Effects of perioperative topical dorzolamide hydrochloride–timolol maleate administration on incidence and severity of postoperative ocular hypertension in dogs undergoing cataract extraction by phacoemulsification

Rachel B. Matusow DVM
Ian P. Herring DVM, MS
J. Phillip Pickett DVM
Natalia Henao-Guerrero DVM, MS
Stephen R. Werre PhD

From the Department of Small Animal Clinical Sciences (Matusow, Herring, Pickett, Henao-Guerrero) and Laboratory for Study Design and Statistical Analysis (Werre), Virginia-Maryland College of Veterinary Medicine, Virginia Tech, Blacksburg, VA 24061. Dr. Matusow’s present address is Cornell University Veterinary Specialists, 880 Canal St, Stamford, CT 06901.

Address correspondence to Dr. Matusow (rachel.matusow@gmail.com).

OBJECTIVE
To assess the effects of topically applied 2% dorzolamide hydrochloride–0.5% timolol maleate ophthalmic solution (DHTM) on incidence and severity of postoperative ocular hypertension (POH; ie, intraocular pressure [IOP] > 25 mm Hg) in dogs undergoing cataract extraction by phacoemulsification.

DESIGN
Randomized, masked, controlled study.

ANIMALS
103 dogs (180 eyes).

PROCEDURES
Pertinent history, signalment, and ophthalmic examination findings were recorded. Dogs received 1 drop of DHTM or sham treatment solution (sterile, buffered, isotonic eye drops) in both eyes 14 hours and 2 hours before anesthetic induction and at the time of corneal incision closure (ie, end of surgery); IOPs were assessed by rebound tonometry 2, 4, 6, and 8 hours after surgery and between 7:30 and 8:00 AM on the following day. Dogs with IOPs of 26 to 45 mm Hg received 1 drop of 0.005% latanoprost solution topically; the surgeon’s treatment of choice was used for dogs with IOPs > 45 mm Hg. Incidence of POH and postoperative IOPs were compared between treatment groups.

RESULTS
DHTM treatment resulted in significantly lower incidence of POH than did sham treatment at the level of the dog (18/53 [34%] vs 31/50 [62%]) and the eye (24/94 [26%] vs 42/86 [48%]). Mean IOP did not differ between groups at the time of POH detection. The DHTM-treated eyes that developed POH were significantly more likely to have a 1-hour follow-up IOP < 25 mm Hg after latanoprost administration than were sham-treated eyes (19/25 [76%] vs 18/35 [51%]; OR, 3.87).

CONCLUSIONS AND CLINICAL RELEVANCE
Multidose perioperative administration of DHTM in dogs undergoing phacoemulsification reduced the incidence of POH and improved responsiveness of POH to latanoprost treatment. (J Am Vet Med Assoc 2016;249:1040–1052)

Phacoemulsification and aspiration for cataract extraction in dogs is an elective procedure commonly performed by veterinary ophthalmologists. Benefits include restoration of vision and reduction of cataract-related complications, such as glaucoma and chronic uveitis.1 Reported success rates (on the basis of treated eyes) for the surgery range from 27 of 34 (79%) to 148 of 179 (83%), whereas long-term failure rates (on the same basis) have been reported as < 10% until after the 3-year follow-up point (blindness at > 1 to 2 years, 10/132 [8%]; blindness at > 2 to 3 years, 5/80 [6%]).1–3 Postoperative complications are not infrequent, however, and poor outcomes may result. Complications that can potentially cause blindness include retinal detachment, glaucoma, endophthalmitis, corneal endothelial degeneration, posterior lens capsule opacification, and POH.2–7

In contrast to glaucoma, which is associated with a persistent pathological high IOP in dogs, POH is a distinct clinical syndrome characterized by a transient but sometimes severe increase in IOP after cataract extraction surgery. In dogs, POH is generally defined as an IOP > 25 to 27 mm Hg occurring in

ABBREVIATIONS
CAI Carbonic anhydrase inhibitor
DHTM 2% dorzolamide hydrochloride–0.5% timolol maleate ophthalmic solution
IOP Intraocular pressure
LOCF Last outcome carried forward
POH Postoperative ocular hypertension
VIAT Viscoelastic irrigation-aspiration time

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the acute postoperative period.\textsuperscript{2,4,8–12} It is a common occurrence in dogs undergoing routine phacoemulsification for cataracts, affecting up to 45.5% of eyes\textsuperscript{2,4,8–14} with a reported peak incidence at 2 to 5 hours after surgery.\textsuperscript{4,9,11,12} While POH is generally transient and is infrequently associated with permanent, clinically detectable vision deficits, it does have the potential to cause blindness in dogs undergoing cataract surgery, rendering the surgery a failure and resulting in poor client satisfaction.\textsuperscript{10,15–17} Because of this, some clinicians choose to hospitalize dogs after surgery to facilitate monitoring and intervention for POH, and hospital stays can be further prolonged if POH does occur. Additionally, in a 2012 survey\textsuperscript{18} of veterinary ophthalmologists, 64 of 185 (35%) respondents reported routinely prescribing postoperative antiglaucoma medications for all dogs undergoing cataract surgery to ameliorate the potential for POH, and an additional 75 of 185 (41%) respondents reported doing so for all dogs that develop POH.\textsuperscript{4} This potentially puts the animal at risk for adverse effects from medication, incurs greater cost to the owner, and increases the complexity of postoperative medication regimens. Lastly, POH may be associated with subsequent development of glaucoma in affected eyes.\textsuperscript{4,8}

Studies\textsuperscript{2,4,10,13} evaluating risk factors for POH in dogs have produced conflicting results, suggesting a multifactorial etiopathogenesis. Increases in age and phacoemulsification time, for example, have been associated with higher risk of POH in some studies, but not in others.\textsuperscript{2,4,10,13} Investigators have consistently found that sex, preoperative lens-induced uveitis, placement of an intraocular lens, diabetes mellitus, and gonioscopy findings lack a statistical relationship with POH, whereas breed-related predisposition to the syndrome has been repeatedly found for Boston Terriers and Labrador Retrievers.\textsuperscript{4,10,11,13} To our knowledge, gonioscopic examination of the iridocorneal angle has not been routinely performed in any study of POH in dogs, and when it has been reported, results were generally recorded for only a small percentage of the patient population.\textsuperscript{18–23} In studies of people,\textsuperscript{19,24,25} the single greatest predictor of postoperative IOP is preoperative IOP; glaucoma patients and those with intraoperative posterior lens capsule rupture are at highest risk of developing POH. A literature search identified no reports of studies investigating preoperative IOP as a risk factor for POH in dogs.

