Evaluation of the effects of nephrotomy on renal function in clinically normal cats

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Objective—To evaluate the effects of nephrotomy on renal function in clinically normal cats.

Animals—20 specific-pathogen-free, 9- to 11-month-old female mixed-breed cats.

Procedure—Serum chemistry analyses, CBC determinations, urinalyses, microbiologic urine cultures, renal ultrasonography, abdominal radiography, and single-kidney and total glomerular filtration rate (GFR) determinations by use of renal scintigraphy and measurements of plasma disappearance of technetium 99m-diethylenetriaminepentaacetic acid were performed before surgery and at 3, 12, 26, 52, and 78 weeks after surgery in 10 cats that underwent unilateral nephrotomy and in 10 control cats that underwent a sham surgical procedure.

Results—Two cats (1 from each group) did not complete the study, and their data were eliminated from analyses. Unilateral nephrotomy resulted in a 10% to 20% reduction in mean single-kidney GFR, compared with that of nephrotomy contralateral control kidneys. However, mean total GFR in nephrotomy-group cats was not significantly different from that of sham-group cats. Over the 78 weeks of study, mean total GFR declined 34% and 40% in nephrotomy- and sham-group cats, respectively. Adverse events associated with nephrotomy included persistent microscopic hematuria, renal pelvis hyperechogenicity with distant shadowing on ultrasonographic evaluation, dilatation of renal pelves, and hydronephrosis.

Conclusions and Clinical Relevance—Nephrotomy in normal functioning feline kidneys results in a modest relative reduction in renal function, compared with contralateral kidney controls, but has minimal effect on total GFR when compared with sham-operated control cats. However, any detrimental effects of nephrotomy may be magnified in cats with diseased kidneys, which may have little or no capacity for repair or compensation. (Am J Vet Res 2008;69:1400-1407)

Urolithiasis is one of the most common urinary tract disorders encountered in feline practice. Although most feline uroliths are identified in the urinary bladder and urethra, uroliths located in the kidneys (nephroliths) pose unique diagnostic and therapeutic challenges. Nephroliths may be clinically silent and unassociated with substantial morbidity or mortality. Conversely, cats affected with actively enlarging nephroliths may have signs of pain, fever, or renal failure attributable to fibrosis, infection, or urethral outflow obstruction. The optimal method for managing feline nephroliths has not been determined. In humans, extracorporeal shock wave lithotripsy is widely used for the management of nephroliths. However, in a preliminary study of extracorporeal shock wave lithotripsy in 4 cats with nephroliths, 2 stones did not fragment and only partial fragmentation was achieved in the stones of the remaining cats. The ineffectiveness of extracorporeal shock wave lithotripsy in these cats may be related to the finding that the shock wave dose must be substantially reduced in cats, compared with humans and dogs, to minimize shock wave–induced renal injury.

Most feline nephroliths are composed of calcium salts, with calcium oxalate being the most common mineral type. Because nephroliths composed of calcium salts are generally not amenable to medical dissolution, surgical removal by nephrotomy or pyelolithotomy remains the most commonly used methods of managing nephroliths in cats. However, clinical observations suggest that nephrotomy may adversely affect renal morphology in cats with preexisting renal disease. Progressive reduction in kidney size was observed in a cat during a 3-year period following unilateral nephrotomy for removal of multiple calcium phosphate nephroliths. Although the contralateral nonoperated kidney contained a similar number of nephroliths, the nonoperated kidney did not change in size or morphology during the 3-year follow-up period. Unfortunately, renal function was not evaluated in this patient. There have been several short-term studies of the effect of nephrotomy on renal function in dogs. In one 2-day study and another 6-week study of nephrotomy in dogs, investigators observed a 15% to 50% decline in glomerular filtration rate (GFR), compared with presurgical values. In 2 subsequent studies, nephrotomy did not appear to adversely affect GFR in dogs during a 30- to 42-day postoperative observation period. Nephrotomy in humans with nephrolithiasis may be associated with significant declines in renal function. The decline in renal function following nephrotomy was believed to be the result of direct nephron damage; ischemic damage as a result of vascular occlusion; and alterations in nephron...
function as a result of inflammation, edema, neovascularization, fibrogenesis, and wound contraction. Partial recovery of renal function after nephrotomy was believed to be the result of subsiding healing processes, repair of some nephrons, and an increase in function (compensatory hypertrophy) of the surviving nephrons. In contrast to other species, the short- and long-term effects of nephrotomy on renal function in either clinically normal cats or cats with preexisting renal disease have not been investigated.

