Effects of renal autograft ischemia and reperfusion associated with renal transplantation on arterial blood pressure variables in clinically normal cats

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Objective—To evaluate the effect of renal autograft ischemia and reperfusion associated with renal transplantation on pulse rate and pressure and arterial blood pressure variables in clinically normal cats.

Animals—10 cats.

Procedures—A radiotelemetric implant was placed in each cat to measure hemodynamic variables; baseline data were recorded before surgery. Standard heterotopic renal implantation and contralateral nephrectomy were performed (day 0). Autografts were stored in cold sucrose phosphate solution for 30 minutes (n = 5) or 3 hours (5); cats were anephric during this period. Hemodynamic variables were recorded every 5 minutes for up to 16 days after surgery; mean daily values were calculated.

Results—Data from 6 cats were available for analysis. Two cats developed ureteral obstructions and became azotemic at 111 and 197 hours after kidney reperfusion. Mean serum creatinine and BUN concentrations were greater than baseline values on days 1 and 2. Although changes from baseline hemodynamic values were detected in some cats, arterial blood pressure measurements did not change significantly from baseline at any time point. Compared with baseline data, mean pulse rate was increased on days 1 and 2 and days 6 through 12; mean pulse pressure was increased on days 1 and 2.

Conclusions and Clinical Relevance—In clinically normal cats, hypertension was not induced by clinically relevant periods of ischemia-reperfusion injury of renal autografts and was not an inherent consequence of the transplantation process. Causes of marked posttransplantation hypertension in cats with chronic kidney disease require further investigation. (Am J Vet Res 2009;70:1426–1432)

In humans and other animals that undergo renal transplantation, the development of hypertension is common.1–3 In a study1 of 1,666 human renal transplant recipients, only 3.5% were normotensive without medication at 1 year after transplantation. The etiology of chronic posttransplantation hypertension in humans is multifold and includes genetic factors, concomitant disease, immunosuppressive treatment regimens, graft ischemic injury, the presence and severity of chronic allograft nephropathy, lifestyle, and effects of the native kidneys.1 In people, acute hypertension following renal transplantation has also been reported and has been identified as a risk factor for early acute graft rejection and delayed graft function.4,5

In cats, the prevalence of and risk factors for development of chronic hypertension following renal transplantation are unknown; however, the causes of posttransplantation hypertension in cats are likely similar to those in human transplant recipients. In 2 studies3,6 of cats that underwent renal transplantation, acute severe hypertension (systolic arterial blood pressure ≥ 170 mm Hg) developed during the perioperative period in 9 of 30 (30.0%) and 21 of 34 (61.7%); treatment of hypertension resulted in control of acute neu-
rologic signs following transplantation in some of those affected cats. Similar to findings in human transplant recipients, acute severe hypertension often develops immediately following graft reperfusion and persists after surgery in cats that undergo transplantation. In addition to hypertensive encephalopathy, chronic post-transplantation hypertension contributes to other end organ damage and may theoretically increase anastomotic complications early in the postoperative period.

The cause of acute hypertension following renal transplantation in humans or cats is unknown. Suggested causes include persistent activation of the renin-angiotensin-aldosterone system or other blood pressure regulatory factors from the native kidneys, uremic vasculitis, surgery-related pain, ischemia-reperfusion injury to the allograft, and inflammation. Another potential cause of hypertension following transplantation is volume overload, particularly given that systemic neurohumoral blood pressure regulatory systems are disrupted in association with CKD. Furthermore, renal artery stenosis or patchy areas of ischemia in the renal parenchyma secondary to arterial vasospasm or microembolism may cause release of renin from normal (unaffected) renal parenchyma. Although hypertension is common in cats with CKD, there is no apparent association between pre- and postoperative hypertension.

Because CKD in cats can induce several interrelated metabolic and vascular changes, identification of a specific cause of posttransplantation hypertension is difficult. The purpose of the study reported here was to evaluate the effects of renal autograft ischemia and reperfusion associated with renal transplantation on DBP, SBP, MBP, PR, and PP in clinically normal cats during a period of at least 14 days following surgery. Our hypothesis was that renal transplantation in cats would result in increases in PP and arterial blood pressure variables without significant changes is PR, compared with preoperative baseline values.