Reduced aqueous humor outflow is considered the most likely mechanism of POH,\textsuperscript{12,10,17} and the main pharmacological target for treatment and prophylaxis is alteration of aqueous humor dynamics. Various intracameral, topical, and systemic antiglaucoma medications have been evaluated as potential prophylactic agents against POH in human patients undergoing cataract surgery, but the veterinary literature addressing this subject to date has been limited to just 2 prospective investigations\textsuperscript{9,13} and 1 retrospective study.\textsuperscript{11} Although pharmacological intervention has the potential to ameliorate POH, preoperative treatment with antiglaucoma medications was routinely given to canine patients undergoing phacoemulsification by only 18 of 186 (10%) veterinary ophthalmologists who responded to the question in the previously described survey.\textsuperscript{4}

Topically administered CAIs or fixed-combination medications containing a CAI and a β-adrenergic receptor antagonist reduce aqueous humor production and are routinely used for treatment of glaucoma in dogs.\textsuperscript{26–28} In people, these drugs may be more effective than topical prostaglandin analogs for preventing or reducing the severity of POH.\textsuperscript{29–31} However, to our knowledge, no study in the veterinary literature has evaluated the effects of topically administered CAIs, β-adrenergic receptor antagonists, or combination products on POH in dogs. The present study was conceived to improve our understanding of risk factors for POH in dogs and to provide evidence to help establish a scientific basis for the perioperative administration of antiglaucoma medications in canine patients undergoing cataract surgery. The primary objective of the study was to assess the effects of topically applied DHTM on the incidence and severity of POH in dogs undergoing cataract extraction by phacoemulsification. We hypothesized that dogs receiving perioperative DHTM treatment would have a lower incidence or severity of POH, compared with dogs that received a control (sham) treatment.

**Materials and Methods**

**Animals and study design**

Canine patients admitted to the Virginia-Maryland College of Veterinary Medicine veterinary teaching hospital for phacoemulsification between March 1, 2013, and July 31, 2014, were considered candidates for enrollment in the study. All of the dogs had been previously evaluated and found to be acceptable candidates for surgery. The population included dogs with unilateral or bilateral juvenile or senile cataracts and cataracts secondary to diabetes mellitus. Dogs with cataracts that had associated conditions which precluded the likelihood of a successful surgical outcome (eg, retinal degeneration or retinal detachment) were not considered surgical candidates. Eligible study candidates were subsequently excluded only when deviation from the study protocol was necessary for optimal patient care or if the owner declined participation. Patient care factors precluding study enrollment included preexisting glaucoma requiring medical treatment and severe lens-induced uveitis requiring additional preoperative cycloplegic medication.

Study dogs were assigned to 1 of 2 groups (DHTM\textsuperscript{b} or control [sham treatment]) by use of a computer-generated random numbers table. The DHTM and the sham treatment solution (sterile, buffered, isotonic lubricating eye drops)\textsuperscript{e} were of similar physical appearance and viscosity and were dispensed in identical bottles by pharmacy staff. Clients, clinicians,
students, and staff were masked to the treatment solution administered for the duration of the study. The study protocol was approved by the Virginia Tech Institutional Animal Care and Use Committee, and informed owner consent was obtained prior to enrollment of dogs in the study.

**Historical data collection and patient evaluation**

Standard preoperative evaluation for study dogs involved collection of pertinent historical data including signalment, diabetes mellitus status, and previous cataract-related treatments, together with an ophthalmic examination, which included evaluation of white-light pupillary light and dazzle reflexes and slit-lamp biomicroscopy. Indirect ophthalmoscopy was performed when possible (depending on completeness of the cataract). Ocular ultrasonography and flash electroretinography were performed when visibility of the fundus was not adequate to rule out retinal detachment and retinal degeneration. Ophthalmic examination was performed by 1 of 2 board-certified ophthalmologists (IPH or JPP) or 1 of 2 ophthalmology residents (including RBM). Direct gonioscopy was performed with a Layden or Koeppen goniolens and a slit-lamp biomicroscope to provide magnification, with attempted visual examination of approximately 270° of the iridocorneal angle (dorsal quadrant excluded). Angles were first scored as normal (open) or abnormal. Abnormal angles were further graded according to the estimated percentage of the examined region that was affected by narrowing, closure, or pectinate ligament dysplasia or dysgenesis. Angles judged to be <10% affected by ≥1 abnormality were classified as mildly affected, those with 10% to 50% involvement by ≥1 abnormality were considered moderately affected, and those with >50% involvement by ≥1 abnormality were classified as severely affected. Additional examination data recorded for purposes of statistical evaluation included whether the left, right, or both eyes were undergoing surgery; presence or absence of biomicroscopically evident anterior uveitis at the time of evaluation or at the drop-off appointment for hospitalization (presence of aqueous flare, keratic precipitates, or synchiae); and stage of cataract (incipient, immature, mature, or hypermature).

All study dogs underwent routine physical examination. Preoperative laboratory evaluation was determined at the attending clinician’s discretion and ranged from minimal (PCV, serum total solids concentration, estimate of BUN concentration by use of a reagent strip test, blood glucose concentration via glucometer, and urine specific gravity) to fairly comprehensive (CBC, serum biochemical analysis, urinalysis, and microbial culture of urine). Topical corticosteroid treatments were routinely administered prior to surgery, with the duration of treatment determined primarily by clinician preference, the timing of surgery relative to the preoperative evaluation appointment, and the presence of clinical lens-induced induced uveitis.

**Study treatment protocol**

To standardize the total applied dose and account for any potential ocular effects related to systemic absorption of the test medication, study treatments were applied to both eyes regardless of whether unilateral or bilateral surgery was performed. One drop of DHTM or the sham treatment was administered to each eye 14 hours before planned anesthetic induction time, 2 hours before planned anesthetic induction time, and at the time of corneal incision closure.

**IOP measurements and surgical procedures**

Intraocular pressures of eyes undergoing surgery were measured and recorded at several predetermined time points for each study animal. The day prior to surgery, IOP was measured when the patient was dropped off at the hospital, and this was considered the baseline value. Immediately after the baseline IOP was obtained, a mydriatic provocative test was performed as follows: 1 drop of 1% tropicamide solution was applied to the eye or eyes to undergo surgery, and IOP was measured again 1 hour later (postdilation IOP); eyes that had an increase in IOP to >25 mm Hg were considered to have a positive result and to be at risk for glaucoma; the difference between postdilation IOP and baseline IOP was also calculated, and eyes were grouped as those that had ≥5 mm Hg increase in IOP (clinically relevant increase) and those that did not. Subsequent IOP measurements were obtained immediately after corneal incision closure (closure IOP); at 2, 4, 6, and 8 hours after surgery (with the end of surgery designated as the end of corneal incision closure [ie, completion of the last knot]); and between 7:30 AM and 8:00 AM on the next day (16 to 20 hours after surgery). If POH was detected and rescue medications were administered, IOP in affected eyes was measured 1 hour after rescue treatment. Additional measurements were performed at the clinician’s discretion on the basis of clinical need. The IOPs in awake animals were measured by use of a designated handheld rebound tonometer with the patient in sternal recumbency or in a seated or standing position. This task was performed by students, technicians, or clinicians trained in appropriate use of the instrument. Because of intraoperative patient positioning limitations precluding use of a rebound tonometer, IOPs at the completion of corneal incision closure were measured with a hand-held application tonometer by 1 of 3 ophthalmology surgery technicians trained in its use. The IOP measurements were performed in triplicate at all time points; the first 3 values obtained with low or no error were recorded, and the mean value was determined. During the course of the study, it was determined that the effects of preoperative DHTM and sham solution administration on preoperative IOP in cataractous eyes should
be evaluated. Thereafter, IOP was measured at the time of the first dose of DHTM or sham treatment solution (14 hours before planned induction time) and 6 and 11 hours after this initial dosing.

