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ORIGINAL REPORT

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Iris angiography in ADAMTS10 mutant dogs with open-angle glaucoma (*ADAMTS10-OAG*)

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Abstract

Objective: To evaluate anterior segment angiographic findings in hypertensive ADAMTS10-open-angle glaucoma (*ADAMTS10*-OAG) eyes as compared to normotensive control eyes.

Animals Studied: Nine *ADAMTS10-OAG* beagles and four *wild-type* control dogs.

Procedures: Anterior segment angiography was performed under general anesthesia following intravenous injection of indocyanine green (ICG; 1 mg/kg) and sodium fluorescein (SF; 20 mg/kg) using a Heidelberg Spectralis® confocal scanning laser ophthalmoscope. Time to onset of iridal angiographic phases and the presence/severity of dye leakage into the iris stromal and/or aqueous humor were recorded. Group findings were compared, and multiple linear regression analysis was performed to identify potential factor associations with disease status.

Results: Time to onset of all angiographic phases visualized using ICG was significantly prolonged while time to onset of SF leakage into the aqueous humor was significantly reduced in glaucomatous eyes compared to controls. Only glaucomatous eyes ($n = 9$) demonstrated evidence of SF stromal leakage. Mean intraocular pressure (IOP) and age were significantly higher, while mean cardiac pulse was significantly lower in glaucomatous eyes compared to controls. Blood pressure and ocular perfusion pressure were not significantly different between groups. Multiple linear regression analysis, controlling for age, IOP, and pulse demonstrated glaucoma, was not predictive of the time to onset of any angiographic phase, stromal, or aqueous humor leakage. However, pulse was a significant factor contributing to the severity of aqueous humor leakage.

Conclusions: A compromised vascular supply to the anterior segment exists in dogs with *ADAMTS10-OAG*. These observations warrant further exploration of what role altered perfusion and/or disruption to the blood–aqueous barrier may play.

KEYWORDS
ADAMTS10-open-angle glaucoma (*ADAMTS10*-OAG), angiography, canine, uvea

1 | INTRODUCTION

Glaucoma is an important ophthalmic disease in canines due to the associated intraocular pressure (IOP) elevation and subsequent optic neuropathy.[1] Primary open-angle glaucoma (POAG) represents the most prevalent form of primary glaucoma in humans,[2] whereas primary angle-closure glaucoma (PACG) is the predominant form of primary glaucoma in dogs.[3] Canine PACG represents a disease by which acute closure of the iridocorneal angle, appreciated gonioscopically and/or by ultrasound biomicroscopy, is influenced by factors such as pectinate ligament dysplasia.[4] Canine open-angle glaucoma (OAG) is best characterized in beagles with a G661R missense mutation in the *ADAMTS10* gene[5] and typically shows a more insidious elevation of IOP compared to PACG.[3] In some forms of human OAG, low diastolic perfusion pressure has been suggested to contribute to the progression of glaucomatous optic neuropathy.[6] In addition, ocular hypertension is associated with the progression of glaucomatous disease due to low ocular perfusion pressure (OPP).[7] Examination of ophthalmic vessel blood flow velocities via color Doppler imaging in OAG beagles suggested a pressure-associated increase in vascular resistance,[8] which was not apparent in normal beagles.[9] However, the potential effects on perfusion of the anterior uvea have not been reported.

The use and comparison of sodium fluorescein (SF) and indocyanine green (ICG) angiography to assess iridal vasculature in canines free of ophthalmic and systemic disease have been previously described.[10] Due to the tendency of SF to leak through iridal vessels into the aqueous humor,[11] employing SF angiography in glaucomatous dogs may show increased leakage; if vascular compromise and subsequently increased vessel permeability exist. Unlike SF, the comparatively increased peak absorbance wavelength of ICG permits enhanced visualization of the iridal vasculature via reduced wavelength scatter and improved wavelength penetrability of pigmented structures, such as darkly pigmented irises.[10] Therefore, any existent delays in perfusion to the anterior segment vasculature should be detected by ICG. To our knowledge, the effects of glaucoma on anterior segment perfusion have not been explored in dogs.

This pilot study compared anterior segment indocyanine green angiography and anterior segment sodium fluorescein angiography findings between nine purpose-bred *ADAMTS10-OAG* beagle dogs with four *wild-type* control beagles free of glaucomatous disease. Compromised blood supply to the uvea, secondary to elevated IOP and decreased OPP, could lead to the disruption of the blood–aqueous barrier and subsequent elevation of IOP. Parameters such as anterior segment perfusion, blood pressure, and OPP could represent future prognostic biomarkers for primary canine glaucoma.

2 | MATERIALS AND METHODS

2.1 | Animals

Nine purpose-bred *ADAMTS10*-mutant beagle dogs with OAG and four wild-type, control beagles free of glaucomatous disease were utilized. All *ADAMTS10-OAG*-affected dogs were categorized as hypertensive, exhibiting an average diurnal IOP ≥20 mmHg (mean ± SD = 25.3 ± 4.3 mmHg) with optic nerve head changes (atrophy and cupping), as documented by indirect ophthalmoscopy and optical coherence tomography over the previous 6 months. Four glaucomatous dogs had been receiving dorzolamide hydrochloride 2%-timolol maleate 0.5% (Micro Labs Inc, Basking Ridge, NJ) one drop in both eyes every 12 hours, while one dog had been receiving dorzolamide hydrochloride 2%-timolol maleate 0.5% one drop in both eyes every 12 hours and neomycin–polymyxin B–dexamethasone (Bausch and Lomb, Bridgewater, NJ) one drop in both eyes every 12 hours. The remaining four glaucomatous dogs had not been receiving any medications. Glaucomatous dogs on medications received their last medication the afternoon prior to anesthesia and angiographic imaging. No control dogs utilized in the study received topical medications.

