Kidney Allografts and Remaining Contralateral Donor Kidneys Before and After Transplantation: Assessment by Quantitative ^{99m}Tc-DMSA SPECT

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We used ^{99m}Tc-dimercaptosuccinic acid (DMSA) quantitative SPECT (QDMSA) to assess the function of kidneys before harvesting and after transplantation as well as the function of remaining donor kidneys. **Methods:** Nineteen kidney donors underwent a baseline QDMSA study before nephrectomy. The allografts of these kidneys were studied in recipients at 1 wk, 1–2 mo, and 6–15 mo after transplantation. The kidneys remaining in 16 donors were studied at 1–2 mo and 6–15 mo after harvesting. The parameters obtained in each SPECT study included functional volume, concentration of ^{99m}Tc-DMSA per cubic centimeter of renal tissue, and total kidney uptake. Clinical evaluation and determination of serum creatinine levels took place at the same time as SPECT. **Results:** On the basis of the clinical evaluation, 14 grafts had normal function and 5 were impaired. The mean ± SD of kidney uptake values expressed as percentage of baseline values were 131% ± 30% in normal grafts versus 57% ± 5% in impaired grafts at 1 wk ($P < 0.01$), 173% ± 57% versus 65% ± 10% at 1–2 mo ($P < 0.001$), and 190% ± 50% versus 69% ± 14% at 6–15 mo after transplantation ($P < 0.01$). Uptake values in the donors' remaining kidneys were 159% ± 27% of baseline values at 1–2 mo and 164% ± 30% at 6–15 mo after nephrectomy. Allografts and remaining kidneys showed a similar increase in total kidney uptake as a result of an increase in both functional volume and concentration. **Conclusion:** QDMSA may be a noninvasive assessment tool in kidney transplantation from living donors.

Key Words: transplantation; SPECT; ^{99m}Tc-dimercaptosuccinic acid

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Dimercaptosuccinic acid (DMSA) labeled with ^{99m}Tc is a renal cortical agent that detects the functioning proximal tubular mass. Its uptake correlates with effective renal plasma flow, glomerular filtration rate, and creatinine clearance. Its quantitative measurement is therefore a good index for renal function. Previous studies have shown that ^{99m}Tc-DMSA uptake differentiates between normal and diseased kidneys (*1–3*).

A quantitative SPECT technique has been described by Iosilevsky et al. for in vivo quantitation of radiopharmaceutical concentration and organ volume (*4*). Previous studies have applied this technique for assessment of kidney function using ^{99m}Tc-DMSA as the injected radiopharmaceutical. A good correlation was found between quantitative SPECT ^{99m}Tc-DMSA total kidney uptake and creatinine clearance in patients with a single kidney. The technique was used for assessment of the adaptive changes occurring in functioning kidneys remaining after nephrectomy and was reproducible, with differences of <10% having been observed in healthy volunteers in repeated studies (*5–8*). Quantitative ^{99m}Tc-DMSA SPECT (QDMSA) appears to be a practical noninvasive technique for monitoring changes in individual renal volume and function on follow-up.

An accurate determination of renal mass and function is critical both before transplantation for kidney donor selection and after transplantation for follow-up. In this study, we assessed the potential role of QDMSA in the clinical setting of renal transplantation. The remaining donor kidney and the donated kidney were evaluated before and after transplantation.

MATERIALS AND METHODS

Patients

Paired kidneys from 19 consecutive living donors (8 men, 11 women; age range, 24–71 y; mean age, 41 ± 13 y) were analyzed before nephrectomy (13–56 d; mean, 26.4 ± 14 d) by a QDMSA scan, which served as a baseline study. The kidneys were transplanted in 19 recipients (10 men, 9 women; age range, 20–55 y; mean age, 40 ± 10 y). All allografts were analyzed 1–2 mo after transplantation. Eight allografts were analyzed also at 1 wk after transplantation, and 12 allografts were analyzed at 1 y after surgery. The scintigraphic findings were correlated with clinical outcome and with serum creatinine levels measured at the time of the QDMSA study. The remaining kidney after nephrectomy was studied in 16 donors at 1–2 mo after harvesting and, in 10 of these donors, also at 6–15 mo after surgery.

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QDMSA

SPECT scintigraphy of the kidneys was performed 4 h after intravenous injection of 148 MBq (4 mCi) ^{99m}Tc-DMSA using either single-head or double-headed rotating cameras with all-purpose parallel-hole collimators. Data acquisition lasted 20 min and yielded 120 projections, 3° apart, in a matrix size of 64 × 64. The total number of counts per study was 3–5 × 10^5. Data were reconstructed by the filtered backprojection technique using a Hanning filter with a cutoff of 0.5 cycle per centimeter. Reconstructed images were displayed in transaxial, coronal, and sagittal slices with a slice thickness of 1 pixel (0.68 cm in the 64 × 64 matrix size used). The exact injection dose required for quantitation was obtained by measuring the syringe uptake immediately before and after injection, and a decay correction from time of injection to time of scintigraphy was performed.