Although renal function may be assessed by a variety of methods, quantitative estimation of total GFR by urinary or plasma clearance methods is considered the best global indicator of renal function. Total GFR may be estimated by measuring plasma clearance of the radiopharmaceutical technetium 99m-diethylenetriaminepentaacetic acid (99mTc-DTPA). Plasma 99mTc-DTPA clearance has been shown to correlate well with the other methods of estimating total GFR in cats. A disadvantage of this and other plasma and urine clearance methods for estimating GFR is that these tests measure only total GFR. However, the relative contribution of each individual kidney to total GFR (ie, single-kidney GFR) can be determined noninvasively by quantitative 99mTc-DTPA renal scintigraphy. Alternatively, single-kidney GFR may be estimated by simultaneously performing qualitative renal scintigraphy and measuring total GFR by plasma clearance with a single IV bolus injection of 99mTc-DTPA.

On the basis of clinical observations and results of studies in other species, we hypothesized that nephrotomy in clinically normal cats would adversely affect renal function of the operated kidney. The specific aims of this study were to prospectively evaluate the effects of nephrotomy on renal function in clinically normal cats by use of 99mTc-DTPA plasma clearance to estimate total GFR and 99mTc-DTPA renal scintigraphy to estimate relative single-kidney GFR, describe radiographic and ultrasonographic morphologic changes associated with nephrotomy in clinically normal cats, and identify clinical complications associated with nephrotomy in clinically normal cats.

Materials and Methods

Animals—Twenty specific-pathogen-free, healthy female mixed-breed cats between 9 and 11 months of age were acquired from a commercial vendor. The cats were routinely vaccinated and group housed in the University Laboratory Animal Resources facility for the first 16 weeks of the study. After the initial 16 weeks, 18 cats were placed in private homes for the duration of the study. Cats that were not adopted remained group housed in the university facility. All cats were fed the same dry commercial maintenance diet for the duration of the study. The Michigan State University All University Committee on Animal Use and Care approved this study.

Experimental protocol—Cats were randomly assigned to the following 2 groups: the nephrotomy group in which one of the cat’s kidneys underwent a nephrotomy surgical procedure and the sham group in which one of the cat’s kidneys underwent a procedure mimicking nephrotomy but without kidney incision and suturing. Once assigned to the nephrotomy or sham group, the right or left kidney within each cat was randomly assigned to receive the specified group treatment (treatment) or to remain a control (contralateral control). Clinical assessments and testing procedures were conducted for each cat and each kidney within a cat at each of the following 6 times: time 0 (before surgery) and at 3, 12, 26, 52, and 78 weeks after surgery.

Surgical procedures—One day after the preoperative scintigraphy, cats were premedicated with acepromazine (0.05 mg/kg, IM) and butorphanol (0.2 mg/kg, IM) and anesthetized with 1% to 2% halothane in oxygen. All cats received 10 mL/kg/h of lactated Ringer’s solution during anesthesia. All surgical procedures were performed by the same surgeon (CB). Using an aseptic surgical technique, a standard ventral midline celiotomy was performed. In cats in the nephrotomy group, 1 kidney was assigned by random selection to undergo a nephrotomy. The kidney was mobilized from its peritoneal attachment and the renal vessels digitally occluded by the assistant surgeon during the procedure. To access the renal pelvis, an incision was made in the renal capsule along the greater curvature of the kidney, extending not more than two thirds of the length between the cranial and caudal pole. The renal parenchyma was then bluntly dissected by use of a scalpel handle. The 2 halves of the kidney were spread apart by use of a hemostat to expose the renal pelvis. The renal pelvis was visually examined, explored with a hemostat, and flushed with sterile saline (0.9% NaCl) solution. The kidney was closed by manually apposing the 2 halves of the kidney for approximately 1 minute and by placing simple interrupted sutures of 5-0 polydioxanone in the renal capsule, avoiding the renal parenchyma. Total renal ischemia time averaged approximately 10 minutes for all the procedures, during which time the incision, renal pelvis inspection, and closure were completed. Hemorrhage was controlled by gentle digital pressure. The kidney was then placed back into its original position in the abdomen. No procedures were performed on the contralateral control kidney. A routine ovariohysterectomy was performed prior to closure.