During the 24 hours preceding surgery, all eyes undergoing phacoemulsification were treated with topical ophthalmic 1% prednisolone acetate suspension and neomycin-polymyxin B-gramicidin solution (both administered every 8 hours). A standardized topical ophthalmic preoperative medication regimen was implemented on the morning of surgery; 1% tropicamide solution was applied to eyes undergoing surgery 3 hours prior to anesthetic induction to facilitate dilation for the preoperative examination, and this treatment was repeated every 30 minutes starting 2 hours prior to induction. Neomycin-polymyxin B-gramicidin, 0.1% diclofenac sodium, and 1% prednisolone acetate treatments were also applied to eyes undergoing surgery every 30 minutes beginning 2 hours prior to induction, and 1 dose of topical 10% phenylephrine solution was applied 30 minutes prior to induction.

The anesthetic protocol was standardized to include premedication with acepromazine maleate and hydromorphone hydrochloride (IM; doses at discretion of the attending anesthesiologist), induction with propofol IV to effect, and maintenance of anesthesia with isoflurane in 100% oxygen. Neuromuscular blockade was achieved with rocuronium bromide (0.2 mg/kg [0.09 mg/lb], IV, as a loading dose followed by a continuous rate infusion at 0.8 mg/kg/h [0.36 mg/lb/h]). All dogs received 1 dose of buprenorphine (IV; doses at discretion of the attending anesthesiologist) after surgery.

Systemic medications were administered (orally or by injection) on the basis of surgeon preference and the dog’s diabetes mellitus status: before surgery, dogs received anti-inflammatory drugs (NSAIDs if diabetic and prednisone or prednisolone if nondiabetic). Most dogs received cefazolin (22 mg/kg [10 mg/lb], IV, q 90 min) intraoperatively; however, some received orally administered antimicrobials preoperatively instead.

Routine phacoemulsification was performed on all study dogs by 1 of 4 surgeons. Sterile irrigation solution was supplemented with 5,000 U of heparin/500 mL. Upon anterior chamber entry, 0.3 mL of dilute (1:10,000) injectable epinephrine was routinely administered intracameraly. A sodium hyaluronate viscoelastic preparation was injected intraocularly, as needed, and removal was performed at the completion of surgery via irrigation and aspiration. The duration of VIAT was recorded but was not standardized. Phacoemulsification time was recorded for each eye. Foldable acrylic lenses were placed within the lens capsule unless the surgeon deemed it contraindicated because of factors such as severe lens capsule instability or lens capsule tears. Clear corneal incision closure was accomplished by suturing in a continuous symmetrical sawtooth pattern (3 surgeons) or by placement of 5 simple interrupted sutures (1 surgeon), according to surgeon preference. Suture materials included 8-0 polyglactin 910, 8-0 polyglycolic acid, or 9-0 polyglactin 910. Five minutes after application of the study solution following completion of corneal incision closure, 2.5% hydroxypropyl methylcellulose solution was applied to provide ocular lubrication and protection from desiccation during the remainder of surgery (for dogs undergoing bilateral procedures) and recovery from anesthesia.

Placement of intraocular lens implants, capsular tension rings, and tarsorrhaphy sutures was recorded, and any surgical complications were noted and described. In rare instances, when the surgeon elected to administer 0.01% carbachol intracameraly to address vitreous prolapse or capsular instability with resultant lens capsule or lens subluxation, the study protocol was stopped and the patient removed from the study.

**Definition and treatment of POH**

Postoperative ocular hypertension was defined as any IOP measurement > 25 mm Hg identified at the predetermined postoperative IOP measurement times. Rescue protocols in place were as follows: eyes with IOP of ≤ 25 mm Hg were considered to have normal pressures and were monitored at the described IOP measurement intervals; eyes with IOPs of 26 to 45 mm Hg were treated with 1 drop of 0.005% latanoprost solution and reassessed in 1 hour, with a positive response defined as subsequent IOP of < 25 mm Hg; eyes not responding to latanoprost and those with IOP of > 45 mm Hg at any time point were treated according to surgeon preference, including some combination of topical 0.005% latanoprost solution treatment, orally or topically administered CAIs, topically applied β-adrenergic receptor antagonists, aqueous paracentesis, or manual leakage of fluid via the corneal incision.

**Statistical analysis**

A 2-eye model, requiring that statistical analysis take into account the correlation between eyes of the same individual, was used for the study. This method also accounted for the fact that data were collected from 2 eyes in dogs having bilateral surgery and from 1 eye in those undergoing unilateral surgery. Two-eye model analysis methods have been recommended in human and veterinary medical literature.

The primary exposure was treatment group, and the primary outcome was POH. Potential prognostic factors evaluated included sex, diabetes mellitus status, breed, age, and gonioscopy results for the patient; preoperative topical corticosteroid administration; evidence of lens-induced uveitis; baseline IOP, mydriatic provocative test results, VIAT, phacoemulsification time (total time during which phacoemulsification energy was delivered into the eye [measured automatically by the equipment]), closure IOP, cataract stage, surgical time (time from corneal incision to closure) for each eye, and surgeon (designated as surgeons A, B, C, or D).
B, C, and D). Probability plots confirmed the normal distribution of age, VIAT, phacoemulsification time, surgical time, and all IOP measurements at the predetermined time points. Associations between treatment group and each of the potential prognostic factors were assessed by means of a χ² test (dog-level factors of sex, breed, diabetes mellitus status, and surgeon), binary logistic generalized estimating equations (normal vs abnormal gonioscopy and mydriatic provocative test results, presence or absence of lens-induced uveitis, and whether the patient received preoperative topical corticosteroid treatment), ordinal logistic generalized estimating equations (iridocorneal angle grade and cataract stage), mixed-model ANOVA (baseline IOP, VIAT, phacoemulsification time, and closure IOP), and 2-sample t tests (age and surgical time).

Associations between prognostic factors and the outcome (POH) were assessed with the χ² test (sex, breed, treatment group, diabetes mellitus status, and surgeon, with dog-level POH used for these factors) and binary logistic generalized estimating equations (age, normal vs abnormal gonioscopy and mydriatic provocative test results, preoperative topical corticosteroid treatment, presence or absence of lens-induced uveitis, iridocorneal angle grade, baseline IOP, VIAT, phacoemulsification time, closure IOP, surgical time, and cataract stage). Associations between the gonioscopy result category (normal or abnormal) and iridocorneal grade with POH value (IOP at time of POH diagnosis) were assessed by mixed-model ANOVA. Intracocular pressure, modeled as a continuous variable, was compared between eyes that received DHTM and those that received the sham treatment by mixed-model ANOVA, and logistic generalized estimating equations were used to assess the effect of treatment group on development of POH as a categorical variable (yes or no). In addition to the first occurrence of eye-level POH as the outcome, cumulative occurrence (at 2, 4, 6, and 8 hours after surgery) was evaluated through an LOCF method (eg, an eye that developed POH 2 hours after surgery would have a positive indicator for POH inserted at the 4, 6, and 8 hour time points). Where appropriate, ORs and their 95% confidence intervals were computed as the exponentials of their logistic coefficients and their Wald 95% confidence limits, respectively. Patient age was tested for association with phacoemulsification time by mixed-model linear regression, and treatment group was tested for association with dog-level POH (designated as unilateral or bilateral POH) with the χ² method. All mixed-model ANOVA, regression, and generalized estimating equations models specified dog as a blocking factor to account for the correlation between eyes of dogs undergoing bilateral surgery. Tests for associations between pairs of prognostic factors and multivariable analyses were performed on an ad hoc basis to further investigate any potentially spurious associations observed. All analyses were performed with statistical software. Values of $P < 0.05$ were considered significant.