The ^{99m}Tc-DMSA concentration and functional volume of the kidney were quantified using a quantitative SPECT technique that has been described previously in detail (*4*,*9*). The method uses an empiric threshold value to separate target from background pixels. The operator selects the reconstructed slices containing the entire functioning kidney tissue that takes up ^{99m}Tc-DMSA. The pixel that contains the maximal number of counts within the kidney is selected by the computer, and the threshold value is expressed as a percentage of the counts within the pixel. The threshold value suitable for ^{99m}Tc-DMSA measurements was empirically obtained by phantom studies and by in vivo measurements versus in vitro measurements in humans and was found to be 43% (*4*,*5*). Only nonzero pixels (activity greater than threshold) are used for volume and concentration measurements. The functional volume (cubic centimeters) is defined as the total number of nonzero pixels multiplied by the slice thickness (1 pixel). Concentration is defined as the percentage of injected dose (%ID) corrected for decay per cubic centimeter of kidney tissue. The total kidney uptake was obtained by multiplying volume by concentration. Functional volume, concentration, and kidney uptake were the 3 parameters used in the results analysis.

Statistical Analysis

The results (mean ± SD) for volume, concentration, and uptake in allografts were expressed as percentage of baseline values before harvesting. Normal functioning allografts were compared with impaired allografts. Normal functioning allografts were also compared with the remaining contralateral single kidneys in donors. The comparisons were made using an unpaired *t* test. The significance of the change in actual concentration, volume, and uptake (concentration × volume) values of kidneys before harvesting and after transplantation was assessed using a paired *t* test. $P < 0.05$ was considered statistically significant.

RESULTS

Transplanted Kidneys

On the basis of clinical outcome and blood creatinine levels measured at the time of the SPECT studies, 14 allografts had normal function (group A) and 5 had impaired function (group B).

Comparison Between Kidneys Before Harvesting and After Transplantation. The concentration measured in group A allografts was significantly higher after transplantation than before harvesting ($P < 0.01$, $t = 3.34$). In group B, the concentration was lower after transplantation than before harvesting. The difference, however, was not of statistical significance, probably because of the small group size. The volume of group A allografts was higher after transplantation than before harvesting (208 ± 35 cm^3 vs. 256 ± 46 cm^3, $P < 0.001$, $t = 4.5$). An increase in volume was also measured in group B allografts but was not of statistical significance, probably because of the small group size (159 ± 20 cm^3 vs. 219 ± 71 cm^3). The total kidney uptake value (concentration × volume) after transplantation, compared with that before harvesting, was significantly higher in group A (22.5% ± 7% vs. 13.4% ± 3.5%, $P < 0.001$, $t = 5.07$) and significantly lower in group B (8% ± 0.9% vs. 13.5% ± 2.6%, $P < 0.01$, $t = 5.58$).

Comparison Between Normal and Impaired Allografts. Table 1 summarizes the comparison of total kidney uptake in normal and impaired allografts. Normal allografts had a significantly higher uptake at all times after transplantation. The concentration of ^{99m}Tc-DMSA was 60% ± 16% of baseline values in group B allografts and 131% ± 55% of baseline values in group A allografts ($P < 0.05$, $t = 2.42$) at 1–2 mo after transplantation. Group A and B allografts showed a similar increase in kidney volume relative to baseline measurements: 125% ± 35% in impaired allografts and 128% ± 23% in normal allografts.

Remaining Contralateral Donor Kidneys

Uptake values in the remaining donor kidneys were 159% ± 27% (range, 108%–208%) of baseline values at 1–2 mo after nephrectomy and 164% ± 30% (range, 120%–206%) at 6–15 mo. Uptake values in these remaining kidneys at 1–2 mo after nephrectomy were 82% ± 11% (range, 60%–99%) of the total uptake measured in both kidneys before nephrectomy.

Table 2 and Figure 1 summarize the uptake, functional volume, and concentration of ^{99m}Tc-DMSA in normal functioning single kidneys, which included normal allografts ($n = 14$) and remaining donor kidneys ($n = 16$). Uptake values measured in normal functioning allografts and remaining donor kidneys did not differ significantly either at

TABLE 1
^{99m}Tc-DMSA Total Kidney Uptake in Normal and Impaired Allografts

Allograft type	Time after transplantation		
	1 wk	1–2 mo	6–15 mo
Normal ($n = 14$)	131% ± 30.1% 80%–158% ($n = 4$)	173% ± 57% 64%–275% ($n = 14$)	190% ± 50% 128%–279% ($n = 9$)
Impaired ($n = 5$)	57% ± 5% 53%–65% ($n = 4$)	65% ± 10% 50%–80% ($n = 5$)	69% ± 14% 58%–88% ($n = 3$)
P	0.01	0.001	0.01

Uptake data are expressed as percentage of baseline values (mean ± SD and range) before kidney harvesting.

