Renal Function After Tumor Enucleation: Assessment by Quantitative SPECT of ^{99m}Tc-Dimercaptosuccinic Acid Uptake by the Kidneys

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The purpose of this study was to evaluate the amount of functioning renal mass removed and the amount of remaining individual renal function after tumor enucleation. **Methods:** Renal functional volume, percentage injected dose (%ID) per cubic centimeter of renal tissue and individual renal uptake of 24 operated and 24 contralateral kidneys were studied by two sequential SPECT quantitations of ^{99m}Tc-dimercaptosuccinic acid (DMSA) uptake by the kidneys (QDMSA). The first study was before surgery and the second study was 1 to 6 mo (mean 3.5 mo) after surgery. Mean tumor size was 3.4 ± 0.99 cm and all tumors were confined to the renal parenchyma (stages pT1 and pT2). **Results:** In the operated kidneys, there was a statistically significant decrease in renal cortical volume (170 ± 46 mL after surgery versus 207 ± 45 mL before surgery, $t = 6.2$, $P < 0.001$) and individual renal uptake (10.3% ± 3.0% after surgery versus 13.0% ± 2.9% before surgery, $t = 5.4$, $P < 0.001$). There was no statistically significant change after surgery compared with before surgery in the %ID per cubic centimeter of renal tissue of the operated kidneys, and in the volume, %ID per cubic centimeter and uptake of the contralateral normal kidneys. **Conclusion:** The results suggest that QDMSA is a noninvasive method able to assess changes in separate renal function. The limited functioning parenchymal loss after tumor enucleation had no effect on the opposite kidneys.

Key Words: renal tumors; ^{99m}Tc-dimercaptosuccinic acid; SPECT; renal function

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Preservation of renal function is the main goal of nephron-sparing surgery (NSS). Although controversy still exists about the role of NSS in the presence of a normal contralateral kidney, this technique has been used in patients with a single kidney or bilateral tumors (*1*). Quantitative SPECT measurement of ^{99m}Tc-dimercaptosuccinic acid (DMSA) uptake by the kidneys (QDMSA) is a reproducible method that can reliably be used to monitor serial changes in individual renal function (*2*). QDMSA provides information concerning the percentage injected dose (%ID) per cubic centimeter of renal tissue and functional kidney volumes. By multiplying these two parameters, one can obtain individual kidney uptake, which provides a practical index for evaluation of individual renal function (*3*). In this study, QDMSA was used to evaluate the amount of functioning renal mass removed and the remaining individual renal function after tumor enucleation.

MATERIALS AND METHODS

Patient Population

Twenty-four consecutive patients (15 men, 9 women; mean age 56.7 y) undergoing renal tumor enucleation were studied by two sequential QDMSA examinations. The first study took place before surgery, and the second study occurred 1 to 6 mo (mean 3.5 mo) after surgery. Tumor pathologies were renal cell carcinoma (n = 13), renal angiomyolipoma (n = 2), hyperdense cyst (n = 2) and benign tumors (n = 7). Mean tumor size was 3.4 ± 0.99 cm, and all tumors were confined to the renal parenchyma (stages pT1 and pT2). No patient had prior renal surgery. Concomitant diseases present in those patients were hypertension (HTN) = 6; diabetes mellitus (DM) = 2; peripheral vascular disease (PVD) = 2; HTN, DM and PVD = 2; HTN and PVD = 1; HTN and DM = 1; and urolithiasis = 1. Four patients received concomitant angiotensin-converting enzyme inhibitor medication for HTN. There was no change related to concomitant diseases and medications between the two studies. All patients had normal values for serum creatinine and blood urea nitrogen before and after surgery.

The studies were performed 4–6 h after intravenous injection of 37–111 MBq (1–3 mCi) of the radiopharmaceutical. The exact dose injected was obtained by measuring the syringe in a dose calibrator before and after injection. Renal functional volume, %ID per cubic centimeter of renal tissue and percent of individual renal uptake of 24 operated kidneys and 24 normal contralateral kidneys were studied.