In the sham group, 1 kidney was randomly selected to undergo a procedure mimicking nephrotomy without incision and suturing. The selected kidney was mobilized from its peritoneal attachment by which was held by the assistant surgeon who digitally occluded the renal artery and vein for approximately 10 minutes. The kidney was then placed back into its original position in the abdomen. No procedures were performed on the contralateral control kidney. A routine ovariohysterectomy was performed prior to closure.

After surgery, all cats received lactated Ringer’s solution IV (4 mL/kg/h) and buprenorphine (0.01 mg/kg, IM) every 8 hours for the first 24 hours following surgery. The cats were closely monitored during the first 10 days after surgery by means of daily physical examinations and assessment of records of food and water consumption.

Clinical evaluations—A physical examination, CBC determination, serum chemistry analysis, urinalysis, quantitative aerobic microbiologic culture of urine, renal ultrasonography, abdominal radiography, and single-kidney and total GFR determinations by use of renal scintigraphy and measurement of plasma disappearance of 99mTc-DTPA were performed before surgery and at 3, 12, 26, 52, and 78 weeks after surgery in each cat. Survey radiography and ultrasonography were used to evaluate renal morphologic changes associated with nephrotomy and sham nephrotomy procedures. Standard survey lateral and ventrodorsal abdominal radiographic views were obtained for each cat. The length of each kidney in each cat was measured along the longitudinal axis in the ventrodorsal radiographic view and expressed as a
ratio of kidney length to length of the second lumbar verte-
bra as seen on the same radiograph. Renal ultrasonographic
examination was performed by use of a 7.5-MHz linear trans-
ducer probe to evaluate renal morphology and measure kid-
ney length. Longitudinal (sagittal) plane images of each kid-
ney were made with the cat in lateral recumbency, and the
length of the kidneys was measured in centimeters. The same
radiologist (DSR) performed all ultrasonographic examina-
tions and was masked as to the treatment of each cat.

Renal function was evaluated by estimating total and
singly kidney GFRs for each cat at each of the 6 times.
General anesthesia was used to facilitate placement of IV
catheters and collection of urine and blood samples and to
ensure that cats remained motionless during renal scintig-
raphy. For preoperative GFR studies, anesthesia was
induced with isoflurane in oxygen as a single agent admin-
istered by mask. An orotracheal tube was placed, and anes-
thesia was maintained with isoflurane in oxygen. However,
because many cats had varying degrees of muscular spasm
and excitation during recovery from isoflurane alone, all
cats were subsequently sedated with acepromazine
(0.05 mg/kg, IM) and butorphanol (0.2 mg/kg, IM) prior to
the induction of anesthesia with isoflurane for all follow-
up evaluations. An IV catheter was placed in a cephalic
vein for IV administration of fluids and 99mTc-DTPA. A cen-
tral venous catheter was placed in either a jugular vein or
a medial saphenous vein for blood collection. To ensure ade-
quate hydration and support blood pressure during
anesthesia, each cat received a volume of lactated Ringer’s
solution that was equal to 3% of its body weight prior to
clearance studies.20

The relative contribution (%) of each individual kidney
to total GFR was estimated by qualitative renal
scintigraphy of anesthetized cats by use of a round, large
field-of-view gamma camera equipped with a low-energy,
high-resolution parallel hole collimator coupled to a dedi-
cated computer with nuclear imaging software.21 The cam-
era was calibrated before each use with a Cobalt flood
source. Cats were placed in dorsal recumbency with the cam-
era positioned 7 centimeters under the patient and
centered at the kidneys. Approximately 37 MBq of 99mTc-
DTPA (1 mCi in a volume of approx 1 mL saline solution)
was administered by rapid IV injection through the cephal-
ic catheter, followed by 2 mL of heparinized saline solution
flushing the catheter. Radioactivity delivered to each cat
was calculated as the difference between dose activity
before injection and residual syringe activity after injec-
tion, as measured in a well counter.1 Injection time (time 0)
was recorded, and dynamic imaging was initiated simulta-
neously with the 99mTc-DTPA injection by use of the fol-
lowing protocol: 10 s/frame for 60 frames (10 minutes
total) and a 128 × 128 matrix. Frame numbers 6 to 18 were
summed into a static image to draw regions of interest
(ROI) around each kidney. Background correction was per-
fomed. Individual kidney uptake was calculated by use of
frames 6 to 18, which represented the nephrogenic phase
of the study between 60 and 180 seconds after injection.13

The relative contribution (%) of an individual kidney
to the total GFR was estimated by use of the following for-
formula: radioactivity counts in 1 kidney (ROI) × 100/radioactivity counts in both kidneys (sum of the 2 ROIs).

