Quantitative renal scintigraphy has been validated as a rapid and accurate method for determining the quantitative estimate of GFR in dogs and cats.\textsuperscript{1–3} Quantitation of GFR by use of \textsuperscript{99m}Tc-DTPA in dogs and cats is often used to determine global GFR or GFR for each kidney to detect early impairment of renal function, evaluate response to treatment, evaluate a contralateral kidney prior to nephrectomy, and determine severity of subclinical renal disease in subjects receiving nephrotoxic treatments.\textsuperscript{4}

Glomerular filtration rate is determined by a balance of hydrostatic and colloid osmotic forces acting across the capillary membrane and the capillary filtration coefficient, which is the product of the permeability and filtering surface area of the capillaries.\textsuperscript{5} When mean arterial pressure ranges from 80 to 180 mm Hg, RBF remains constant by intrinsic autoregulation.\textsuperscript{6–8} Autoregulatory mechanisms play an important role in maintaining GFR despite decreases in RBF or decreases in systemic blood pressure,\textsuperscript{9} and the systemic effects of sedation and anesthesia on GFR are thought to be mitigated at the level of the kidneys via these mechanisms. However, hypovolemia and stimulation of the sympathetic nervous system can decrease RBF by increasing renal vascular resistance regardless of renal autoregulation. Autoregulation of RBF is not abolished by the administration of most anesthetic drugs.\textsuperscript{10}

Measurement of GFR by use of nuclear scintigraphy has been described.\textsuperscript{1} It is important that the subject remain motionless for 2 minutes to enable acquisition of the data needed for GFR calculation, although motion correction software can be used to adjust for movement.\textsuperscript{4} In clinical veterinary medicine, sedation protocols are often used to ensure cooperation and safety or...

### Effect of sedation protocol on glomerular filtration rate in cats as determined by use of quantitative renal scintigraphy

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**Objective**—To evaluate the effect of several sedation protocols on glomerular filtration rate (GFR) in cats as measured by use of quantitative renal scintigraphy and to analyze interobserver differences in GFR calculation.

**Animals**—5 cats (1 sexually intact male, 1 neutered male, and 3 sexually intact females).

**Procedures**—Effects on GFR of 3 sedation protocols commonly used at the Iowa State University College of Veterinary Medicine were evaluated. The protocols were medetomidine (11 \( \mu \)g/kg) and butorphanol tartrate (0.22 mg/kg) administered IM; ketamine hydrochloride (10 mg/kg) and midazolam (0.5 mg/kg) administered IV; and ketamine (10 mg/kg), midazolam (0.5 mg/kg), and acepromazine maleate (0.05 mg/kg) administered IM. Results for the 3 protocols were compared with results of GFR measurements obtained in these same cats without sedation (control protocol).

**Results**—No significant difference between GFR measurements was associated with the 3 sedation protocols, compared with GFR measurements for the control protocol. The greatest mean GFR values were for the medetomidine-butorphanol and ketamine-midazolam protocols. There were no significant differences between observers for calculation of GFR.

**Conclusions and Clinical Relevance**—Results suggested that none of the 3 sedation protocols had significant effects on GFR calculated by use of quantitative renal scintigraphy, compared with results for GFR evaluations performed in the cats when they were not sedated. No significant interobserver error was evident. However, the statistical power of this study was low, and the probability of a type II error was high. (Am J Vet Res 2011;72:1222–1225)

### Abbreviations

- \textsuperscript{99m}Tc-DTPA Technetium Tc 99m diethyltriaminepentacetic acid
- GFR Glomerular filtration rate
- QRS Quantitative renal scintigraphy
- RBF Renal blood flow

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to ease discomfort of the patient. Many of the drugs in these protocols exert effects on heart rate and systemic blood pressure. Medetomidine, an α₂-adrenoceptor agonist, causes initial peripheral vasoconstriction via stimulation of α₁-adrenoceptors, which is followed by vasodilation attributable to centrally mediated decreases in activity of the sympathetic nervous system. The increase in systemic vascular resistance may alter RBF.