Materials and Methods

Animals—Ten purpose-bred young adult (6-month-old) cats were used. The mean ± SEM weight of the cats was 2.5 ± 0.07 kg. Each cat was considered clinically normal on the basis of results of a physical examination, CBC, serum biochemical analyses, and urinalysis prior to the study. Certain data obtained from some of these cats have been published. All procedures were approved by the University of Georgia Animal Care and Use Committee.

Telemetry catheter system—Each cat was anesthetized, and a radiotelemetry catheter was aseptically implanted in the right carotid artery of each cat. Cats were premedicated with acepromazine (0.01 mg/kg, IM), buprenorphine (0.04 mg/kg, IM), and ketamine hydrochloride (7 mg/kg, IM). Anesthesia was induced with isoflurane delivered via a face mask. Cats were intubated, and anesthesia was maintained by use of isoflurane delivered in 100% oxygen. An approximately 4-cm-long cutaneous incision was made longitudinally at the ventral cervical midline between the cricoid cartilage and the thoracic inlet. The paired sternohyoideus muscles were separated on midline. The carotid artery was isolated with 2 lengths of 4-0 silk suture. An arteriotomy was performed, and the telemetry catheter was advanced retrograde approximately 3 to 4 cm. Stay sutures were used to ligate the carotid artery around the catheter. The transmitter portion of the catheter was sutured to the musculature of the ventral aspect of the neck with 3-0 polypropylene suture. The sternohyoideus muscles, subcutaneous tissue, and skin were closed with 4-0 polypropylene suture in a simple continuous pattern.

After catheter implantation, cats were given buprenorphine (0.03 mg/kg) orally every 12 hours for 24 hours. Every 2 hours for the first 6 hours after surgery, then every 8 hours for the next 42 hours, a subjective scoring system score was used by 1 of 3 investigators (CWS, ADM, or MMG) to assess discomfort (Appendix). An additional dose of buprenorphine (0.02 to 0.04 mg/kg) was given to any cat that was assigned a score > 8 (maximum possible discomfort score, 15).

Cats were housed individually, fed standard diets, and given water ad libitum. Each cage was equipped with 3 radiotelemetry receivers. Cat data, along with ambient barometric pressure data, were routed through two 20-channel matrices to a computer. Values of PR, PP, DP, SBP, and MBP were acquired and stored by use of a software program. For all parameters in each cat, hemodynamic data were recorded for 30 seconds every 5 minutes.

For all variables of interest, baseline preoperative data in each cat were recorded. Radiotelemetry catheters were placed a minimum of 4 days prior to renal transplantation, and a minimum of 2 days was allowed after catheter placement prior to accumulation of baseline data. If any cat required additional analgesic administration at > 48 hours after catheter implantation, a minimum of 12 hours was allowed to elapse after the final analgesic drug administration prior to recording baseline data. To establish baseline data, hemodynamic data were recorded for 30 seconds every 5 minutes. Daily means of these data were calculated for every cat and for all study cats. For baseline data, the daily mean value for all cats was used in the statistical analysis; days prior to transplantation were assigned a negative number with day 0 designated as the day of transplantation. For each day after transplantation (days 1 through 15), mean values of each variable in all cats were computed for each 6-hour period for comparison with the daily means determined during the baseline period.

Renal transplantation—Each cat underwent a standard heterotopic renal autotransplantation and contralateral nephrectomy (day 0). Anesthesia was induced and maintained with the regimen used for radiotelemetry catheter placement, except all cats received crystalloid fluids IV at a rate of 10 mL/kg/h for the first hour, followed by 5 mL/kg/h thereafter. Hetastarch was also administered (10 mL/kg) to all cats during the anesthetic period, and body temperature was maintained by use of a hot water blanket and a hot air patient warming system. Cats were kept at a surgical plane of anesthesia (stage III; light plane) except during periods of cold storage of the autografts when cats were kept at a lighter plane of anesthesia (stage III; light plane). Depth of anesthesia was monitored by evaluation of eye position,

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jaw tone, heart rate, respiratory rate, and blood pressure variables. Anesthesia and fluid rate were adjusted to maintain MAP > 60 mm Hg.