Total GFR was estimated by plasma clearance of 99mTc-
DTPA.20–21 Three EDTA-anticoagulated blood samples were
collected from the central venous catheter at 90, 120, and
180 minutes after 99mTc-DTPA injection. One hundred-micro-
liter aliquots of each plasma sample were analyzed for
radioactivity along with an equal aliquot of 99mTc-DTPA stan-
dard solution in a single-channel analyzer system attached to
a sodium iodide well crystal.1 The standard solution was pre-
pared by placing approximately 1 mCi of 99mTc-DTPA in a vol-
umetric flask and adding distilled water to make a total vol-
ume of 1.000 mL. Activity of each sample was corrected for
decay over time. Total GFR was estimated by constructing a
99mTc-DTPA plasma clearance curve by use of a single-expo-
rential, 1-compartment model. Total GFR results were
expressed as millimeter per minute per kilogram of body
weight.

Quantitative single-kidney GFR (split kidney function)
was estimated by use of the following formula:total GFR
(estimated from the plasma clearance analysis)/100 × individ-
ual kidney percentage GFR (obtained from the qualitative
renal scintigraphy).24 Single-kidney GFR results were
expressed as milliliters per minute per kilogram of body
weight.

Statistical analyses—To describe the effect of nephroto-
my on renal function and kidney length, the following null
hypotheses were tested: in clinically normal cats, no diff-
ence exists in single-kidney GFR or individual kidney length
over time between nephrotomized kidneys and their con-
tralateral controls and no difference exists in single-kidney
GFR or individual kidney length over time between nephro-
tomized kidneys and kidneys subjected to a sham proced-
ure. Outcome variables of interest were single-kidney GFR
and kidney length in clinically normal cats. Summary statistics
were computed for each outcome variable.2 Evaluation of
data for normality and identification of potential outliers was
performed.20 Data were summarized and presented as mean ± SE values. A value of P < 0.05 was considered signifi-
cant.

A multivariable mixed-effects model was used to evalu-
ate this repeated-measures experimental study.21,24 The fixed
effects of group (nephrotomy or sham) and treatment
(surgery or contralateral control) and repeated effects of time
(0, 3, 12, 26, 52, and 78 weeks) were modeled to determine
their association with single-kidney GFR and length. For
each, a direct product autoregressive (first order) covariance
structure was selected to simultaneously account for a poten-
tial correlation between kidneys within each cat and between
repeated measurements over time within each cat. The fully
saturated model was reduced after comparing the difference
between the full and final model –2 log likelihood. An assess-
ment of hypotheses of interest, on the basis of the model
parameters, was then conducted.21,24

Results

Of the 20 cats entering the study, 2 cats (1 from
each group) did not complete the study. One nephro-
tomy-group cat died from trauma shortly after being
stuck by an automobile shortly after the 52-week evaluation.
One sham-group cat was lost to follow-up when the
adoptive owner declined further participation in the
study.

With exception of the 2 cats eliminated from the
study, there were no missing data values in the data set.
Results of physical examinations, CBC determinations,
and serum chemistry profiles were within reference
range limits for all cats at all times. With the exception
of 1 nephrotomy-group cat with cystostecesis-induced
microscopic hematuria, results of presurgical urinaly-
ses were within reference range limits. In nephrotomy-
group cats, microscopic hematuria was observed in 7
of 9 cats at postsurgery weeks 3, 12, 26, and 78 and in
8 of 9 cats at week 52. In the nephrotomy-group cat,
hematuria was observed in only 1 sham-group cat at
12 weeks after surgery and in 2 sham-group cats at 26
weeks after surgery. Cultures for aerobic bacteria in urine from all cats were negative at all times.