Medetomidine infusion in sheep decreases RBF significantly, and 1 dose administered IV to dogs decreases GFR. Butorphanol is an opioid that is a weak μ-receptor antagonist or a partial μ-receptor agonist and a relatively powerful κ-receptor agonist. The renal effect of butorphanol is minimal. Administering a combination of medetomidine and butorphanol via IM injection to dogs results in a slight increase in GFR. Ketamine, a dissociative anesthetic, increases heart rate and blood pressure via a secondary increase in centrally mediated tone of the sympathetic nervous system. The increase in cardiac output and vasoconstriction could alter RBF and GFR. Administration of a combination of ketamine and midazolam (a benzodiazepine) reduces the increase in plasma catecholamines induced by administration of ketamine alone and may enable renal autoregulation of RBF. Acepromazine is a phenothiazine tranquilizer that blocks α₁-adrenoceptors in the peripheral circulation. This blockade of α₁-adrenoceptors may lead to vasodilation and prevent vasoconstriction associated with circulating catecholamines (ie, norepinephrine and epinephrine), which may allow the kidneys to autoregulate flow at even lower mean blood pressures.

The effect of sedation protocols on the determination of GFR in dogs by use of nuclear scintigraphy has been described. However, to the authors' knowledge, the effect of sedation on GFR in cats as determined by use of nuclear scintigraphy has not been reported. The purpose of the study reported here was to evaluate effects of several sedation protocols on GFR as measured by use of QRS and to examine the degree of sedation obtained with each protocol. Interobserver differences in calculated GFR were also analyzed.

Materials and Methods

Animals—Six cats (2 sexually intact males, 1 neutered male, and 3 sexually intact females) were obtained from laboratory animal resources at the Iowa State University College of Veterinary Medicine. At the start of the study, a physical examination and routine laboratory evaluations (CBC, blood biochemical analysis, and urinalysis) were performed. All values were within reference limits. However, 1 sexually intact male cat was found to have polycystic renal disease and was excluded from the study. The remaining cats were provided with food and water ad libitum. All protocols were reviewed and approved by the Institutional Animal Care and Use Committee at Iowa State University.

Sedation and monitoring—A randomized crossover design was used. Three sedation protocols commonly used at the Iowa State University College of Veterinary Medicine were evaluated: medetomidine (11 μg/kg) and butorphanol tartrate (0.22 mg/kg) administered IM; ketamine hydrochloride (10 mg/kg) and midazolam (0.5 mg/kg) administered IV; and ketamine (10 mg/kg), midazolam (0.5 mg/kg), and acepromazine maleate (0.05 mg/kg) administered IM. Effects for these 3 protocols were compared with results of GFR evaluations performed in nonsedated cats (control protocol). Each cat was evaluated once for each of the 4 protocols over a 3-week period. The QRS evaluations were performed on each of 4 days with a recovery interval of ≥72 hours between subsequent QRS evaluations. All QRS evaluations were performed at approximately the same time of day (2 PM to 5 PM), and the cats were evaluated in the same order, although the order of protocols was randomized.

Prior to QRS, a physical examination was performed on each cat. Hydration status was assessed subjectively by a board-certified veterinary anesthesiologist. No additional blood biochemical analyses or CBCs were performed. A 22-gauge catheter was placed in a cephalic vein or medial saphenous vein. A 3-cm cuff was placed around the base of the tail, and systolic blood pressure was measured by use of a Doppler flow probe at 0 and 3 minutes after radiopharmaceutical injection. Heart and respiratory rates were also measured at these time points. Sedation score was assessed by use of a semiojective 4-point scale on the basis of recumbency, head position, palpebral reflex, and eye position, as described elsewhere (Appendix).