A midline laparotomy was performed. The left renal artery was inspected. If a single left renal artery was present, the left kidney was selected for transplantation preferentially; a standard nephrectomy was performed on the kidney that was not selected for transplantation. The renal artery and vein of the kidney selected for transplantation were isolated. The associated ureter was isolated to the urinary bladder and harvested with the ureteral papilla intact. The renal artery and vein were clamped and transected. The kidney was flushed with an ice-cold (approx 4°C) sucrose phosphate solution until the renal parenchyma was uniformly blanched and the renal vein effluent appeared clear. The autograft was then placed in a bowl containing ice-cold (approx 4°C) sucrose phosphate solution surrounded by a frozen slush of saline (0.9% NaCl) solution. Of the 10 kidneys removed for transplantation from the 10 cats, 5 were stored for 30 minutes and 5 were stored for 3 hours in the ice-cold solution prior to implantation; the cats were anephric during the storage period. The caudal vena cava was partially occluded, and the renal vein was sutured end-to-side with 10-0 polyester suture in 2 simple continuous suture lines. The caudal aorta was then clamped, an aortotomy was performed, and the renal artery was sutured with 9-0 nylon in 2 simple continuous suture lines. The clamps were released, and additional simple interrupted sutures were used as necessary to control hemorrhage. If needed, acepromazine (approx 0.025 to 0.05 mg) was used topically to control arterial vasospasm. A 4-mm-diameter defect was made in the seromuscular layer of the bladder with a skin punch. The bladder mucosa was incised, and a mucosal defect was created to approximate the shape of the ureteral papilla. By use of 8-0 polypropylene suture, the ureteral papilla was sutured to the bladder in 2 layers with simple continuous suture lines.

During and immediately after surgery, cats were given hydralazine hydrochloride SC to effect if SBP values were > 180 mm Hg (ie, 1-mg injection, followed by a 1.5-mg injection if still hypertensive, followed by a 2.5-mg injection if still hypertensive).

Following transplantation, a transdermal fentanyl patch (25 μg of fentanyl/h) was applied to the skin of the lateral abdomen of each cat. Analgesia was augmented via SC administration of hydromorphone (0.1 mg/kg) as needed (on the basis of discomfort score assigned during monitoring [Appendix]). Lactated Ringer’s solution (60 to 70 mL/kg/d) was administered SC for the first 48 hours after surgery or until the cat started eating and drinking. To assure the well-being of the cats, each animal was monitored twice daily for signs of pain (discomfort score assigned) and to assess appetite, thirst, urination, and defecation. Serum creatinine and BUN concentrations were measured once daily for the first 6 days, then on days 10 (± 2) and 15 (± 1). Each cat was euthanized by use of an IV injection of euthanasia solution’ 15 (± 1) days after transplantation, and a complete necropsy was performed by 1 pathologist (CAB).

Statistical analysis—A repeated-measures ANOVA that accounted for multiple observations for each cat was used to test for differences in baseline and daily mean hemodynamic values as well as differences between serum creatinine and BUN concentration from baseline (day 0) and days 1, 2, 3, 4, 5, 6, 10 (± 2), and 15 (± 1). For hemodynamic data, the mean of the daily baseline values was compared with the 6-hour means of a particular posttransplantation day. The full model included a fixed factor of time and a random factor of cat. Multiple comparisons were adjusted for by use of a Dunnett test. An unstructured covariance structure was used in all repeated-measures models. A repeated-measures model was evaluated for each cat individually and for the mean values of all 6 cats. All hypothesis tests were 2-sided, and the significance level was α = 0.05. Analysis was performed by use of statistical software. Data are described as mean ± SEM and range.

Results
Radiotelemetry catheter placement was performed without complication in all cats. No cat required additional analgesic treatment > 24 hours after catheter placement. Preoperative baseline data were collected for at least 40 hours in each cat (mean ± SEM, 111 ± 68 hours [range, 40 to 239 hours]).