Mean preoperative (time 0) total GFRs for the nephrotomy- and sham-group cats as estimated by plasma clearance of $^{99m}$Tc-DTPA were $3.5 \pm 0.4$ mL/min/kg and $3.5 \pm 0.3$ mL/min/kg, respectively. Mean total GFRs at the final measurement (time 78) for the nephrotomy- and sham-group cats were $2.3 \pm 0.2$ mL/min/kg and $2.1 \pm 0.1$ mL/min/kg, respectively. No significant difference was found in mean total GFR between the nephrotomy and sham-group cats at any of the times assessed (time 0, $P = 0.69$; time 3, $P = 0.74$; time 12, $P = 0.48$; time 26, $P = 0.43$; time 52, $P = 0.43$; and time 78, $P = 0.13$; Figure 1). Similarly, repeated-measures, mixed-model analyses did not reveal any significant association between single-kidney GFR and group (both kidneys in nephrotomy-group cats vs both kidneys in sham-group cats) over time ($P = 0.81$; Table 1). However, a significant 34% and 40% decline was found in total GFR between the preoperative measurement (time 0) and final measurement (time 78) in both the nephrotomy- and sham-group cats, respectively ($P = 0.01$ and $P < 0.001$, respectively). Likewise, repeated-measures, mixed-model analyses revealed a significant overall association between single-kidney GFRs and time ($P < 0.001$).

A significant decrease in single-kidney GFR was identified in the nephrotomy kidneys, compared with their contralateral controls, over the 78-week study period (repeated-measures, mixed-model analyses, $P > 0.001$; Table 2; Figure 2). Mean pretreatment (time 0) single-kidney GFRs for the nephrotomy kidneys and their contralateral controls were $1.7 \pm 0.2$ mL/min/kg and $1.8 \pm 0.2$ mL/min/kg, respectively. Mean single-kidney GFRs at the final measurement (time 78) for the nephrotomy kidneys and their contralateral controls were $1.0 \pm 0.1$ mL/min/kg and $1.2 \pm 0.1$ mL/min/kg, respectively. Overall, this represented a 10% to 20% relative reduction in single-kidney GFR of nephrotomy kidneys, compared with their contralateral control kidneys. This relative reduction in single-kidney GFR was most evident at 26 ($P = 0.11$), 52 ($P = 0.02$), and 78 ($P = 0.10$) weeks after surgery. In contrast, no significant differences in mean single-kidney GFRs were identified over time for sham

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**Table 1—Overall effects of nephrotomy (9 cats) or sham procedure (9) on single-kidney glomerular filtration rate (GFR) over a 78-week study period.***

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Numerator DF</th>
<th>Denominator DF</th>
<th>F value</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group kidneys (N + NC vs S + SC)</td>
<td>1</td>
<td>16</td>
<td>0.06</td>
<td>0.81</td>
</tr>
<tr>
<td>Treatment kidneys (N + S vs NC + SC)</td>
<td>1</td>
<td>16</td>
<td>11.03</td>
<td>0.004</td>
</tr>
<tr>
<td>Group and treatment kidneys (N vs S vs NC vs SC)</td>
<td>1</td>
<td>16</td>
<td>15.27</td>
<td>0.001</td>
</tr>
<tr>
<td>Kidneys (N + NC + S + SC) over time</td>
<td>5</td>
<td>85</td>
<td>10.40</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>(weeks 0 vs 3 vs 12 vs 26 vs 52 vs 78)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Evaluated by use of the final multivariable mixed model of the fixed effects of group (nephrotomy or sham) and treatment (surgery or nonoperated contralateral control) and repeated effects of time (0, 3, 12, 26, 52, and 78 weeks).

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**Table 2—Comparative effects of nephrotomy (9 cats) or sham procedure (9) on single-kidney GFR over a 78-week study period.**

