
Young-Woo Park, DVM; Won-Gyun Son, DVM; Man-Bok Jeong, DVM, PhD; Kangmoon Seo, DVM, PhD; Lyon Y. Lee, DVM, PhD, DACVA; Inhyung Lee, DVM, PhD

Objective—To evaluate the prevalence of and risk factors for development of corneal ulcers after nonocular surgery performed with general anesthesia in dogs.

Design—Retrospective case-control study.

Animals—14 dogs with development of corneal ulcers after nonocular surgery and 718 control dogs.

Procedures—Medical records of dogs evaluated at the Veterinary Medical Teaching Hospital of Seoul National University from January 2009 to June 2011 were reviewed for assessment of risk factors for development of corneal ulcers.

Results—Among the 732 reviewed cases, 14 (1.9%) dogs of 6 breeds developed a corneal ulcer after nonocular surgery. Duration of anesthesia was significantly longer in dogs with ulcers than dogs without ulcers. The number of medications received and procedures performed were also significantly higher in dogs with ulcers than dogs without ulcers. Dogs with a small skull (OR, 8.59; 95% CI, 1.04 to 70.90) and dogs that received neurosurgery (OR, 21.12; 95% CI, 5.77 to 77.25) were more susceptible to development of corneal ulcers. Also, postoperative application of a fentanyl patch was a risk factor for development of corneal ulcers (OR, 4.53; 95% CI, 1.05 to 19.60).

Conclusions and Clinical Relevance—Several risk factors were identified for development of corneal ulcers after nonocular surgery was performed with general anesthesia in dogs. Perioperative eye protection strategies and postoperative ophthalmic examination are needed to reduce the occurrence of corneal ulcers and their progression, especially for high-risk dogs and procedures. (J Am Vet Med Assoc 2013;242:1544–1548)

All anesthetic and preanesthetic agents have an effect on various organs and body systems, in particular the cardiovascular and pulmonary systems. Common perianesthetic complications are associated with cardiovascular and respiratory functions, including hypotension, cardiac dysrhythmias, hypercapnea, hypoxia, and death. Anesthetic procedures and anesthetic agents can also alter eye conditions and in rare cases, damage the eyes. Specifically, tear production can be reduced with anesthesia during the perioperative period in humans and other animals. The corneal epithelium is more resistant than the latter in humans. The corneal epithelium can be damaged via several mechanisms during the perioperative period: direct trauma by the anesthetist’s hands, anesthetic equipment (laryngoscope and face mask), or surgical drapes and instruments; chemical injuries caused by antiseptic solution and inhalation anesthetic agents; and reduction of tear production caused by anticholinergics, perioperative analgesics, and inhalation anesthesia itself; and exposure of the cornea associated with incomplete approximation of the eyelids (lagophthalmos). Also, blood flow to the retina and visual cortex can be reduced by anesthesia. From these changes, perioperative ophthalmic complications can occur. Perioperative corneal ulcer and acute vision loss are possible complications after general anesthesia in humans and other animals.

Although perioperative corneal abrasion and acute vision loss are rare complications, the former is more prevalent than the latter in humans. The corneal epithelium can be damaged via several mechanisms during the perioperative period: direct trauma by the anesthetist’s hands, anesthetic equipment (laryngoscope and face mask), or surgical drapes and instruments; chemical injuries caused by antiseptic solution and inhalation anesthetic agents; reduced tear production caused by anticholinergics, perioperative analgesics, and inhalation anesthesia itself; and exposure of the cornea associated with incomplete approximation of the eyelids (lagophthalmos). Vestre et al reported that tear production in dogs markedly decreases after 60 minutes of inhalation anesthesia and suggested that an artificial tear solution should be applied for dogs undergoing prolonged anesthesia to prevent corneal ulcers from forming. However, to the authors’ knowledge, there have been no clinical reports of corneal ulcers associated with general anesthesia in dogs. Therefore, the purpose of the study reported here was to investigate the occurrence and risk.
factors of corneal ulcer formation after nonophthalmic surgery performed with general anesthesia in dogs.