NSS consisted of tumor enucleation after temporary occlusion of the renal vascular pedicle and regional hypothermia using ice-slush saline. The technique involves circumferential incision of the capsule around the tumor. A plane is identified between the

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fibrous pseudocapsule and the renal parenchyma. The tumor is then bluntly enucleated with the butt end of the scalpel together with approximately 1 cm of normal renal parenchyma around the tumor. Intraoperative biopsies are taken from the tumor bed to verify the complete removal of the tumor (*4*).

Quantitative SPECT

QDMSA was measured using the same methodology as in previous studies (*2,3*). In brief, studies were performed using a rotating gamma camera and an all-purpose, low-energy collimator (SP-4; Elscint Ltd., Haifa, Israel). Data acquisition lasted 20 min and required 120 projections (3° apart), and the entire study accumulated 3×10^5 to 5×10^5 counts. Raw data were reconstructed by filtered backprojection with a Hann filter with a cutoff point of 0.5 cycle/cm. After reconstruction, each image was sectioned at 1-pixel (0.68-cm) intervals in the transaxial, coronal and sagittal planes using a 64×64 byte matrix. Kidney volumes and radioactive concentration measurements were calculated on the reconstruction data using the threshold method (*5*).

Threshold is the most used method for organ or tumor segmentation in SPECT studies (*6,7*). The threshold selection depends on the level of the surrounding activity and the organ size (*6,7*). The high target-to-nontarget ratio of DMSA in the kidney and kidney size (>30 mL) makes this method suitable for QDMSA (*5,6*). A threshold value of 43% was found to be optimal for ^{99m}Tc after a series of phantom measurements with known volumes and concentrations was performed (*3,5*). The study required only 20 min, and data analysis was practically automated and operator-independent, with low intra- and interobserver variability (*5*). The method does not deny that tissue attenuation is present but assumes that cancellation of attenuation effects occurs. Consideration of the theoretic role of attenuation and the inability to correct for it has led us to use the empirical threshold method and to demonstrate its usefulness and reliability by extensive phantom studies and by the only meaningful gold standard—the in vivo-in vitro correlation (*5*).

The operator chose the slice to define the kidney and drew a region of interest (ROI) around the organ. For volume measurements (cm^3), the number of pixels in all sections multiplied by the slice thickness was summed. For concentration measurements, the threshold value was subtracted from all pixels in the ROI in all slices. All the nonzero pixels that had higher counts than the threshold value were used to calculate the concentration. Counts per voxel were converted into concentration units (MBq/cm^3 [$\mu Ci/cm^3$]) using the regression line obtained previously by phantom measurements (*5*). The %ID per cubic centimeter of renal tissue was calculated using this value corrected for radioactivity decay. Kidney uptake was then obtained by multiplying kidney volume (cm^3) and %ID per cubic centimeter (*3*).

Statistical Methods

Values are expressed by their mean ± 1 SD. The paired t test was used to compare volume, %ID per cubic centimeter and kidney uptake before and after surgery.

RESULTS

Volume

In the operated kidneys, there was a statistically significant decrease in the renal cortical volume after surgery (170 ± 46 mL) compared with the study before surgery (207 ± 45 mL; $t = 6.2$, $P < 0.001$). In the contralateral nonoperated kidneys, there was no significant difference in the functional volume after surgery compared with before surgery (206 ± 47 mL versus 205 ± 44 mL; $t = 0.5$, not significant, respectively) (Table 1).

Percentage Injected Dose per Cubic Centimeter

In the operated kidneys, there was no statistically significant difference in the %ID per cubic centimeter of renal tissue after surgery compared with before surgery (0.064 ± 0.02 %ID/cm^3 and 0.064 ± 0.02 %ID/cm^3, respectively; $t = 0.18$, not significant). Similar results were observed in the nonoperated kidneys (0.069 ± 0.02 %ID/cm^3 versus 0.066 ± 0.02 %ID/cm^3; $t = -1.5$, not significant, respectively) (Table 1).