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Difference in mean GFR</th>
<th>SE</th>
<th>DF</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nephrotomy group kidneys (N vs NC)</td>
<td>−0.18</td>
<td>0.03</td>
<td>16</td>
<td>&lt; 0.001</td>
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<tr>
<td>Sham group kidneys (S vs SC)</td>
<td>0.01</td>
<td>0.03</td>
<td>16</td>
<td>0.884</td>
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<tr>
<td>Treated kidneys (N vs S)</td>
<td>−0.07</td>
<td>0.09</td>
<td>16</td>
<td>0.459</td>
</tr>
<tr>
<td>Nontreated kidneys (NC vs SC)</td>
<td>0.12</td>
<td>0.10</td>
<td>16</td>
<td>0.269</td>
</tr>
<tr>
<td>Kidneys (N + NC + S + SC) over time</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0–3 weeks</td>
<td>0.29</td>
<td>0.07</td>
<td>85</td>
<td>0.002</td>
</tr>
<tr>
<td>3–12 weeks</td>
<td>0.12</td>
<td>0.07</td>
<td>85</td>
<td>0.108</td>
</tr>
<tr>
<td>12–26 weeks</td>
<td>0.08</td>
<td>0.07</td>
<td>85</td>
<td>0.269</td>
</tr>
<tr>
<td>26–52 weeks</td>
<td>0.14</td>
<td>0.07</td>
<td>85</td>
<td>0.054</td>
</tr>
<tr>
<td>52–78 weeks</td>
<td>0.10</td>
<td>0.07</td>
<td>85</td>
<td>0.197</td>
</tr>
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</table>

*Evaluated by use of selected linear function estimates computed from the final multivariable mixed model of the fixed effects of group (nephrotomy or sham) and treatment (surgery or nonoperated contralateral control) and repeated effects of time (0, 3, 12, 26, 52, and 78 weeks).

See Table 1 for remainder of key.
kidneys, compared with their contralateral controls (Figure 3), and nephrotomy kidneys, compared with sham kidneys (Figure 4). Mean single-kidney GFRs of nephrotomy contralateral controls were increased, compared with sham contralateral controls, at 26 (P = 0.10), 52 (P = 0.04), and 78 (P = 0.04) weeks after surgery (Figure 5).

Superimposition of the colon on kidneys precluded radiographic assessment of both renal silhouettes in the lateral or ventrodorsal view in 19 of 54 (35%) radiographs. However, mineralization of the renal pelvis was observed radiographically in 1 nephrotomized kidney at 78 weeks after surgery. No abnormalities were observed in any of the kidneys during the study period.

Ultrasonography did not reveal any significant differences in the length of individual kidneys at any of the times assessed (P ≥ 0.2). Morphologic changes in the kidneys observed by ultrasonography included mineralization and dilatation of renal pelves and hydronephrosis. Renal pelvis hyperechogenicity with distant shadowing, likely attributable to mineralization, was observed in 6 of 9 (67%) nephrotomized kidneys at postsurgery week 78. Renal pelvis hyperechogenicity was not observed in any of the control kidneys. Renal pelvis dilatation extending in the direction of the surgical approach was observed in 4 of 9 (44%) nephrotomized kidneys. Of these, 2 had mild, 1 had moderate, and 1 had severe renal pelvis dilatation. No abnormalities were observed in the contralateral kidneys of the nephrotomy- or sham-group cats.

It is also notable that severe unilateral hydronephrosis developed in 1 cat following nephrotomy. Ultrasonographic and scintigraphic findings consistent with obstruction were first observed in this cat 3 weeks after surgery; however, the cause of the obstruction was not evident. The hydronephrosis progressed over the next 12 months and was accompanied by a compensatory increase in renal size and single-kidney GFR in the contralateral kidney (data not shown). No changes in the results of blood and urine tests were noted, and the cat was clinically normal. Unfortunately, this cat died from trauma after being stuck by an automobile shortly after the 52-week evaluation; therefore, data from this cat were excluded from all statistical analyses.