**Materials and Methods**

**Selection of cases and controls**—Medical records of the Veterinary Medical Teaching Hospital of Seoul National University from January 2009 to June 2011 were examined. Dogs that had undergone nonophthalmic surgeries during inhalation anesthesia were included in the study. Dogs in which surgery was performed by use of injectable anesthesia and procedures of short duration (< 10 minutes), such as the simple reduction of a joint dislocation or intraoral examination, were excluded. Also, dogs with records with insufficient information (eg, case history, anesthesia protocol, duration, and follow-up) were not included. Case dogs were those that developed a corneal ulcer after surgery. Corneal ulcer was confirmed by use of fluorescein stain, and evaluation for corneal ulcers was performed up to 14 days after surgery. Control dogs did not develop a corneal ulcer after surgery.

**Medical record review**—Pertinent data, including age, sex, breed, skull size (small, medium, or large), body weight, occurrence of corneal ulceration, duration of anesthesia, surgical area (head and neck, trunk, and extremities), type of surgery (soft tissue surgery, orthopedic surgery, neurosurgery, and dentistry), and perioperative medications received and procedures performed (anticholinergics [atropine and glycopyrrolate], acepromazine, butorphanol, diazepam, hydromorphone, morphine, ketamine, tramadol, fentanyl patch, local lidocaine infiltration, lidocaine patch, regional nerve block [brachial plexus block, infraorbital nerve block, intercostal nerve block, mandibular nerve block, mental nerve block; para- lumbar nerve block; radial, ulnar, musculocutaneous, and median nerve block; and sciatic nerve block], and epidural anesthesia), were collected.

In cases of corneal ulceration observed by veterinarians or owners, complete ophthalmic examinations were performed by ophthalmologists (KS and MJ), including the Schirmer tear test, tonometry, indirect ophthalmoscopy with a 30-diopter condensing lens, slit-lamp biomicroscopy, and fluorescein staining. In addition, data on the treatment and prognosis of corneal ulcers were collected. After diagnosis of corneal ulcers, the cornea was examined at 1-week intervals via slit-lamp biomicroscopy, and healing of the corneal ulcer was confirmed by use of fluorescein staining.

**Statistical analysis**—Numeric variables were determined as mean ± SD values and compared by use of the independent samples t test. Categoric variables were evaluated on the basis of the frequency of their occurrence in affected versus nonaffected dogs. Variables with 2 categories were compared by use of the Pearson χ² test and logistic regression. Variables with > 2 categories were compared by use of logistic regression. When the regression model was not justified by the χ² goodness-of-fit test, fitting the sequential model with stepwise regression was used until P < 0.05. All statistical analyses were performed with statistical software. A value of P < 0.05 was considered significant.