With regard to heterotopic renal autotransplantation and contralateral nephrectomy, all cats survived the perioperative period. There were no major intraoperative complications in any cat. The left kidney was autotransplanted in all cats. In all cats, no additional abnormalities were detected at the anastomosis site at the time of abdominal closure.

Three cats died in the early morning following surgery (day 1) and were found dead in their cages. On the basis of telemetry data, it was determined that these 3 cats became increasingly hypotensive prior to death. At necropsy, 2 cats had free abdominal blood and an extravascular thrombus at the anastomosis site. The cause of death in the third cat could not be determined because there was no free abdominal fluid and the cat appeared normal the night before (day 0). A fourth cat began vomiting, became dyspneic, and had detectable crackles in all lung lobes on the evening of day 2. The serum creatinine concentration in this cat was 1.4 mg/dL on day 1 and 2.1 mg/dL on day 2. At necropsy, the cat had pulmonary changes consistent with aspiration pneumonia and intravascular renal artery thrombosis. Data obtained from these 4 cats were excluded from analysis.

Of the 6 cats that survived, 2 cats (cats 1 and 5) developed obstructions in the distal portion of the transplanted ureter secondary to periureteral fibrovascular proliferation at the neoureterocystostomy site. These cats were euthanatized when the serum creatinine concentration reached 8 mg/dL. Data from these cats were censored when these cats became azotemic (serum creatinine concentration > 2.1 mg/dL) at 111 and 197 hours after kidney reperfusion. Among the 6 cats that survived, the duration of autograft cold ischemia was 30 minutes and 3 hours for 4 and 2 cats, respectively.
Cat 3 became anemic and hypotensive at 5 hours after kidney reperfusion and required a fresh whole blood transfusion. Cat 4 developed uroperitoneum following surgery, which resolved after 3 days by use of an indwelling urinary catheter. In cat 3, the ureteral papilla was damaged during harvest of the left kidney; thus, a mucosal apposition technique was used for the neoureterocystostomy.

Among the 6 cats, mean time to complete anastomosis was 83 ± 5.2 minutes (range, 70 to 102 minutes). Cat 5 was administered hydralazine (1.0 mg, SC, and then 1.5 mg, SC, 10 minutes later) just prior to extubation; this cat responded well to the second dose and did not require additional doses.

Generally, serum creatinine concentration was increased immediately after surgery and peaked at day 2 (mean serum creatinine concentration, 3.1 ± 0.84 mg/dL [range, 1.5 to 6.7 mg/dL]; Figure 1). Compared with the baseline value, mean serum creatinine concentration was significantly elevated on days 1 (P = 0.020) and 2 (P = 0.002). In the individual cats, serum creatinine concentration returned to reference limits (0.9 to 2.1 mg/dL) by day 3 to 6. In all cats, serum creatinine concentration was within reference limits at day 6. Serum creatinine concentrations in cats that received a renal transplant after the kidney underwent 30 minutes of cold ischemia (n = 4) did not differ significantly from concentrations in cats that received a renal transplant after the kidney underwent 3 hours of cold ischemia (2).

Similar to changes in serum creatinine concentration, serum BUN concentrations were also significantly elevated on days 1 (P = 0.013) and 2 (P = 0.005) and gradually returned to baseline concentrations by the conclusion of the experimental period (Figure 1).

A fentanyl patch was applied to each of the 6 cats after transplant surgery; none of the cats required additional analgesia after 24 hours. Hemodynamic data were recorded after transplantation while the fentanyl patch was in place (patch was removed on day 3). On

**Figure 1**—Mean ± SEM serum creatinine (A) and BUN (B) concentration in 6 cats before and after renal autotransplantation and contralateral nephrectomy. Autografts were stored in cold sucrose phosphate solution for 30 minutes (n = 4) or 3 hours (2) prior to transplantation; cats were anephric during this period. The day 0 datum point represents the preoperative baseline value (day 0 was the day of transplantation), and other datum points are the mean values for each 24-hour period after kidney reperfusion. The number of cats from which data were collected at each time point varied from 2 to 6. *For a given variable, value at this time point is significantly (P < 0.05) increased, compared with the day 0 value.