QRS—The QRS procedures were modified from the methods described elsewhere. A low-energy all-purpose collimator was fitted to a gamma camera. A dose of approximately 2 mCi (74 MBq) of 99mTc-DTPA was used for each procedure; the radiopharmaceutical activity was measured by use of an ion chamber immediately before and immediately after IV injection. Counts were obtained before IV injection with the dose syringe placed on an acrylic resin table and the gamma camera positioned 26 cm below the table. Each cat was placed in dorsal recumbency on the table, and the gamma camera was positioned in contact with the table adjacent to the dorsal aspect of the cat. The radiopharmaceutical was injected, and images were acquired in a 64 × 64 × 16 matrix at 6 s/frame for 6 minutes.

Counts after IV injection were obtained immediately after image acquisition by use of the same procedure described for preinjection counts. The cats were subsequently housed and monitored until dosimetry readings obtained at the level of the kidneys and urinary bladder were <2 milliroentgen/h.

Image evaluation—Scintigraphic images were reviewed at a workstation with nuclear medicine software and evaluated for evidence of movement that might have interfered with GFR calculation. As described elsewhere, summed images were created and regions of interest were drawn around each kidney and around background regions by an investigator (MDW) and another observer. Depth correction was not performed. Percentage dose for each kidney, net kidney counts, and GFR were calculated by use of regression analysis, as described elsewhere.

Statistical analysis—Statistical analysis was performed by use of a commercially available statistics
Multiple measurement techniques have also been reported. Reproducibility of GFR measurements obtained via multiple protocols* and for a control protocol (no sedation).

Table 1—Mean ± SD GFR results determined by use of QRS for 5 cats (1 sexually intact male, 1 neutered male, and 3 sexually intact females) as calculated by 2 observers for each of 3 sedation protocols and for a control protocol (no sedation).

<table>
<thead>
<tr>
<th>Protocol</th>
<th>GFR (mL/kg/min)</th>
<th>Observer 1</th>
<th>Observer 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>No sedation</td>
<td>2.03 ± 0.38</td>
<td>2.60 ± 0.71</td>
<td></td>
</tr>
<tr>
<td>Medetomidine-butorphanol</td>
<td>2.49 ± 1.45</td>
<td>2.82 ± 1.39</td>
<td></td>
</tr>
<tr>
<td>Ketamine-midazolam</td>
<td>2.34 ± 0.42</td>
<td>2.81 ± 0.67</td>
<td></td>
</tr>
<tr>
<td>Ketamine-midazolam-acepromazine</td>
<td>1.79 ± 0.39</td>
<td>2.17 ± 0.63</td>
<td></td>
</tr>
</tbody>
</table>

*The 3 sedation protocols were medetomidine (11 µg/kg) and butorphanol (0.22 mg/kg) administered IM, ketamine (10 mg/kg) and midazolam (0.5 mg/kg) administered IV, and ketamine (10 mg/kg), midazolam (0.5 mg/kg), and acepromazine (0.05 mg/kg) administered IM.

Results

Calculated GFR, sedation score, and blood pressure recorded for each sedation protocol were summarized. There was no significant (P = 0.232) difference between GFR measurements associated with each of the 3 sedation protocols, compared with GFR for the control protocol. However, the greatest mean GFR values were for the medetomidine-butorphanol and ketamine-midazolam protocols (Table 1). Mean sedation score did not differ significantly among the 3 sedation protocols (2.4, 1.8, and 2.2 for the medetomidine-butorphanol, ketamine-midazolam, and ketamine-midazolam-acepromazine protocol, respectively). Similarly, mean ± SD systolic blood pressure did not differ significantly among the control (128.8 ± 24.9 mm Hg), medetomidine-butorphanol (114.0 ± 21.6 mm Hg), ketamine-midazolam (146.4 ± 52.2 mm Hg), and ketamine-midazolam-acepromazine (93.0 ± 23.4 mm Hg) protocols.

Interobserver differences in GFR calculation were analyzed. We did not detect significant (P = 0.066) differences in variation between observers for the region of interest and calculated GFR (Table 1).