Results

Study population

During the study period, 130 dogs (223 eyes) were evaluated by the ophthalmology service at the study facility after being screened and deemed acceptable candidates for cataract extraction by phacoemulsification. One hundred twelve dogs (195 eyes) were enrolled in the study, and 103 of these dogs (180 eyes) completed the protocol and were included in data analysis. Twenty-seven dogs (43 eyes) were excluded or enrolled and subsequently removed from the study for a variety of reasons, including severe lens-induced uveitis or miosis requiring additional preoperative treatment with mydriatic agents (7 dogs [10 eyes]), scheduling conflicts with the preoperative medication protocol (3 dogs [6 eyes]), preoperative diagnosis of glaucoma or treatment with antiglaucoma medications (4 dogs [6 eyes]), IOP > 30 mm Hg after the mydriatic provocative test requiring topical antiglaucoma treatment in ≥ 1 eye (3 dogs [5 eyes]), lack of client consent (3 dogs [4 eyes]), intraoperative administration of carbachol (3 dogs [4 eyes]), cardiomyopathy-related anesthetic death prior to surgery (1 dog [2 eyes]), treatment with additional mydriatics (1 dog with ocular melanosis [2 eyes]), lack of postoperative IOP data at the 2-hour time point (1 dog [2 eyes]), and early discharge from the hospital because of excessively anxious behavior (1 dog [2 eyes]). Of these, a total of 27 eyes of 18 dogs were excluded because of conditions preventing adherence to the study protocol (substantial lens capsule subluxation with vitreal prolapse prompting intracameral carbachol administration, ocular melanosis or marked preoperative lens-induced uveitis requiring preoperative cycloplegic medications, and preexisting glaucoma or a positive mydriatic provocative test with IOP > 30 mm Hg requiring ocular hypotensive medications). Of 103 dogs completing the study, 77 had bilateral and 26 had unilateral phacoemulsification. Fifty-three dogs received DHTM, and 50 received the sham treatment, with 94 and 86 eyes, respectively, undergoing surgery in the 2 treatment groups. In total, 49 of 103 (48%) dogs developed POH in 66 of 180 (37%) eyes that underwent surgery. There were no significant differences between treatment groups for any potential prognostic factor for POH.

The 103 dogs included 53 females (49 spayed and 4 sexually intact) and 50 males (46 neutered and 4 sexually intact). Mean ± SD age at the time of phacoemulsification surgery was 8.3 ± 3.2 years (range, 1 to 16 years). The most commonly represented purebred dogs included Yorkshire Terrier (n = 11), Miniature Schnauzer (7), Boston Terrier (5), Pug (5), Cocker Spaniel (5), Toy Poodle (4), Miniature Pinscher (4), Jack Russell Terrier (4), Miniature Dachshund (3), Bichon Frise (3), Miniature Poodle (3), and Rat Terrier (3). There were 23 other purebred dogs (≤ 2 each) and 23 mixed-breed dogs. Fifty-five (53%) dogs had a diagnosis of diabetes mellitus. Development of POH was not significantly associated with age ($P = 0.729$),
breed (P = 0.610), sex (P = 0.838), or diabetes melitus status (P = 0.129).

Of the 180 eyes undergoing surgery, 154 were treated with twice-daily topical corticosteroids prior to surgery; most were treated for 1 to 3 weeks before surgery (mean ± SD duration, 17.4 ± 13.0 days [median, 14 days; range, 1 to 90 days]). For the remaining 26 eyes, topical treatment was not initiated prior to surgery owing to lack of owner compliance or the decision to perform surgery the day following evaluation because of scheduling limitations or marked lenticular intumescence prompting urgent surgical intervention. Preoperative topical corticosteroid administration was not associated with development of POH (P = 0.187).

**Preoperative ophthalmic factors**

Cataracts were most commonly categorized as mature (82/180 [46%] eyes), followed by immature (58/180 [32%] eyes) and hypermature (40/180 [22%] eyes). Biomicroscopically detectible evidence of quiescent or active lens-induced uveitis at the initial evaluation by the ophthalmology service or at the drop-off appointment for surgery (flare, keratic precipitates, or posterior synechia) was present in 15 of 180 (7%) eyes. Neither cataract stage (P = 0.146) nor lens-induced uveitis (P = 0.591) were predictors of POH.

Mean ± SD baseline IOP in eyes undergoing surgery was 11.7 ± 3.9 mm Hg [median, 11 mm Hg; range, 3.6 to 24.0 mm Hg]). Mydriatic provocative test data were available for 176 eyes, of which 3 had positive results (IOP > 25 mm Hg 1 hour after topical tropicamide administration). Twenty-nine of 180 (16%) eyes had an increase in IOP of ≥ 5 mm Hg at the 1-hour time point, compared with the baseline value. Neither baseline IOP nor a mydriatic provocative test result of ≥ 5 mm Hg increase in IOP was significantly associated with development of POH.

Gonioscopy findings were available for 175 of 180 (97%) eyes; the data were unavailable for 5 eyes because of record-keeping errors or clinician failure to perform the examination. The iridocorneal angle was considered normal (open) in 90 of 175 (51%) evaluated eyes; grades of mild, moderate, and severe were categorically assigned to 17 (10%), 34 (19%), and 34 (19%) eyes, respectively. For gonioscopy findings grouped as normal versus abnormal and for iridocorneal angle grades of normal, mildly affected, moderately affected, or severely affected, effect was measured both for incidence and severity of POH. Neither incidence (P = 0.992) nor severity (P = 0.348) of POH was associated with gonioscopic classification of normal versus abnormal. Neither incidence (P = 0.948) nor severity (P = 0.793) of POH was associated with categorical iridocorneal angle grades.

**Surgical factors**

Surgical factors evaluated included surgeon, VIAT, surgical time for each eye, phacoemulsification time, and closure IOP. On initial analysis, the factor of surgeon was significantly (P = 0.008) associated with development of POH, which was identified in 18 of 23 (78%), 10 of 26 (38%), 7 of 15 (47%) and 14 of 39 (36%) dogs for which phacoemulsification was performed by surgeons A, B, C, and D, respectively. The distribution of patients in the 2 treatment groups did not differ significantly among surgeons. Surgical times were variable, ranging from 30 to 110 minutes for eyes that developed POH and from 25 to 90 minutes for eyes that did not. Longer surgical time (from incision to closure of the cornea for each treated eye) was positively associated with development of POH (P = 0.020), although data were available for only 82 of 180 eyes (29 and 53 that did and did not subsequently develop POH, respectively, including 37 sham-treated and 45 DHTM-treated eyes). Data for most dogs were missing owing to variability in recording the start and end times on the anesthesia record.