Uptake

In the operated kidneys, there was a statistically significant decrease in kidney uptake after surgery compared with before surgery (10.3% ± 3.0% and 13.0% ± 2.9%, respectively; $t = 5.4$, $P < 0.001$). In the contralateral nonoperated kidneys, there was no significant difference between the two studies (13.9% ± 3.7% versus 13.2% ± 3.2%; $t = 1.4$, not significant, respectively) (Table 1).

DISCUSSION

Radical nephrectomy has been the treatment of choice for renal cell carcinoma in the presence of a normal contralateral kidney since the early 1960s (*1*). NSS by partial nephrectomy or tumor enucleation techniques has also been used for many years in patients with bilateral tumors or in the presence of a solitary functioning kidney to prevent renal replacement therapy (*1*). The widespread use of noninvasive imaging techniques for other indications has resulted in early diagnosis of renal tumors that are smaller and of lower grade and stage and, consequently, are more likely to be resected for cure (*1,8*). Several studies have shown that the overall survival of patients who undergo NSS for renal cell carcinoma is similar to that of patients with comparable stage carcinoma who had radical nephrectomy (*1,8–13*). In fact, due to these favorable results, more and more centers are using NSS in treating small localized renal tumors in the presence of a normal contralateral kidney (*1,8,13*).

The goal of NSS is to preserve functioning renal tissue. In an aging population, preservation of renal tissue is important because many conditions such as HTN, stone disease or DM can affect the kidney and because tumors may occur bilaterally (*1,8*). Little information on individual renal function after NSS is available (*14,15*). Substantial ablation of renal mass may cause adaptive hyperfunction with hypertrophy and hyperfiltration of the remaining nephrons (*14,16*). These changes may lead to progressive glomerulosclerosis and renal failure (*14,16,17*). In two small series of patients, it was empirically estimated that one fourth to one sixth of the solitary kidney was removed by tumor enucleation (*14*) and that one fourth to three fourths of the renal parenchyma was removed by partial nephrectomy (*15*).

QDMSA is a reproducible method for monitoring serial changes in individual renal function (*2*). QDMSA is a

TABLE 1
Results of QDMSA Before and After Tumor Enucleation

Patient no.	Operated kidneys (n = 24) Before Volume (mL)	Operated Before %ID/cm³	Operated Before Kidney uptake (%)	Operated After Volume (mL)	Operated After %ID/cm³	Operated After Kidney uptake (%)	Contralateral kidneys (n = 24) Before Volume (mL)	Contralateral Before %ID/cm³	Contralateral Before Kidney uptake (%)	Contralateral After Volume (mL)	Contralateral After %ID/cm³	Contralateral After Kidney uptake (%)
1	156	0.09	14.3	152	0.07	11.0	144	0.08	10.8	131	0.07	9.0
2	241	0.07	17	168	0.07	11.0	229	0.05	12.0	249	0.06	15.0
3	137	0.05	7.3	111	0.05	6.1	127	0.05	6.6	126	0.05	6.0
4	242	0.06	14.3	230	0.07	15.6	249	0.06	14.0	232	0.07	16.0
5	142	0.08	11.2	84	0.09	7.7	149	0.09	13.2	148	0.10	14.6
6	203	0.07	13.6	198	0.05	9.3	220	0.07	15.0	205	0.05	11.0
7	171	0.12	20.0	129	0.09	12.0	175	0.11	19.4	182	0.12	21.5
8	195	0.07	13.1	137	0.07	9.7	213	0.08	16.6	215	0.08	17.4
9	213	0.06	12.1	179	0.07	12.5	203	0.06	12.0	205	0.07	13.5
10	165	0.07	12.1	165	0.06	9.4	159	0.07	11.6	159	0.07	12.6
11	182	0.06	11.6	133	0.09	12.3	171	0.07	12.0	165	0.10	16.0
12	245	0.05	13.0	243	0.08	15.0	248	0.05	13.0	233	0.07	17.0
13	208	0.09	18.9	192	0.09	17.7	190	0.11	21.0	192	0.10	19.0
14	344	0.04	13.5	263	0.03	7.9	301	0.05	15.2	315	0.05	15.7
15	173	0.07	12.6	165	0.07	11.1	147	0.07	11.7	160	0.07	11.5
16	213	0.06	13.2	178	0.06	10.0	220	0.07	14.0	207	0.06	11.0
17	170	0.06	10.9	143	0.06	9.0	174	0.05	9.4	183	0.06	10.7
18	222	0.07	14.8	181	0.07	12.6	208	0.07	15.1	227	0.08	17.4
19	232	0.04	10.2	205	0.04	8.4	241	0.05	12.0	245	0.05	11.6
20	244	0.03	8.1	138	0.05	6.3	211	0.04	8.0	195	0.04	8.9
21	202	0.06	13.0	117	0.06	7.0	217	0.07	15.0	218	0.08	17.8
22	272	0.04	9.8	261	0.03	7.0	293	0.03	10.7	313	0.03	9.8
23	223	0.07	14.9	180	0.06	11.6	229	0.07	15.9	239	0.07	17.3
24	186	0.07	12.3	146	0.05	7.6	207	0.07	14.7	212	0.06	13.3
Mean	207	0.06	13.0	170	0.06	10.3	205	0.066	13.2	206	0.069	13.9
1 SD	45	0.02	2.9	46	0.02	3.0	44	0.02	3.2	47	0.02	3.7