TABLE 2
QDMSA Results in Normal Allografts and in Donors' Remaining Kidneys After Nephrectomy

	Time after nephrectomy					
	1–2 mo			6–15 mo		
Parameter	Graft kidney	Donor kidney	*P*	Graft kidney	Donor kidney	*P*
No. of patients	14	16		9	10	
Uptake						
Mean	173%	159%	NS	190%	164%	NS
SD	57%	27%		50%	30%	
Range	64%–275%	108%–208%		128%–279%	120%–205%	
Concentration						
Mean	138%	145%	NS	151%	140%	NS
SD	49%	22%		45%	19%	
Range	54%–233%	103%–181%		105%–243%	102%–170%	
Volume						
Mean	125%	109%	0.01	121%	120%	NS
SD	19%	11%		17%	14%	
Range	88%–157%	82%–124%		83%–142%	90%–139%	

Data are expressed as percentage of baseline values before kidney harvesting and transplantation. Probability values are for comparison between allografts and remaining donor kidney after nephrectomy using unpaired *t* test.
NS = not statistically significant.

1–2 mo or at 6–15 mo after surgery. Both allografts and remaining donor kidneys showed an increase in volume relative to the volume measured before harvesting. Allografts showed a higher increase in volume than did remaining donor kidneys at 1–2 mo after surgery (125% ± 19% vs. 109% ± 11%, $P < 0.01$, $t = 2.77$). A sizable hematoma was probably the cause for the single normal allograft that decreased in volume compared with the baseline volume measured before harvesting. At 6–15 mo after surgery, allografts and donor kidneys showed a similar increase in volume relative to baseline values (121% ± 17% and 120% ± 14%, respectively). Allografts and remaining donor kidneys also showed a similar increase in the concentration of ^{99m}Tc-DMSA per cubic centimeter, compared