Although surgical time and surgeon were each significant predictors of POH when evaluated individually, further analysis with mixed-model ANOVA revealed a significant (P = 0.001) association between the 2 factors, and surgical time became nonsignificant (P = 0.074) after adjusting for surgeon in the multivariable logistic generalized estimating equations model. Similarly, a significant (P = 0.029) relationship was initially detected between higher VIAT and development of POH (mean ± SD VIAT was 63 ± 22 seconds [median, 60 seconds; range, 32 to 135 seconds] for eyes that developed POH, whereas that for eyes that did not develop POH was 56 ± 20 seconds [median, 50 seconds; range, 22 to 120 seconds]); however, mixed-model ANOVA identified a significant (P < 0.001) association between VIAT and surgeon, and after adjusting for surgeon in the multivariable logistic generalized estimating equations model, VIAT also became a nonsignificant (P = 0.804) factor.

Phacoemulsification time had a significant (P < 0.001) positive association with dog age, with a mean increase of 26.23 seconds (95% confidence interval, 17.64 to 34.81 seconds) for each additional year of age (n = 103 dogs). No significant (P = 0.936) difference in phacoemulsification times was found between eyes with (mean ± SD, 275 ± 143 seconds [median, 234 seconds; range, 42 to 696 seconds]; n = 65) and without (mean ± SD, 279 ± 181 seconds [median, 222 seconds; range, 0 to 1,032 seconds]; 114) POH. Similarly, closure IOP was not significantly (P = 0.791) associated with development of POH, with a mean ± SD closure IOP of 6.88 ± 4.24 mm Hg for all eyes (n = 176 eyes), 7.12 ± 5.49 for eyes that developed POH (62), and 6.74 ± 3.40 mm Hg for eyes that did not develop POH (114).

**Treatment effects**

Overall, 53 dogs (94 eyes undergoing surgery) received DHTM treatment and 50 dogs (86 eyes undergoing surgery) received the sham treatment. Assessment of IOPs prior to surgery in a subset of 74 eyes in
39 patients (38 eyes of 20 patients and 36 eyes of 19 patients that received DHTM and the sham treatment, respectively) revealed that the mean ± SD IOP was not different between the treatment groups at baseline (11.75 ± 3.22 mm Hg and 12.23 ± 4.77 mm Hg for eyes that received the DHTM and sham treatments, respectively; P = 0.672) or 6 hours after administration of the first dose of the assigned treatment (11.37 ± 2.94 mm Hg and 12.64 ± 3.90 mm Hg, respectively; P = 0.230). However, by 11 hours after this treatment, eyes that received DHTM had a significantly (P = 0.029) lower mean ± SD IOP than those that received the sham treatment (10.27 ± 2.72 mm Hg vs 12.57 ± 3.56 mm Hg, respectively). Application of DHTM also resulted in a significantly (P = 0.025) lower IOP at the 11-hour time point, compared with the baseline IOP, whereas administration of the sham treatment did not (P = 0.825). The mean IOP for DHTM-treated eyes was significantly (P < 0.001) lower than that of eyes that received the sham treatment at all contiguous postoperative time points when the LOCF method was used to account for dropout of dogs when POH developed (Figure 1). The effect of treatment over time was also significant (P < 0.001).

The incidence of POH (at dog level) was 31 of 50 (62%) among dogs that received the sham treatment, versus 18 of 53 (34%) among those that received DHTM treatment (P = 0.004). Forty-two of 86 (49%) sham-treated eyes that underwent surgery had POH identified at one of the predetermined postoperative IOP measurement time points, with a significantly (P = 0.005) smaller proportion (24/94 [26%]) of DHTM-treated eyes having this result. The odds for development of POH were significantly lower following DHTM treatment than after sham treatment, whether evaluated on the basis of affected eyes (OR, 0.36 [95% confidence interval; 0.18 to 0.73; P = 0.005]) or at the level of dog (OR, 0.32 [95% confidence interval, 0.14 to 0.58]; P = 0.001) (Figure 2). The greatest number of new cases of POH was found at the 2-hour time point, and most (60/66 [91%]) POH cases were diagnosed by the 4-hour time point. See Figure 1 for key.

Figure 1—Mean ± SD IOPs at contiguous predetermined time points up to 8 hours after cataract removal by phacoemulsification in 180 eyes of 103 dogs in a prospective study to evaluate the effects of perioperative DHTM administration on the incidence and severity of POH (defined as IOP > 25 mm Hg at any of the predetermined postoperative IOP measurement times). Dogs received 1 drop of topically applied DHTM (light gray bars) or a sham treatment solution (sterile, buffered, isotonic eye drops; dark gray bars) in both eyes, regardless of whether unilateral or bilateral surgery was performed, at 3 time points: 14 hours before planned anesthetic induction time, 2 hours before planned anesthetic induction time, and the time of corneal incision closure (considered the end of surgery). The IOPs in awake animals were measured with a designated handheld rebound tonometer with the patient in sternal recumbency, sitting, or standing. *Mean IOP was significantly (P < 0.001) lower for DHTM-treated than for sham-treated eyes (LOCF method).

Figure 2—New cases of POH identified at predetermined study time points (2 to 8 hours after surgery and between 7:30 and 8:00 AM on the following day) for the same 180 eyes of dogs in Figure 1. In total, 66 eyes in 49 dogs developed POH as identified by the study protocol; the greatest number of new cases of POH was found at the 2-hour time point, and most (60/66 [91%]) POH cases were diagnosed by the 4-hour time point. See Figure 1 for key.

Figure 3—Cumulative frequency of POH at contiguous predetermined time points up to 8 hours after surgery in the same 180 eyes of dogs in Figure 1. The cumulative frequency of POH by the 8-hour time point was 24 of 94 (26%) and 42 of 86 (49%) for DHTM- and sham-treated eyes, respectively. *Cumulative frequency of POH was significantly (P ≤ 0.003) lower for DHTM-treated than for sham-treated eyes (LOCF method). See Figure 1 for remainder of key.
to 0.71; \( P = 0.005 \)). This effect was enhanced after adjusting for surgeon (OR, 0.19; 95% confidence interval, 0.07 to 0.50; \( P < 0.001 \)). When the 77 dogs that underwent bilateral surgery were evaluated separately, DHTM treatment was associated with a significantly (\( P = 0.029 \)) lower incidence of POH, whether unilateral or bilateral. Of 36 sham-treated dogs, 12 (33%) had no POH, 13 (36%) had unilateral POH, and 11 (31%) had bilateral POH. Of 41 DHTM-treated dogs, 26 (63%) had no POH, 9 (22%) had unilateral POH, and 6 (15%) had bilateral POH.

