutes after intravenous administration of iodine contrast media. The authors conclude that for characterization of the expansive processes of the kidney, the speed at which iodine contrast medium accumulates in the expansive process is as important as the rate at which contrast medium leaves the expansive formation. Indirectly, it can be concluded that for CT characterization of expansive processes of the kidneys, careful composition of imaging protocol is more important than technical capabilities of radiological equipment. Several parameters have been used in assessing local extension of malignant tumors of the kidney: penetration through the kidney fibrous capsule, penetration in the collecting system, spread in the main renal vein, and local lymph node status. Perinephric stranding was accepted as a sign of the possible penetration through the connective capsule, although in previous studies perinephric stranding was described as a sign of low specificity because it can be found with kidney inflammation, edema and venous stasis. Inflammatory changes in perirenal adipose tissue were the cause of a large number of false-positive results (19 of 51 pa-
The selected criterion for penetration through the renal capsule was probably the main reason for the results of diagnostic value measurements obtained. CT assessment of the penetration of malignant kidney tumors through the renal capsule is not sufficiently reliable without visualization of a clearly shaped cluster of tumor tissue in the perirenal adipose tissue. Catalano et al. performed CT studies on a multidetector row CT scanner (MDCT) and achieved much better results in diagnosing perirenal fat infiltration with 96% sensitivity, 93% specificity and 95% accuracy.

Comparing the results of conventional retrograde urography and MSCT urography in the evaluation of upper urinary tract tumors, McCarthy and Cowan found that 98% of all lesions were diagnosed with MSCT and 78% with conventional retrograde urography. A retrospective study by Caoli et al. included 370 MDCT urography examinations; 18 of 27 tumors were prospectively diagnosed with MDCT urography and six neoplasms more after retrospective review. Three ureteral neoplasms were not depicted. All detected lesions were visualized on axial excretory phase images. The thickness of the postcontrast sections of 3-5 mm is suboptimal by today’s standard MSCT protocol in urinary collecting system invasion evaluation because 1-mm slice thickness is associated with better diagnostic test parameters.

The criterion for involvement of lymph node with metastases from malignant kidney tumor of a diameter equal to or greater than 10 mm was chosen because it was used in most previous studies and systems of renal tumor staging. The study conducted by Nussbitt et al. in 1997 included 163 patients who underwent nephrectomy and dissection of lymph nodes due to RCC. Applying the above mentioned criterion, false-negative results were obtained in 4% of cases. Reactive hyperplasia of lymph nodes was the main cause of false-positive findings as it was the cause in most previous studies too. Lymph nodes had a diameter of 15-18 mm in one patient with RCC clear cell type, but pathologic analysis revealed reactive lymphoid hyperplasia. Allam et al. conclude that the overall agreement between triphasic spiral CT and pathologic findings in T stage of RCC is perfect, while agreement in N staging is poor.

The tumor spread in the main renal vein is one of the most important information that the radiologist should give to the operator for planning the intervention. Tumor thrombus is located in the main renal vein in 23% and in inferior vena cava in 4%-10% of RCC cases. In previous studies, the signs of tumor thrombus in renal vein were described as a hypodense area surrounded by contrast medium opacified blood in the renal vein, inhomogeneous perfusion of tumor thrombus with contrast medium and a direct link of tumor thrombus with the tumor. In a study conducted by Welch and LeRoy, CT achieved PPV of 92% and NPV of 97% in assessing the spread of renal tumors into the vein. These criteria of tumor invasion in renal vein were used in our study. Some authors recommend three series of postcontrast scans on diagnostic evaluation of kidney tumors with CT including corticomedullary phase scans for diagnosis of tumor thrombus in renal vein. The single-slice helical CT device used in the present study lacks adequate technical capabilities that would permit recording a larger number of postcontrast scans with short pauses between each two phases. Analysis of the results obtained in the present study allowed to assume that, had the patients been scanned during later arterial phase (scan delay of 25-35 seconds) with the use of thinner sections (1 mm), the imaging material would be more suitable for more

Fig. 6. Postcontrast axial image in nephrographic phase: left kidney is affected by renal cell carcinoma clear cell type, which penetrated kidney capsule and propagated into the canal system and main renal vein. Enlarged local lymph nodes with a mean size of 15 mm, in which pathologic analysis revealed only reactive hyperplasia and no metastases.
detailed analysis of tumor penetration into the main renal vein and inferior vena cava and for presentation of renal arterial supply.

In earlier studies, the difference between the mean tumor size measured on CT image and in renal specimen amounted to 0.5 cm\(^3\). In the present study, correlation between the mean tumor size measured on CT scan and in renal specimen showed a high level of correspondence between CT and pathologic methods in the assessment of the mean tumor size.

Precise assessment of local spread of malignant kidney tumors at the beginning of treatment is important since it directly correlates with the prognosis of the disease, which justifies the use of multiphase CT scanning despite the risk of higher doses of ionizing radiation\(^{22-34}\). MR diagnosis of renal tumors, as well as CT is based on the finding of expansive formation, radiomorphological features, and the manner and speed of tumor perfusion with intravenously applied contrast material\(^6\). In the evaluation of lymph nodes, differentiation between normal and lymph nodes affected with metastases of malignant tumors is based on the lymph node size, as well as the CT view. Based on data obtained by three-dimensional gradient echo sequence scans performed after intravenous application of gadolinium it is possible to get as good depiction of renal tumors and vasculature as with multiphase scanning protocol on CT\(^9\). MR is the method of choice in patients with known allergy to iodine contrast materials and for patients with suspected bone metastases\(^8\).

According to the results presented, the multiphase spiral CT of kidneys with imaging protocol consisting of unenhanced and postcontrast scans in arterial and nephrographic phases has an appropriately high level of validation of diagnostic test parameters. CT findings are important factors in evaluation of tumor operability and planning of treatment. In uncertain cases, CT should be supplemented with other non-invasive imaging methods such are MR and nuclear medicine methods.

References


17. HERTS BR, COLL DM, LIEBER ML, et al. Triphasic helical CT of the kidneys: contribution of vascular phase scan-
Multiphase computed tomography of malignant kidney tumors: radiologic-pathologic comparison

I. Žokalj, M. Marotti, H. Sagbir, S. Gašparov, B. Kolaric and A. Plešnar

Cilj ove retrospektivne studije bio je procjena parametara valjanosti dijagnostičkog testa višefazne spiralne kompjutorizirane tomografije (CT) bubrega u dijagnostičkoj obradi malignih tumora bubrega. Pregledane su snimke CT pregleda 51 bolesnika. Protokol snimanja uključivao je nativne i postkontrastne presjeke učinjene tijekom arterijske i nefrografske faze. Na osnovu CT pregleda su uspoređeni parametri valjanosti procjene dijagnostičkog testa, to je osjetljivost, specifičnost, pozitivna i negativna prediktivna vrijednost. Tomografske snimke su analizirane na osnovu konzultacije i saradnje sa patologom. Tomografija je dosegla osjetljivost od 96,3% u otkrivanju i karakterizaciji tumor. Specifičnost u otkrivanju tumor je iznosila 96,3%, a bezvremena točnost u otkrivanju tumor je iznosila 96,3%. Spearmanov koeficijent korelacije između srednjih veličina tumora na tomografskim snimcima i otkrivenim tumora iznosio je 0,916. U zaključku, višefazna spiralna CT je dosegao zadovoljavajuće vrijednosti parametara valjanosti testa otkrivanju i karakterizaciji tumor. Osim toga, CT je dosegao pozitivnu prediktivnu vrijednost u procjeni zahvaćenosti regionalnih limfnih čvorova.