**Discussion**

In both groups of cats, we observed a significant decline in total GFR over the study period. This decline was most evident between the preoperative and 3-week postoperative evaluations. A more gradual...
decline in total GFR was observed over the following 75 weeks. Because the magnitude of change was similar in both groups, factors other than nephrectomy are most likely responsible for the decline in total GFR over time. Factors that may influence GFR include renal injury, gender, advancing age, physiologic variables (eg, diet, hydration, posture, and exercise), and pharmacologic agents.25,30 Although GFR is most accurately estimated in unrestrained animals, the nature of the clearance technique used in our study required that cats remain motionless for a short time; thus, chemical restraint was necessary. Most sedatives and anesthetics are likely to affect GFR by altering renal blood flow or indirectly via changes in the cardiovascular activity, neuroendocrine activity, or both. No standardized anesthetic protocols exist for estimating GFR in cats. Previous studies of renal function in cats involved nonanesthetized animals12,13,14 or animals restrained by use of thiopental sodium,15 pentobarbital sodium,16,21 ketamine hydrochloride;22,23 halothane;25,26 tiletamine hydrochloride and zolazepam hydrochloride (telazol),27 or medetomidine hydrochloride and butorphanol tartrate administration.39 In our study, the first scintigraphic evaluation to estimate preoperative GFR was performed on cats anesthetized by use of isoflurane as a single agent to facilitate catheter placements, collection of samples, and restraint for scintigraphy. No chemical restraint was used during the subsequent 180-minute plasma clearance period. Because many cats had varying degrees of muscular spasm and excitation during recovery from isoflurane anesthesia, premedication with acepromazine and butorphanol was used in all subsequent studies. It is possible that the initial steep decline in total GFR was the result of renal injury induced by anesthesia, surgical procedures, or both. However, preoperative mean total GFRs for the nephrectomy-group cats (3.5 ± 0.4 mL/min/kg) and sham-group cats (3.5 ± 0.3 mL/min/kg) were substantially greater than GFRs estimated by plasma clearance of 99mTc-DTPA reported in other studies21,25,39 of awake or anesthetized clinically normal adult cats (2.02 ± 0.27 mL/min/kg to 2.6 ± 0.72 mL/min/kg). Furthermore, values for follow-up total GFRs in both groups were well within the reported reference range for clinically normal adult cats.21,23,39 Interestingly, in a study of 20 humans anesthetized with isoflurane, nitrous oxide, lorazepam, and fentanyl, values for mean GFR, renal vascular resistance, and filtration fraction at 1 hour after anesthesia were 27% higher than preanesthesia values.40 This significant increase in postanesthesia GFR was attributed to persistently increased glomerular efferent arteriolar vasconstrictor induced by persistently elevated postanesthesia angiotensin II concentrations. Similar studies have not been performed in cats. However, cats anesthetized with isoflurane had increased values for mean heart rate, arterial blood pressure, and systemic vascular resistance 30 to 60 minutes after emergence from anesthesia, compared with preanesthesia values.41 We hypothesized that preoperative GFRs obtained in our study by use of isoflurane as a single anesthetic agent were artificially increased as a result of postanesthesia rebound of GFR during the plasma clearance period. It is also likely that addition of acepromazine and butorphanol premedications in subsequent evaluations mitigated the postanesthesia rebound of GFR. Proof of these hypotheses requires further investigations.

After the initial decrease in total GFR at the 3-week postoperative evaluation, we observed a more gradual decline in GFR in both groups over the following 75 weeks. The reasons for this decline are unknown. At the beginning of the study, all cats were between 9 and 11 months of age. In clinically normal humans and rats, GFR declines with advancing age.26,30 Similar studies have not been performed in cats. However, it is possible that the gradual decline in total GFR may reflect a normal physiologic response to maturation. Alternatively, it is possible that progressive renal injury was induced by surgical procedures and repeated anesthetic events. Unfortunately, the long-term nature of our study and requirement that cats be adopted to private homes precluded postmortem light microscopic examination of operated and unoperated kidneys. Further studies are needed to investigate these hypotheses.