For most eyes with POH (60/66 [91%]), the condition developed by the 4-hour time point; the greatest number of new cases (40 [61%]) was detected at the 2-hour time point (Figure 2). When the LOCF method was used to compare differences between treatment groups over time, the cumulative frequency of POH was significantly lower at 2 (\( P < 0.001 \)), 4 (\( P = 0.002 \)), 6 (\( P = 0.003 \)), and 8 (\( P = 0.003 \)) hours after surgery in DHTM- versus sham-treated eyes (Figure 3). The final time point for IOP measurements (between 7:30 and 8:00 AM on the day after surgery) was not contiguous and was therefore not included in the LOCF analysis of POH; only 1 eye (in the DHTM group) had POH newly diagnosed at this time point, and statistical analysis was not possible.

Mean ± SD IOP at the time of POH detection was 32.67 ± 6.39 mm Hg (median, 31.0 mm Hg; range, 25.33 to 51.67 mm Hg) for DHTM-treated eyes and 37.17 ± 10.47 mm Hg (median, 33.5 mm Hg; range, 25.33 to 66.67 mm Hg) for those that underwent sham treatment; this difference was nonsignificant (\( P = 0.069 \)). Sixty eyes had IOPs of 26 to 45 mm Hg and were initially treated for POH with 1 drop of latanoprost solution according to the study protocol. When POH was identified, 19 of 25 (76%) DHTM-treated eyes and 18 of 35 (51%) eyes that received sham treatment had an acceptable response to treatment (IOP < 25 mm Hg 1 hour after latanoprost administration). Odds of an acceptable response in DHTM-treated eyes were 3.87 times those of eyes that received the sham treatment (OR, 3.87; 95% confidence interval, 1.03 to 14.51 [\( P = 0.045 \)]). However, the difference in mean ± SD IOPs between treatment groups 1 hour after latanoprost administration (21.41 ± 7.89 mm Hg vs 27.49 ± 14.67 mm Hg for DHTM- and sham-treated eyes, respectively) was nonsignificant (\( P = 0.090 \)).

**Discussion**

To the best of our knowledge, the present study was the first masked, controlled prospective investigation of DHTM as prophylaxis against POH in dogs undergoing phacoemulsification. Perioperative administration of DHTM resulted in a lower incidence of POH in this study, compared with the sham treatment. Overall, POH developed in 66 of 180 (37%) eyes and in 49 of 103 (48%) dogs that underwent surgery, in agreement with results of other studies\(^\text{4,9-14,35}\) (with POH identified in 41/179 [23%]\(^\text{2} to 68/139 [49%]\(^\text{10}\) eyes and 5/25 [18%]\(^\text{19} to 35/51 [69%]\(^\text{10}\) dogs).

In the present study, POH was identified in 18 of 53 (34%) versus 31 of 50 (62%) dogs following DHTM and sham treatment, respectively (\( P = 0.004 \)). Twenty-four of 94 (26%) DHTM-treated and 42 of 86 (49%) sham-treated eyes developed POH (\( P = 0.005 \)). Additionally, among dogs undergoing bilateral surgery, the proportion of dogs that did not develop POH in either eye was significantly (\( P = 0.029 \)) greater among those that received DHTM (26/41 [63%] vs 12/36 [33%]). The DHTM administration protocol used in this study, which required topical administration at 5 perioperative time points, was determined on the basis of a review of human medical literature, which indicated that administration of a single pre- or postoperative dose might be less effective than multidose prophylaxis regimens.\(^\text{36-38}\)

Previous studies evaluating the effect of prophylactic medications on development of POH in dogs have been limited to topically administered latanoprost and intracameral administered carbachol, producing mixed results. In a retrospective study, Crasta et al\(^\text{11}\) found no significant effect of routine postoperative administration of latanoprost on occurrence of POH (6/21 [29%] and 15/46 [33%] in treated and untreated dogs, respectively). Stuhr et al\(^\text{13}\) prospectively evaluated intracameral carbachol treatment in a small sample (1 eye in each of 32 dogs) undergoing elective cataract surgery and detected POH in 0 of 16 treated and 12 of 16 untreated control eyes. Conversely, Crasta et al\(^\text{11}\) found significantly higher IOP 2 hours after surgery in carbachol-treated eyes, compared with untreated control eyes, and no significant difference in the incidence of POH between these groups. Moeller et al\(^\text{14}\) reported that carbachol treatment was associated with increased risk of POH in Labrador Retrievers and decreased risk in dogs of other breeds following phacoemulsification. Additionally, carbachol is known to cause brow pain in human patients,\(^\text{39}\) and both carbachol and latanoprost induce marked miosis that precludes postoperative examination of the posterior segment; both effects are undesirable traits in a pharmacological agent for POH amelioration.

The highest number of new cases of POH in the present study was found at 2 hours after surgery (with the end of surgery designated as the end of corneal incision closure); 40 of 66 (61%) eyes had POH identified at that time, and 60 (91%) of the affected eyes had POH identified by 4 hours after surgery. These results conformed to the findings of studies by Crasta et al\(^\text{11}\) (with POH present in 36/38 cases by 2 hours after surgery), Chahory et al\(^\text{9}\) (with 7/14 and 13/14 cases identified by 3 and 5 hours after surgery, respectively), and Miller et al\(^\text{12}\) (with 17/17 dogs having IOP > 30 mm Hg within 3 hours after surgery). However, it is impossible to rule out the occurrence of POH at unmonitored time points. One of the aforementioned studies\(^\text{11}\) did not include IOP measurements between 4 hours after surgery and the following morning, and another\(^\text{9}\) had no postoperative measurements between the 5- and 18-hour time
points. A retrospective study by Smith et al.\textsuperscript{10} found a mean onset of POH at 4.9 hours after surgery in eyes undergoing phacoemulsification; however, IOP measurement times were not standardized. In the present study, IOP monitoring was limited to 2, 4, 6, and 8 hours after surgery and between 7:30 AM and 8 AM on the day after surgery; and 3 dogs were known to have developed POH late in the study or after the predetermined 8 AM cutoff for the last IOP measurement but were not included in the totals of dogs with POH for the analyses. One DHTM-treated dog had bilateral POH diagnosed when the clinician measured its IOPs 10 hours after surgery (inadvertently deviating from the protocol); this was not one of the preselected time points, and subsequent IOPs were excluded from the 8 AM data set because antiglaucoma medications had been administered. Two additional dogs that received DHTM treatment developed POH after the last study time point on the morning after surgery and underwent treatment prior to discharge from the hospital.

It was not possible to determine whether any residual pharmacological effects of DHTM remained at or after the 8 AM time point the day after surgery. To the authors’ knowledge, neither the duration of action nor point of maximal efficacy of DHTM on IOP has been specifically evaluated in the human or veterinary literature; additionally, we administered 3 doses of DHTM during our treatment protocol (14 and 2 hours before planned surgical induction and at time of corneal incision closure), and this dosage regimen has not been specifically evaluated in dogs. However, Moisseiev et al.\textsuperscript{10} found that treatment with DHTM 3 times daily resulted in lower IOPs with no impact on safety, compared with twice-daily administration in human patients, and topical treatment with DHTM every 8 hours is commonly prescribed by ophthalmologists in our group for treatment of glaucoma in dogs, without resulting in complications. It seems likely that the effect of DHTM in our study would have been reduced by the time of the last IOP measurement, given that the final dose in the study was administered approximately 16 hours to 20 hours before that time. However, further study of the DHTM protocol used in this study would be required before we could estimate the duration of efficacy for POH prophylaxis in dogs undergoing phacoemulsification.