**Results**

Prevalence and prognosis of perioperative corneal ulcer—A corneal ulcer developed in 14 (23 eyes) of 732 (1.9%) dogs evaluated in this study. In all dogs, there were no previous opthalmic problems before surgery as evaluated on the basis of history reported by owners and medical records. Both eyes were affected in 9 dogs, and only the left eye was affected in the remaining dogs. Six breeds were represented, including 5 Malte, 4 Shih Tzus, 1 American Cocker Spaniel, 1 Cavalier King Charles Spaniel, 1 Pekingese, 1 Miniature Pincher, and 1 Yorkshire Terrier. There was no significant difference in number of males and females. Corneal ulcers were diagnosed at days 0 (the day of surgery), 1, 2, 3, 10, and 13 after surgery in 2 eyes (2 dogs), 7 eyes (4 dogs [including 1 from the previous group]), 6 eyes (3 dogs), 4 eyes (3 dogs), 1 eye (1 dog), and 3 eyes (2 dogs), respectively. Corneal ulceration developed after neurosurgery [hemilaminectomy (7 dogs) and ventral slot procedure (2 dogs)], soft tissue surgery (exploratory laparotomy [1 dog], pyeolithotomy [1 dog], ovariohysterectomy [1 dog], and ligation of patent ductus arteriosus [1 dog]), and dental prophylaxis (1 dog). Medical treatments (antimicrobial eye drops [23 eyes]; 1 drop of ciprofloxacin, levofloxacin, ofloxacin, or tobramycin), anticoagulase eye drops [12 eyes; acetylcy Steele and 1% EDTA], autologous serum [10 eyes], artificial tear [23 eyes; carboram 940, carbosmyethylcellulose sodium, or sodium hyaluronate], 1% atropine eye drop [11 eyes], 0.2% cyclosporine ointment [3 eyes], and flurbiprofen eye drop [5 eyes] with or without surgical treatments (debridement and grid keratotomy [22 eyes] or third eyelid flap [3 eyes]) were applied according to the results of ophthalmic examination and severity of the corneal ulcer. After medical treatment with or without surgical treatment, the corneal ulcer was resolved within 14 days without complications in 12 eyes (8 dogs). Mean ± SD healing time in eyes without complications was 10.3 ± 2.6 days. A persistent corneal ulcer was identified in 2 dogs (4 eyes), for which the duration of the ulcer was 23 and 38 days. Two dogs (3 eyes) died on days 2 and 7 after surgery of postsurgical complications (myelomalacia and peritonitis, respectively). The corneal ulcer progressed to perforation in 3 eyes (2 dogs). One of the dogs (2 eyes) was treated by direct corneal suturing, and the other dog was treated with a conjunctival pedicle graft. The corneal wounds were successfully healed 14 days after surgery in both perforation cases. There was an unknown prognosis in 1 dog (1 eye) because the dog was not returned for a recheck examination.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Dogs without ulcer (n = 718)</th>
<th>Dogs with ulcer (n = 14)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body weight (kg)</td>
<td>6.6 ± 7.0</td>
<td>4.7 ± 3.2</td>
<td>0.265</td>
</tr>
<tr>
<td>Age (y)</td>
<td>8.1 ± 4.0</td>
<td>7.7 ± 4.3</td>
<td>0.706</td>
</tr>
<tr>
<td>Duration of anesthesia (min)</td>
<td>104.7 ± 62.7</td>
<td>175.0 ± 84.6</td>
<td>0.008</td>
</tr>
<tr>
<td>No. of perioperative medications</td>
<td>2.6 ± 1.2</td>
<td>3.8 ± 1.3</td>
<td>0.013</td>
</tr>
<tr>
<td>received and procedures performed</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 1—Mean ± SD values of variables evaluated as possible risk factors for development of corneal ulcers after nonocular surgery in dogs.
Risk analysis—Among the numeric variables, the duration of anesthesia was determined to be a significant risk factor for corneal ulcer development after general anesthesia (Table 1). Dogs with corneal ulcers received significantly longer duration of anesthesia than dogs without ulcers. The numbers of perioperative medications received and procedures performed were significantly higher in dogs with ulcers than dogs without ulcers. Neither age nor body weight was a risk factor for development of corneal ulceration in dogs.

Results of the present study indicated that use of more perioperative medications and procedures were risk factors for perioperative corneal ulcer development. Anticholinergics have been used to inhibit or treat brady-cardia during the perioperative period in veterinary medicine but are well-known to decrease tear production after systemic or topical application in dogs. The results of the present study suggested that a combination of general anesthesia and perioperative pain control, several drugs, such as anticholinergics, phenothiazines, opioids, benzodiazepines, and $\alpha_2$-receptor agonists, are often used as premedication. These tranquilizers, sedatives, and ancillary agents are administered to calm the animal and to achieve a cooperative status, which allows health caretakers to perform detailed examinations. To reduce the unwanted adverse effects of each drug, veterinarians often administer more than 1 class of drugs to achieve perioperative development of corneal ulcers in humans. Factors that could be associated with reduced tear production in the present study were duration of anesthesia and perioperative medications. Reduced tear production during inhalation anesthesia is induced by the inhalation anesthesia itself. After 60 minutes of inhalation anesthesia, tear production is reduced to nearly zero in dogs. Because the cornea is covered with a protective precorneal tear film, a dry cornea is more susceptible to ulceration.

Discussion

Although the possibility of corneal ulcer development associated with general anesthesia has been suggested in a previous study, there have been no clinical reports of this, to the authors’ knowledge. This retrospective study revealed the prevalence and risk factors of perioperative development of corneal ulcers in dogs. Although perioperative corneal ulcers were uncommon, the prevalence of 1.9% was not negligible and 2 cases progressed to globe-threatening complications.

Although the Schirmer tear test was not routinely performed during perioperative periods in most cases included in the study, reduced tear production is the most widely investigated mechanism associated with perioperative development of corneal ulcers in humans. Factors that could be associated with reduced tear production in the present study were duration of anesthesia and perioperative medications. Reduced tear production during inhalation anesthesia is induced by the inhalation anesthesia itself. After 60 minutes of inhalation anesthesia, tear production is reduced to nearly zero in dogs. Because the cornea is covered with a protective precorneal tear film, a dry cornea is more susceptible to ulceration.