**Figure 2**—Mean ± SEM PR (A) and PP (ie, SBP – DBP; B) measured by use of a radiotelemetric implant in 6 cats before and after renal autotransplantation and contralateral nephrectomy. Autografts were stored in cold sucrose phosphate solution for 30 minutes (n = 4) or 3 hours (2) prior to transplantation; cats were anephric during this period. A baseline value was derived from the mean of daily values prior to day 0 (day 0 was the day of transplantation), and other datum points are the mean values for each 24-hour period after kidney reperfusion. The number of cats from which data were collected at each time point varied from 2 to 6. *For a given variable, value at this time point is significantly (P < 0.05) increased, compared with the baseline value.
daily values prior to day 0 (day 0 was the day of transplantation), and other datum points are the mean values for each 24-hour period after kidney reperfusion. The number of cats from which data were collected at each time point varied from 2 to 6. There were no significant differences between pre- and postoperative values for any variable at any time point.

The distal obstruction of the ureter in the remaining cats was characterized histologically by extensive fibrovascular proliferation at the implantation site, which extended around the ureter, with local purulent inflammation and markedly edematous bladder mucosa.

Discussion

Results of the present study indicated that renal autotransplantation and contralateral nephrectomy do not induce clinically relevant changes in arterial blood pressure variables during the 2-week period following surgery in clinically normal cats. Thus, it seems unlikely that the cause of hypertension in cats with naturally occurring CKD that undergo renal transplantation is a result of ischemia-reperfusion graft injury or a consequence of standard surgical technique. This statement is further supported by the fact that the intervals required to complete anastomosis for the autografts in the present study were longer than ideal, which resulted in secondary warm ischemic injury. Furthermore, 2 of the autografts underwent a prolonged period of cold ischemia, yet this injury was not associated with the development of postoperative renal dysfunction or hypertension. The hypertensive responses in cats with naturally occurring CKD that undergo renal transplantation are therefore likely secondary to other factors.

In people, allograft dysfunction and the associated fluid retention and increased peripheral vascular resistance results in systemic hypertension.2 In the cats of the study reported here, there was evidence of transient, mild allograft dysfunction following renal transplantation and only a numerically slight and nonsignificant increase in MBP. Therefore, we are unable to draw conclusions regarding the effect of allograft dysfunction as a cause of hypertension following renal transplantation in cats.

Renal artery stenosis is a common cause of chronic hypertension in people that receive renal transplants.2 Generally, hypertension associated with renal artery stenosis is detected 3 months to 2 years after transplanta-
The prevalence of renal artery stenosis was not evaluated in the present study; nevertheless, it may have a role in the development of chronic hypertension in feline renal transplant recipients.

In cats that receive renal transplants, native kidneys may have a role in the genesis or maintenance of systemic hypertension that develops following surgery via multiple mechanisms, such as chronic activation of the renin-angiotensin-aldosterone or sympathetic nervous system. In humans, the efficacy of bilateral native nephrectomy at the time of renal transplantation with regard to control of postoperative hypertension is controversial. Some data indicate an important benefit, whereas other data do not. Because bilateral nephrectomy is likely to increase the risk of postoperative uremia in cats with postoperative complications, it is generally not accepted in veterinary medicine, especially in centers where hemodialysis is unavailable.

In the cats in the present study, PR was elevated from baseline values following surgery. In the immediate postoperative period, this likely reflected a response to reduced blood volume and postoperative anxiety or discomfort. The reason for the sustained increase in PR at days 6 through 12 is less clear. Cats did not receive analgesics during this period, but signs of pain were not detected during incision-site palpation or other aspects of daily physical examination and discomfort scoring. Packed cell volume and total protein concentration were not evaluated during the second week after transplantation, and there was no clinical evidence of hypovolemia in any cat; therefore, we cannot exclude hypovolemia as a cause of increase in PR.

The effects of unilateral nephrectomy alone on arterial blood pressure variables, PR, and PP have not been evaluated in cats, to our knowledge. Laboratory studies in cats with experimentally induced systemic hypertension have involved renal wrapping (a method of inducing hypertension by wrapping a kidney with cellophane) or partial renal infarction. In dogs, nephrectomy alone resulted in no change in blood pressure variables during the immediate 6-hour postoperative period or more long term (over 2 weeks). In healthy humans that undergo nephrectomy, there is a small (2.4 mm Hg) long-term increase in SBP but no evidence of progressive renal dysfunction.