When POH did develop in our study population, eyes that had been treated with DHTM were significantly (\(P = 0.045\)) more likely to have an acceptable clinical response to 1 drop of 0.005% latanoprost solution than were eyes that received the sham treatment (OR, 3.87). Latanoprost was chosen so that a novel class of antihypertensive medication would be used to treat any eye with POH in light of the fact that the study design precluded the knowledge of which eyes had already been treated with DHTM. Additionally, latanoprost has been shown to have a fairly short time to maximal efficacy in Beagles used for glaucoma research (resulting in a mean decrease in IOP of 6.3 ± 0.3 mm Hg at 4 hours after administration)\textsuperscript{41} and is known to effect a rapid and marked decrease in IOP in dogs with glaucoma.\textsuperscript{42,43} Some researchers and clinicians have expressed concern over treatment with latanoprost in patients with uveitis, as its effects as a prostaglandin analog might exacerbate such inflammation.\textsuperscript{20,45} However, latanoprost was found to be safe for use in human patients with glaucoma and uveitis.\textsuperscript{44} Although the drug may induce mild blood-aqueous-barrier breakdown,\textsuperscript{45} this seems unlikely to cause a substantial difference in eyes with considerable preexisting barrier damage related to the cataract surgery itself. Additionally, in the short term, control of high IOP is arguably a more important goal than control of inflammation. No overt complications were observed during our study, although markers of uveitis were not directly compared between eyes that did and did not receive latanoprost treatment.

We found no association between the signalment factors evaluated (breed, age, and sex) or diabetes mellitus status and the development of POH. Other investigators have found an increased risk of POH after phacoemulsification in Labrador Retrievers, compared with other breeds\textsuperscript{4,11} and the Boston Terrier breed was associated with higher risk of POH in 1 study,\textsuperscript{11} whereas another study\textsuperscript{4} did not detect this association. We had low numbers of both of these breeds in our study, and this could have influenced our findings. Age was positively associated with development of POH in the study by Smith et al.,\textsuperscript{10} whereas, similar to our results, Moeller et al\textsuperscript{4} and Klein et al\textsuperscript{4} did not detect this association. The lack of a significant relationship between POH and sex or diabetes mellitus status in the present study supported the findings of other investigators.\textsuperscript{4,10,11}

Our findings with regard to the relationship of ophthalmologic factors and POH were generally in agreement with previous reports. We found no association between lens-induced uveitis and development of POH, consistent with the results of other investigations.\textsuperscript{2,4,10} However, it should be acknowledged that fluorophotometry demonstrated a loss of blood-aqueous barrier stability indicative of inflammation in the eyes of dogs with all stages of cataracts, despite a lack of clinical signs in some patients\textsuperscript{49}; thus, lens-induced uveitis is a difficult risk factor to assess effectively. Additionally, eyes with marked intraocular inflammation were often excluded from our study on the basis of treatment with confounding medications, leaving 13 eyes in the study with evidence of clinically important historical or ongoing lens-induced uveitis and potentially limiting the strength of our conclusions on the lack of association between this condition and POH. Cataract stage was also not associated with development of POH in our study, confirming the results of other studies.\textsuperscript{3,10,40} We did not identify a protective effect of cataract hypermaturity against development of POH as was reported by Crasta et al.,\textsuperscript{11} in which the authors speculated that the effect may have been related to their exclusion of patients with lens-induced uveitis. Our finding of a lack of association between baseline IOP and development of POH was in agreement with previous results for dogs that
underwent cataract surgery. However, we excluded patients that had preexisting ocular hypertension or were being treated with antiglaucoma medications, and this may explain the difference between our results and those reported in studies of human patients, in which many eyes undergoing phacoemulsification had preexisting glaucoma, preoperative IOP was positively correlated with postoperative IOP and the presence of preoperative glaucoma was a predictor of POH.

On initial analysis of surgical factors, surgeon, surgical time, and VIAT were each identified as significant predictors of POH; however, further analysis revealed that surgeon was significantly associated with the other 2 variables. One surgeon in the study (surgeon A) had a significantly (P = 0.008) higher proportion of patients develop POH than did the remaining 3. After adjusting for surgeon in the multivariable analysis, both surgical time and VIAT lost significance. Several surgical technique factors were not controlled for in the study but were generally very similar among surgeons B, C, and D, whereas surgeon A used several methods not used by the other 3, including endocapsular phacoemulsification, a 2-minute intracapsular incubation of sterile water to facilitate visualization and removal of lens epithelial cells, performing VIAT prior to suture placement for corneal incision closure, and closing the incision with an interrupted rather than a continuous suture pattern. These technique differences were specific to surgeon A; therefore, they could not be evaluated separately as risk factors for development of POH. However, the authors consider that surgical time and corneal suture pattern were both plausible contributors to the high rate of POH among patients treated by 1 surgeon in this study. It is generally accepted that tissue trauma increases with time during intraocular surgery, and postulated mechanisms of POH in dogs include tissue swelling and altered anatomy at the iridocorneal angle-ciliary cleft; however, to the author's knowledge, total surgical time has not been previously evaluated as a risk factor for POH in human or veterinary patients. Considering that surgeon A had both the longest surgical times and the highest proportion of patients that developed POH, it is plausible that increased duration of surgery exacerbated tissue swelling at the drainage angle and predisposed eyes to development of POH. However, the clinical relevance of this association is unclear, given the overlapping and broad ranges of surgical time in each group (30 to 110 minutes and 25 to 90 minutes for eyes that did and did not develop POH, respectively). Watertight wound closure has also been postulated to contribute to the development of POH in people. Although it is possible that a simple interrupted suture pattern is more watertight than a continuous pattern, potentially contributing to development of POH, we found no available data regarding fluid leakage following closure of biplanar incisions such as those created in this study with simple interrupted versus continuous symmetrical sawtooth patterns. Further evaluation of surgical time and various closure techniques would be required for more definitive conclusions.

Intracamerar administration of viscoelastic materials is known to be associated with POH in dogs and removal by irrigation, and aspiration is recommended. Results of an experimental study indicated that complete removal of a viscoelastic preparation (similar to that used in the present study) from human eyes was achieved within 20 to 25 seconds of starting the procedure. Although this has not been specifically evaluated in dogs, a reduced rate of POH was documented in 1 study where VIAT was standardized to ≥ 1 minute in dogs undergoing cataract surgery, compared with the rate of POH prior to standardization (37/137 [27%] and 4/42 [9.5%] of eyes developed POH prior to and after standardization of VIAT). In our study, we found no relationship between VIAT and POH once the statistical analysis was adjusted for surgeon.