Nephrectomy resulted in a 10% to 20% relative reduction in single-kidney GFR, compared with contralateral control kidneys. Although single-kidney GFRs of nephrectomy kidneys were consistently lower than those of sham kidneys or sham contralateral control kidneys from 3 to 52 weeks after surgery, these differences were not significant. In contrast to differences in single-kidney GFRs between the nephrectomy kidney and its contralateral control, mean total GFR in nephrectomy-group cats remained similar to that of sham-operated control cats. This disparity most likely reflects the ability of the nonoperated contralateral kidney to undergo compensatory hypertrophy in response to the decreased GFR in the kidney subjected to nephrectomy.17,18,42 This would be consistent with the observation of increases in single-kidney GFR of nephrectomy contralateral control kidneys, compared with the sham nephrectomy contralateral control kidneys. Unlike previous studies31,15,38,43 in other species, we chose to incorporate sham-operated kidneys and their contralateral controls as additional controls. Lack of a demonstrable detrimental effect of nephrectomy on single-kidney GFR, compared with sham-operated kidneys or their contralateral controls, may reflect little or no compensatory response in kidneys of sham-operated cats or a sample size that is inadequate to detect small treatment effects (ie, type II statistical error).26 To our knowledge, there are no previously reported studies of the effects of nephrectomy on renal function in cats. Furthermore, it is difficult to directly compare the results of our study with those of previous studies in other species because of the diversity of surgical techniques, experimental designs, anesthetic protocols, methods of estimating GFR, and lengths of follow-up.31,15,38 Nevertheless, the magnitude of decline in single-kidney renal function observed in our study was within the range of those reported in most other studies. In short-term (9 weeks or less) studies,15,38,43 of dogs, pigs, and baboons, unilateral nephrectomies closed with only capsular sutures resulted in 0% to
50% reductions in GFR in the operated kidney, compared with the nonoperated contralateral control kidney. In another study, nephrometyses were performed on dogs that had previously undergone a unilateral nephrectomy. Nephrometysis in the remaining hypertrophied kidneys resulted in a 27% decrease in single-kidney GFR at 3 weeks and a 24% decrease at 6 weeks after surgery, compared with prenephrometysis values. However, in a recent study of bilateral nephrometyses in dogs, an inexplicable 176% increase in total GFR was observed at 3 days after surgery, compared with presurgery values; no significant changes in total GFR were observed at 1, 2, and 4 weeks after surgery, compared with presurgery values.

Morphologic changes and adverse events associated with nephrometysis observed in our study included persistent microscopic hematuria, renal pelvis hyperechogenicity with distant shadowing, dilatation of renal pelvis, and hydronephrosis. In dogs, nephrometysis has infrequently been associated with postoperative hematuria, renal mineralization, nephrolithiasis, suppurative pyelitis, and bacterial urinary tract infection. In our study, renal pelvis hyperechogenicity with distant shadowing was observed ultrasonographically in 67% of nephrometized kidneys. Although postmortem examinations were not performed, renal pelvis hyperechogenicity with distinct distant shadow may be associated with mineralization of renal parenchyma, mineralized blood clots in the renal pelvis, or nephroliths. The frequency of postnephrometysis renal hyperechogenicity observed in our study was substantially higher than the frequency of dystrophic mineralization reported in short-term studies of dogs (0% to 17%). This disparity may be related to the longer duration of our study. Alternatively, the dynamics of wound healing and long-term tissue responses to renal injury in cats may differ from that of dogs. Interestingly, mineralization was a consistent light microscopic feature of renal biopsy sites in cats at 8 weeks after the procedure. Further characterization of healing responses to renal injury in cats and their long-term effects on renal function require additional investigation.

Dilatation of the renal pelvis was observed in 5 of 10 kidneys that underwent nephrometysis. Renal pelvic dilatation most commonly occurs secondary to obstruction or infection. In 4 of 5 kidneys with dilatation, no evidence of obstruction or infection based on results of urinalyses, bacteriologic urine cultures, ultrasonography, and qualitative renal scintigraphy was found. Renal pelvis dilatation in affected kidneys extended along the incision and was most likely the result of surgical separation of the renal parenchyma. Severe unilateral hydronephrosis developed in 1 cat following nephrometysis. Ultrasonographic and scintigraphic findings consistent with obstruction were first observed in this cat at the first (3-week) postoperative evaluation. Although the exact cause of the obstruction could not be identified, most likely a blood clot forming in the renal pelvis after surgery caused an outflow obstruction resulting in atrophy of functional renal parenchyma. Hydronephrosis secondary to blood clot formation has been reported as an infrequent complication of renal biopsy in cats and dogs.

In conclusion, our findings suggest that nephrometysis in a normal functioning feline kidney results in a modest relative reduction in single-kidney GFR in the operated kidney, compared with its contralateral nonoperated kidney, and a minimal effect on total GFR, compared with that of sham-operated control cats. However, we emphasize that the detrimental effects of nephrometysis on renal function may be substantially magnified in cats with diseased kidneys, which may have little or no capacity for repair or compensation. Consequently, careful preoperative evaluation and postoperative monitoring are essential for cats undergoing nephrometysis. Additional studies are required to evaluate adverse effects of nephrometysis on renal function in cats affected with nephrolithiasis or other renal diseases.

References