Results of the present study indicated that use of more perioperative medications and procedures were risk factors for perioperative corneal ulcer development. Anticholinergics have been used to inhibit or treat bradycardia during the perioperative period in veterinary medicine but are well-known to decrease tear production after systemic or topical application in dogs. Results of the present study suggested that a combination of many drugs may induce a decrease in tear production during the perioperative period. To achieve safe anesthesia and perioperative pain control, several drugs, such as anticholinergics, phenothiazines, opioids, benzodiazepines, and $\alpha_2$-receptor agonists, are often used as premedication. These tranquilizers, sedatives, and ancillary agents are administered to calm the animal and to achieve a cooperative status, which allows health caretakers to perform detailed examinations. To reduce the unwanted adverse effects of each drug, veterinarians often administer more than 1 class of drugs to achieve

### Table 2—Results of analysis of variables evaluated as potential risk factors for development of corneal ulcers after nonocular surgery in dogs.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Dogs without ulcer (n = 718)</th>
<th>Dogs with ulcer (n = 14)</th>
<th>OR</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (male to female)</td>
<td>1.56</td>
<td>0.54–4.48</td>
<td>0.410</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anticholinergics</td>
<td>1.86</td>
<td>0.58–6.03</td>
<td>0.293</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acrestomine</td>
<td>0.59</td>
<td>0.18–1.91</td>
<td>0.377</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Morphine</td>
<td>2.68</td>
<td>1.00–8.32</td>
<td>0.041</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>3.35</td>
<td>0.72–15.58</td>
<td>0.102</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diazepam</td>
<td>1.90</td>
<td>0.41–8.68</td>
<td>0.402</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lidocaine patch</td>
<td>4.31</td>
<td>1.31–14.15</td>
<td>0.009</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fentanyl patch</td>
<td>9.67</td>
<td>3.09–30.24</td>
<td>&lt; 0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nerve block</td>
<td>2.14</td>
<td>0.47–9.79</td>
<td>0.318</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Epidual anesthesia</td>
<td>0.35</td>
<td>0.05–2.68</td>
<td>0.289</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Table 3—Distribution (No. of dogs) with variables evaluated as risk factors for development of corneal ulcers after nonocular surgery.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Dogs without ulcer (n = 718)</th>
<th>Dogs with ulcer (n = 14)</th>
<th>OR</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skull size</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medium</td>
<td>189</td>
<td>1</td>
<td>Referent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Small</td>
<td>485</td>
<td>13</td>
<td>8.59</td>
<td>1.04–70.90</td>
<td>0.046</td>
</tr>
<tr>
<td>Large</td>
<td>44</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surgical area</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Head and neck</td>
<td>219</td>
<td>3</td>
<td>Referent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trunk</td>
<td>346</td>
<td>11</td>
<td>4.40</td>
<td>0.85–22.88</td>
<td>0.078</td>
</tr>
<tr>
<td>Limb</td>
<td>153</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type of surgery</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Soft tissue surgery</td>
<td>366</td>
<td>4</td>
<td>Referent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neurosurgery</td>
<td>68</td>
<td>9</td>
<td>21.12</td>
<td>5.77–77.25</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Orthopedic surgery</td>
<td>152</td>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dentistry</td>
<td>132</td>
<td>1</td>
<td>2.58</td>
<td>0.17–39.27</td>
<td>0.496</td>
</tr>
</tbody>
</table>

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$P < 0.001$ were significant risk factors for corneal ulcers within the same categories in dogs, but the surgical area was not.
sensation and analgesia. However, the various tranquilizers, sedatives, analgesics, and ancillary agents used as premedication reduce tear production and some of their combinations have a synergistic negative effect on tear production in animals. Although the mechanisms of reduced tear production caused by tranquilizers, sedatives, and analgesics are under investigation, 2 mechanisms can be considered in this study. One is the neural regulation of the lacrimal gland, which can be impaired by sedatives, tranquilizers, or analgesics because of their action on the peripheral and central lacrimogenic pathway. The other is vasosacrification of vessels supplying the tear gland.

Because several medications and procedures were simultaneously applied to most of the dogs in this study, results of the Pearson χ² test could not be directly applied to evaluate the effects of each medication and procedure for perioperative corneal ulcers. Therefore, logistic regression analysis was conducted. Among the 3 significant factors identified by use of the Pearson χ² test, postoperative application of a fentanyl patch was the only risk factor identified by use of logistic regression. The fentanyl patch has been used as a transdermal drug delivery system to achieve slow, continuous drug release and absorption for long-lasting effects of > 72 hours. Adverse effects of fentanyl and the fentanyl patch on the eyes have also been reported in dogs. Biricik et al reported that the mean decrease of Schirmer tear test value 20 minutes after IV administration of fentanyl was approximately 7 mm/min. Pekcan and Koç observed semiclosed eyes after application of the fentanyl patch. Reduced tear production and eyelid function can change corneal conditions, leading to a corneal ulcer.