None of the remaining surgical factors evaluated in the present study were significant predictors of POH. In contrast, a 1996 study by Smith et al found that increased phacoemulsification time was associated with increased risk of POH. Although Klein et al found no significant effect of phacoemulsification power on incidence of POH, the duration of the phacoemulsification procedure was not evaluated in that study.

The relationship between patient age and phacoemulsification time has not been previously investigated to the authors’ knowledge. A significant (P < 0.001) positive association between phacoemulsification time and age was confirmed in this study and was likely attributable to the increase in lens density that develops throughout life. Because age was not a predictor of POH, the lack of association between phacoemulsification time and development of POH was not surprising. Finally, IOP at the time of incisional closure was also not a predictor of POH.

The present study had several shortcomings. Four clinicians, including 2 board-certified veterinary ophthalmologists and 2 veterinary ophthalmology residents, performed ophthalmic examinations, gonioscopy, and surgery on the patients. Frequently, both a board-certified ophthalmologist and a resident performed ophthalmic examination and gonioscopy on a given dog. In such cases, agreement on gonioscopy findings, although not analyzed statistically, was subjectively strong. The intent of the gonioscopy grading scheme was to create a mechanism of scoring that would be indicative of the severity of abnormalities in each patient while remaining sufficiently efficient to fit into our standard cataract evaluation appointment. This meant that we could not adhere to previously published schemata requiring sedation, anesthesia, or gonioscopic photography. To account for the relatively subjective nature of clinical gonioscopy, our desire to grade the percentage of the iridocorneal angle affected by narrowing, closure, or pectinate ligament dysplasia; the small number of
eyes with each condition; and the variability of definitions of gonioscopic abnormalities within the literature, we categorized eyes as minimally, moderately, or markedly affected on the basis of the estimated percentage (< 10%, 10% to 50%, or > 50%, respectively) involvement of the visible portion (270°) of the iridocorneal angle by any of the 3 conditions for purposes of statistical analysis, with neither the presence of any gonioscopic abnormality (normal vs abnormal) nor grouped categorical grades (minimal, moderate, marked) having a significant association with the incidence or severity of POH. The grouping of different gonioscopic abnormalities and the potentially subjective nature of gonioscopic findings were weaknesses of the present study that prevented formation of definitive conclusions on the relationship between iridocorneal angle morphology and incidence of POH.

Tonometry was another potential source of variability in this project, and specific steps were taken to minimize the influence of this source of error. Applanation IOP measurements obtained just after corneal incision closure were performed by 1 of 3 trained veterinary technicians from the ophthalmology service using a handheld applanation tonometer. Postoperative IOPs were measured at time points during which the surgeons and ophthalmology technicians were not consistently available. A designated rebound tonometer was used for all IOP measurements in awake animals because results obtained by inexperienced and experienced users were shown to be well correlated with results of previous studies in which this instrument was used.55,56 Additionally, instructions and training were provided to all users, and for all IOP measurements, 3 low- or no-error readings were required, with the mean of these 3 readings used as the value for each time point. To avoid errors related to the presence of topical agents on the cornea (e.g., ointments), a water-soluble topical lubricant (2.5% hydroxypropyl methylcellulose) that could be easily rinsed from the eye prior to tonometry was used as a protectant from anesthesia-induced reduction of tear production.

Other limitations were mainly related to patient factor variability and the involvement of multiple clinicians and tonometers. Conversely, these factors may broaden the applicability of our results to the treatment of other dogs undergoing cataract removal by phacoemulsification in clinical ophthalmology practice. The exclusion of dogs with complications that precluded adherence to the study protocol was certainly a source of bias, but was ethically unavoidable. A total of 18 dogs (27 eyes) were excluded from the study for this reason. In 4 eyes, the surgeon detected substantial lens subluxation with vitreal prolapse and felt the use of intracameral carbocashed was indicated for optimal surgical outcome. Twelve eyes of 8 dogs were excluded from the study owing to the presence of marked lens-induced uveitis or ocular melanosis-related miosis, necessitating additional preoperative cycloplegic medications. Similarly, the exclusion of dogs with preexisting glaucoma or IOP > 30 mm Hg 1 hour after pharmacological mydriasis was unavoidable but prevented us from establishing efficacy of the treatment protocol in such patients. Additionally, evaluation of only study completer data introduced bias into the analysis; however, this was considered unavoidable, as dogs were excluded or removed from the study on the basis of having received medications confounding interpretation of the primary outcome parameters (IOP and POH) or absence of required data. Despite these limitations, the study identified substantial clinical benefits in the patients that received topical DHTM treatment, compared with those that received the sham treatment. Future research might evaluate the potential of routine postoperative administration of latanoprost in combination with the 3-treatment DHTM protocol used in the present study to assess whether such treatment can be safely used to reduce the incidence or severity of POH in dogs undergoing cataract removal by phacoemulsification.

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Footnotes
b. Hi-Tech Pharmacal Co Inc, Amityville, NY.
c. Abbott Medical Optics Inc, Abbot Park, Ill.
d. TonoVet, Icare Finland Oy, Helsinki, Finland/Jorgensen Laboratories, Loveland, Colo.
f. BSS, Alcon Laboratories, Fort Worth, Tex.
h. Acrivet Inc, S&V Technologies GmbH, Salt Lake City, Utah.
i. SAS, version 9.4, SAS Institute Inc, Cary, NC.
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Comparison of contrast media for visualization of the colon of healthy dogs during computed tomography and ultrasonography

Byunggyu Cheon et al

OBJECTIVE
To evaluate contrast agents for their ability to improve visualization of the colon wall and lumen during CT and ultrasonography.

ANIMALS
10 healthy adult Beagles.

PROCEDURES
Food was withheld from dogs for 36 hours, after which dogs consumed 250 mL of polyethylene glycol solution. Dogs were then anesthetized, a contrast agent (tap water, diluted barium, or air; order randomly assigned) was administered rectally, iodine contrast medium (880 mg of I/kg) was administered IV, and CT and ultrasonography of the colon were performed. After a 1-week washout period, this process was repeated with a different contrast agent until all agents had been evaluated. Two investigators reviewed the CT and ultrasonographic images for colon wall thickness, conspicuity, artifacts, wall layering, and degree of lumen dilation at 4 sites.

RESULTS
Thickness of the colon wall was greatest in CT and ultrasonographic images with water used as contrast agent, followed by barium and then air. The CT images obtained after water administration had a smooth appearance that outlined the colonic mucosa and had the highest score of the 3 contrast agents for wall conspicuity. Although no substantial artifacts related to any of the contrast agents were identified on CT images, barium- and gas-induced shadowing and reverberation artifacts hindered wall evaluation during ultrasonography. For ultrasonography, the degree of conspicuity was highest with barium in the near-field wall and with water in the far-field wall. In contrast to CT, ultrasonography could be used to distinguish wall layering, and the mucosal and muscular layers were distinct with all contrast agents.

CONCLUSIONS AND CLINICAL RELEVANCE
Use of water as a contrast agent for both CT and ultrasonography of the colon in dogs compensated for each imaging modality’s disadvantages and could be beneficial in the diagnosis of colon disease. (Am J Vet Res 2016;77:1220–1226)