Discussion

Analysis of results for the study reported here suggested that the sedation protocols evaluated did not cause changes in calculated GFR as measured by use of QRS, compared with results obtained in healthy, nonsedated control cats. However, the mild differences in GFR among protocols suggest that further investigation is necessary.

Global GFR values calculated for the population of cats in the present study were lower than reported reference values. Global GFR values < 2.5 mL/min/kg are considered indicative of subclinical renal disease. However, global GFR values < 2.5 mL/min/kg have been reported in clinically normal cats. Considerable differences in the reproducibility of GFR measurements obtained via multiple measurement techniques have also been reported.

Several explanations are possible for the low GFR values in the population of cats in the present study. Errors in technique, such as poorly or inaccurately drawn regions of interest for renal or background counts, could have accounted for lower values. The use of an acrylic resin table may have interfered with collection of counts; however, the same device was used for all counts collected and therefore should have had no net effect on GFR calculation. We used a modified technique, with the cats positioned in dorso-lumbar recumbency rather than in lateral recumbency, as has been previously described. This also may have contributed to differences in calculated GFR values because of the relative mobility of the feline kidneys. Although we measured counts for the 99mTc-DTPA remaining in the syringe after IV injection, counts of the 99mTc-DTPA remaining within the catheter were not measured; therefore, they were not included in calculations of GFR. Images were not obtained at the site of injection after the procedure; thus, leakage of radiopharmaceutical into the surrounding tissues at the injection site was not evaluated. These factors may have caused an artifactual decrease in calculated GFR.

Increased protein and caloric intake can increase GFR in partially nephrectomized cats. The cats in this study also had significant increases in blood pressures. The cats in the present study were fed a balanced maintenance diet formulated for cats; however, protein and caloric intake was not measured. It is possible that this could have been a source of error.

Finally, we did not obtain renal biopsy specimens from the cats at the end of the study. Thus, we cannot exclude the possibility that the cats had subclinical renal disease.

Because no significant difference was detected between results of QRS performed by use of sedation protocols, compared with results of QRS for cats receiving no sedatives, the choice of sedation protocol used for QRS may be dependent on the clinical situation. In fractious cats, the use of sedatives administered IM may be of benefit and allow clinicians to insert a catheter into a vein after sedation has been achieved. In cooperative cats that may still move during the procedures, IV administration of sedatives may be most useful, especially if rapid recovery is desired. The administration of ketamine-midazolam IV had the least effect on blood pressure, had a relatively short duration, and was safe and effective. However, there may be some risks in cats with cardiomyopathy.

Differences in interobserver GFR calculations were large, but they were not significant. It is possible that with greater statistical power, this difference could become significant and reflect the effect of interobserver variability in measurement of the region of interest and calculation of GFR by use of QRS.

We concluded that although no significant difference between GFR in sedated and nonsedated cats was detected in the present study, the large SDs and low number of cats included in the study contributed to a low statistical power and the possibility of a type II error. The GFR values calculated for the cats in this study were lower than the reported reference ranges. Although variability in the calculated GFR is multifactorial, the possibility that the regression equation used program. Data did not have a normal distribution; thus, they were logarithmically transformed. A 1-way ANOVA was used to test the hypothesis that sedation protocols* and for a control protocol (no sedation).
References


Appendix

Criteria for a semiobjective sedation score in cats as determined on the basis of recumbency, head position, palpebral reflex, and eye position.

<table>
<thead>
<tr>
<th>Score</th>
<th>Sedation</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>No sedation</td>
<td>NA</td>
</tr>
<tr>
<td>1</td>
<td>Mild sedation</td>
<td>Recumbent, head down, strong palpebral reflex, and normal eye position</td>
</tr>
<tr>
<td>2</td>
<td>Moderate sedation</td>
<td>Recumbent, head down, moderate palpebral reflex, and partial ventromedial eye rotation</td>
</tr>
<tr>
<td>3</td>
<td>Profound sedation</td>
<td>Recumbent, head down, no palpebral reflex, and complete ventromedial eye rotation</td>
</tr>
</tbody>
</table>

NA = Not applicable.