The typical blinking rate of a dog has been estimated at 14.5 and 12.99 blinks/min. Because normal blinking is essential for tear distribution, abnormally reduced blinking can lead to exposure keratitis. Although the blinking rate of dogs with ulcers was not recorded for most dogs in the present study, the blinking rate was approximately 0 or 1 blinks/min in 1 case dog with bilateral corneal perforation.

Thirteen of the 14 dogs with ulcers had a small skull, and this was found to be a risk factor. Because skull conformation calculated by the cephalic index is not consistent even within the same breed and is therefore difficult to classify in some breeds, the size of the skull was used to analyze the risk factor in the present study. Dogs in the present study with a small skull were mostly deemed to be of brachycephalic breeds (although it is ambiguous whether the Maltese is a brachycephalic or mesocephalic breed). Because nerve fiber density of the cornea in brachycephalic dogs is lower than that in mesocephalic dogs, corneal sensitivity of brachycephalic dogs is lower than that of mesocephalic dogs. This difference in innervation may be a cause of predisposition to perioperative corneal ulcers in dogs with a small skull. Also, lagophthalmos is prevalent in brachycephalic breeds and can be a risk factor for corneal ulceration.

The type of surgery can also be a risk factor for the development of a perioperative corneal ulcer. Spinal surgeries, especially lumbar laminectomy, is a risk factor for perioperative corneal abrasion in humans. Also, surgical manipulation during head and neck surgery is another risk factor for perioperative corneal abrasion in human studies. Therefore, the area and type of surgery were investigated in the present study. Although it is a risk factor in humans, head and neck surgery was not a risk factor for development of a corneal ulcer in dogs. In contrast to our expectation, the trunk was the surgical area most frequently associated with postoperative development of corneal ulcers, although the difference was not significant. However, neurosurgery was found to be a risk factor in this study. Similar to a human study, more than half of perioperative corneal ulcer cases (9/14 cases) occurred after neurosurgery, especially hemilaminectomy (7 cases).

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Other possible etiologies are mechanical and chemical trauma, although neither was evident in the present study. Surgical manipulations around the head and neck area can induce direct trauma and corneal edema. Although it is a low-likelihood possibility, perioperative corneal ulcers can be induced by clinicians during anesthetic induction procedures and connection of anesthetic monitoring devices to the patient. Chemical agents used during anesthesia and surgery, such as inhalation anesthetic agents and disinfectants, can also damage the corneal epithelium directly. Occurrence of corneal ulcers, acknowledging the possibility of undetectable corneal ulcers, was investigated up to 14 days after surgery. Two cases of corneal ulcers were diagnosed 13 days after surgery. In these 2 cases, no possible causative events except for anesthesia were evident. In humans, perioperative corneal ulcers have been detected the day of surgery and healing was without complications. Unlike in humans, in the present study, most perioperative corneal ulcers in dogs were diagnosed 1 day after surgery. Later development of corneal ulcers may influence the prognosis; in the present study, some progressed to persistent corneal ulcer (4 eyes) and corneal perforation (3 eyes).

Corneal injury can be effectively prevented via application of eye lubrication during anesthesia in humans. The eyelids should be held closed with adhesive tape to avoid exposure keratitis. In the present study, lubricant was used after induction of anesthesia and at 30-minute intervals while anesthesia was main-
tainied in all cases, but closure of the eyelids with tape was not generally used.

The residence time of eye lubricants is different in relation to their ingredients, concentration, and formulation. The residence time has a positive correlation with viscosity and mucoadhesive formulation. Considering that the residence time of most marketed artificial tears ranges from 20 to 40 minutes in humans, eye lubricant would have to be applied every 30 minutes during anesthesia. Also, tear production profoundly decreases with the duration of anesthesia, so more frequent application or more viscous types of eye lubricants may be considered in prolonged anesthesia.

As part of the prevention strategy for perioperative corneal ulcers, all staff should be educated on the possibility of perioperative corneal ulcers, especially inexperienced staff. The prevalences of corneal injuries were substantially reduced by performance improvement systems in a human study.37

References