QDMSA = quantitative SPECT of dimercaptosuccinic acid uptake; %ID/cm³ = percentage injected dose per cubic centimeter.

noninvasive method that enables measurement of the renal cortical functioning volume (*5,18,19*). The renal uptake of ^{99m}Tc-DMSA correlates well with the effective renal plasma flow, glomerular filtration rate and creatinine clearance (*20,21*). Thus, the renal uptake of ^{99m}Tc-DMSA provides a practical index for evaluating individual renal function (*20,21*).

The renal uptake of ^{99m}Tc-DMSA is dependent on renal blood flow and proximal tubular cell membrane transport function (*20*). It has been shown that the amount of functioning renal tissue removed by unilateral nephrectomy caused hyperperfusion, hyperfiltration and proximal tubule hyperfunction in the remaining kidney (*22,23*). Hyperfunctioning kidneys may show increased %ID per cubic centimeter of renal tissue and increased kidney uptake of ^{99m}Tc-DMSA (*3,24–26*).

To evaluate quantitatively the amount of functional renal mass removed and the individual renal function after tumor enucleation, 24 operated and 24 contralateral kidneys were studied by two sequential QDMSA examinations. One study was conducted before surgery, and the second study was conducted 1 to 6 mo after surgery. A statistically significant decrease in the functioning renal volume was found representing an average of 17.8% volume loss in the operated kidneys. The mean renal functioning volume was 207 ± 46 mL before surgery and 170 ± 46 mL after surgery. This probably represents the loss associated with healthy renal tissue that was removed around the tumor.

This functional parenchyma loss caused an average decrease of 20.7% in the individual renal function as measured by the renal uptake of ^{99m}Tc-DMSA (13.0% ± 2.9% before and 10.3% ± 3.0% after surgery). However, there was no change after surgery in the %ID per cubic centimeter of renal tissue of operated kidneys and in the volume, %ID per cubic centimeter or uptake of the contralateral normal kidneys. These findings indicate that the limited amount of functional renal tissue removed by tumor enucleation caused no adaptive hyperfunction. This technique may be used for pre- and postoperative assessment of individual renal function mainly in patients with a single kidney or a poorly functioning contralateral kidney.

CONCLUSION

The results suggest that QDMSA is a noninvasive method that is able to assess changes in individual renal function. An average loss of 17.8% in parenchymal volume and of 20.7%

in renal function was observed after tumor enucleation. The limited functional renal parenchyma removed by tumor enucleation had no effect on the opposite kidneys.

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