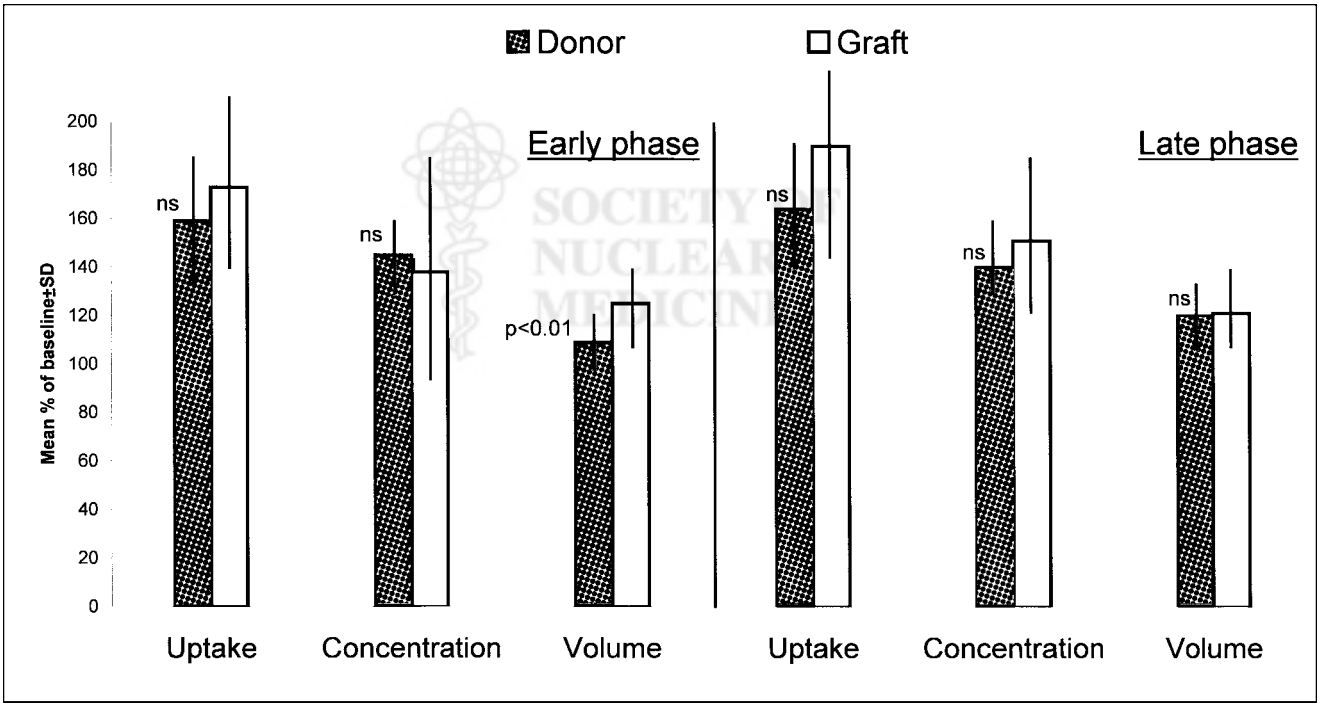

FIGURE 1. Comparison of total kidney uptake, concentration, and volume of ^{99m}Tc-DMSA in normal allografts and in donors' remaining kidneys early (1–2 mo) and late (6–15 mo) after transplantation. ns = not statistically significant.

with the concentration in remaining donor kidneys, at 1–2 mo and 6–15 mo after surgery.

DISCUSSION

Nephron mass and renal function have a major impact on the long-term outcome of kidney transplantation. Their accurate determination is essential both in selection of kidneys for donation and in monitoring of transplantation results. After renal transplantation, patients are often evaluated with radionuclide renal function studies and sonography. The goal of these studies is, however, mainly to assess whether possible complications such as ischemic damage, acute tubular necrosis, and urine leakage are present. Sequential radionuclide function studies may provide data on effective renal plasma flow, excretory index, and glomerular filtration rate, parameters that change when the graft is diseased or responding to treatment (*10–12*). These function studies were also suggested as predictors for survival of cadaver grafts, which are frequently associated with acute tubular necrosis, but not of living related donor grafts, which only infrequently have this complication (*12*). These measurements may be labor intensive, and for more accurate assessment, the external measurement of renal activity should be supplemented by laboratory measurements of blood and urine. Some publications suggest that the indication for serial scintigraphic monitoring for grafts is even less certain (*13*).

In the current study, we assessed the potential use of a practical, noninvasive quantitative SPECT technique (QDMSA) in the clinical setting of living related donor kidney transplantation. The parameters determined using this technique included functional kidney volume and the concentration of the cortical agent ^{99m}Tc-DMSA per gram of tissue (*4*). The total kidney ^{99m}Tc-DMSA uptake obtained by multiplying these 2 parameters is an index of renal function and has been shown to correlate with effective renal plasma flow, glomerular filtration rate, and creatinine clearance (*1–3,5*). The technique is reproducible, and differences of $<$10% were observed in healthy volunteers in repeated studies (*8*). It is, therefore, suitable for serial monitoring of renal function as well.

Kidney donors underwent QDMSA studies, and the function and volume values measured before harvesting were used as points of references for assessing changes associated with kidney harvesting and transplantation. Total ^{99m}Tc-DMSA uptake was significantly different in normal functioning and impaired allografts. Normal functioning allografts maintained their function immediately after transplantation and by 1 mo had already gained compensatory uptake values of 173% $\pm$ 57% of the baseline values before harvesting. In contrast, impaired grafts failed to achieve the uptake values that were measured before transplantation and did not improve significantly with time. These results suggest that uptake measured as early as 1 wk after transplantation can predict future graft function.

The change in concentration and uptake found in normal allografts resembled that found in single kidneys remaining in the donor; that is, both types of single kidneys, the donated transplanted kidney and the remaining contralateral kidney, showed a compensatory increase in function compared with their function before the transplantation. Kidney transplants reached even higher functional volumes early after transplantation than did the remaining donor kidneys. These findings most likely reflect relatively rapid compensatory mechanisms similar to those suggested in animals after nephrectomy and agree with human studies that have shown that, although renal mass is halved after uninephrectomy, the glomerular filtration rate increases to 70%–78% of the preoperative value within days to weeks. The level of renal function stabilizes and is maintained without any demonstrable decline in function (*7,14–20*). Essential to this end, however, is proper selection of donors and kidneys. Measurement of functional volume in potential donor kidneys might have an important role in the selection process before kidney transplantation, because the functioning nephron mass is a major factor in transplantation outcome (*21–25*). In the routine search for kidney donors, selection of suitable kidneys usually depends on donor age, disease history, blood and urine findings, and, occasionally, sonography findings and on tests assessing the function of each kidney separately, such as split renal function testing. The QDMSA technique presented here noninvasively and quantitatively assesses the function and volume of individual kidneys.

CONCLUSION

QDMSA may be a noninvasive assessment tool for kidney transplantation from living donors. Potential uses in this setting may include selection of donor kidneys with a suitable functioning mass, early assessment of transplantation results, and monitoring of changes in the kidneys of both donors and recipients.

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