The telemetry catheter system used in the study of this report provided consistent and accurate arterial blood pressure measurements in cats. The telemetry catheter was placed in a carotid artery in each study cat because of the potential to disrupt the catheter tip during aortic clamping and arterial anastomosis. Additionally, carotid artery placement of the catheter allowed for evaluation of blood pressure during the period of aortic clamping. To our knowledge, carotid artery placement of the telemetry catheter system in cats has not been reported. Carotid artery placement was not associated with catheter-related complications. This technique may prove useful for blood pressure measurements in future laboratory studies involving renal transplantation in cats and in cats with naturally occurring CKD that receive transplants, particularly in those cats with preexisting systemic hypertension.

A potential source of error in the present study was the fact that the duration of autograft cold ischemia was not uniform for all cats. Of the 6 kidneys removed for transplantation, 2 underwent a longer period of cold ischemia than did the other 4; however, the prolonged period of cold ischemia did not have an effect on postoperative hypertension in the recipient cats. Also, 1 cat received 2 doses of an antihypertensive drug (hydralazine), which may have been a confounding factor. This drug was given to prevent hypertensive complications and allow for long-term arterial blood pressure evaluation. The hypertensive episode was just prior to extubation and may represent, at least in part, a strong sympathetic tone resulting from perioperative disorientation and discomfort. Regardless, the 2 doses were administered to only 1 cat over a 10-minute period, which was therefore unlikely to influence the outcome of the study. After renal transplantation, cats received fluid therapy SC in an attempt to maintain hydration and normovolemia. This treatment may have been inadequate in some cats, potentially resulting in hypovolemia and hypotension. The lack of IV administration of fluids represents a deviation from the standard of care in clinical transplant cases and may be a source of error.

The data obtained in the present study indicated that renal transplantation does not substantially influence arterial blood pressure variables in clinically normal cats during the initial 2-week period after transplantation. Further investigation of posttransplantation hypertension is warranted in cats with systemic abnormalities resulting from CKD because structural or functional changes within retained native kidneys, disruptions of volume regulation, or alterations in the systemic neurohumoral milieu may contribute to increased blood pressure. In addition to research applications, carotid artery placement of radiotelemetric catheters may be useful in clinical settings.

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**Appendix**

Criteria used to assign a discomfort score to cats after renal autotransplantation and contralateral nephrectomy.

<table>
<thead>
<tr>
<th>Observation</th>
<th>Score</th>
<th>Criterion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comfort and position</td>
<td>0</td>
<td>Asleep or calm and relaxed</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>Awake; interested in surroundings</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Mild agitation or signs of depression; uninterested in surroundings; hunch body posture</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>Moderate agitation or restless; appears to be uncomfortable; hunch body posture</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>Extremely agitated or thrashing</td>
</tr>
<tr>
<td>Appearance</td>
<td>0</td>
<td>Apparently normal</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>Mild changes (eyes partially closed)</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Moderate changes (eyes sunken or glazed)</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>Severe changes (eyes pale and pupils dilated; abnormal facial expression; guarding or hunch body posture; limbs in abnormal position)</td>
</tr>
<tr>
<td>Behavior (unprovoked)</td>
<td>0</td>
<td>Too sedate to evaluate</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>Apparently normal; grooming</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Minor changes; grooming</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>Moderately abnormal (less mobile or alert than normal and unaware of surroundings or very restless)</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>Markedly abnormal (very restless; vocalization or grunting; self mutilation)</td>
</tr>
<tr>
<td>Interactive</td>
<td>0</td>
<td>Too sedate to evaluate</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>Apparently normal</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Pulls away when surgical site is touched; mobile; looking at wound</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>Violent reaction to touching of surgical site; snapping, hissing, or growling when approached; will not move even when coaxed</td>
</tr>
</tbody>
</table>

*Note:* Cats were assigned a discomfort score by summing the score in each observation category; if any cat was assigned a score > 8, supplemental analgesia was administered.