All dogs received complete physical and ophthalmic examinations the day before anterior segment angiography. Ophthalmic examination included evaluation of a menace response, dazzle and pupillary light reflexes, Schirmer tear test (Merck Animal Health: Madison, NJ, USA), topical fluorescein staining (Ful-Glo: Akorn, Decatur, IL), rebound tonometry (TonoVet, iCare, Vantaa, Finland), slit-lamp biomicroscopy (Kowa SL-17; Kowa Company, Tokyo, Japan), and indirect ophthalmoscopy (Keeler All Pupil II: Keeler Instruments, Broomall, PA, USA; Pan Retinal 2.2D condensing lens; Volk Optical).

All studies were performed in accordance with the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research guidelines and were approved by the Michigan State University Institutional Animal Care and Use Committee.

2.2 | Anesthetic protocol

All dogs received a standard sedation protocol utilizing acepromazine maleate 0.1–0.2 mg intravenously (IV) (Henry Schein Animal Health, Dublin, OH) and butorphanol tartrate 0.2 mg/kg IV (Torbugesic; Zoetis: Parsippany, NJ), immediately followed by diphenhydramine hydrochloride 2 mg/kg intramuscularly (Baxter Healthcare Corp, Deerfield, Il) to prophylactically counteract IV dye induced anaphylaxis. Standard induction protocol with propofol 30 mg IV (PropoFlow, Baxter Healthcare, Deerfield, Il) and midazolam 0.2 mg/kg IV (Midazolam, Akorn Inc, Lake Forest, Il) was utilized and administered through a sterilely placed cephalic catheter 20 min after sedation. All dogs were kept under general anesthesia via isoflurane (between 1% and 4%) in oxygen (1–2 L/min) following tracheal intubation. An IOP of the primary eye imaged was measured from all dogs immediately before sedation (pIOP) and following anesthesia (aIOP) using rebound tonometry (TonoVet, iCare, Vantaa, Finland). Pulse, systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressures (MAP) were obtained every 5 min for all dogs during anesthesia (Mindray PM9000 Vet; Mahwah, NJ). Other vital parameters, including respiratory rate, end-tidal CO2, oxygen saturation, and temperature, were also obtained during anesthesia, but were not utilized in the study's analysis.

2.3 | Anterior segment angiography

A Heidelberg Spectralis® confocal scanning laser ophthalmoscope (Heidelberg Engineering Inc.; Heidelberg, Germany) fit with a 55° lens and automatic Real-time Tracking was used to conduct anterior segment angiography. The imaging sequence for angiography was initiated following injection of dye into the IV catheter, using the appropriate settings (i.e., 488-nm excitation laser and 500-nm barrier filter for SF and 790-nm excitation laser and 830-nm barrier filter for ICG). The sensitivity was set to and maintained at 70. A 60-s video sequence, with a frame rate of 30 images per second, of the anterior segment was obtained and time-stamped to permit accurate analysis at different points in time. Thirty seconds following the complete capture of the 60-s video, still images were captured every minute for 5 min.

The right eye was randomly selected for imaging from five *ADAMTS10-OAG*-affected and one control dog; the left eye was selected for imaging from the remaining dogs (four *ADAMTS10-OAG*-affected and three controls). Following one drop of proparacaine hydrochloride 0.5% ophthalmic solution, USP (Akorn, Decatur, Il), globe positioning was facilitated by placing two 4-0 polypropylene stay sutures in the bulbar conjunctiva. A Barraquer eyelid speculum was applied to maintain the palpebral fissure open.

Following induction and globe centration, standard color (Canon Mark IV 5D, Canon, Tokyo, Japan) and near-infrared images (Heidelberg Spectralis®) were obtained from the eye used for angiography. An IV bolus of 0.25% ICG (1 mg/kg) (C-Green, Akorn Inc, Lake Forest, Il) was administered first. Imaging of the eye was performed as described above. An IV bolus of SF (20 mg/kg) (K-Fluor, Akorn Inc, Lake Forest, Il) was subsequently administered 10 min after ICG administration. Imaging of the eye was performed in the same manner for SF as ICG. During imaging, the cornea was kept moist to avoid ulceration and optimize image clarity via regular application of balanced salt solution (BSS, Alcon Laboratories Inc: Fort Worth, TX).

2.4 | Angiography evaluations

Time of onset of the arterial, capillary, and venous phases were measured and identified by the initial filling of ICG within the major arterial circle of the iris, pupillary capillaries, and iridal veins, respectively (Figure 1). Arterial and capillary phase intervals were measured and defined as the time onset of one phase to the onset of the next phase. Time of start of iris stromal and aqueous humor SF leakage was also measured. The severity score of iris stromal SF leakage was assessed following a previously established grading scheme of 0–4.[12] Severity scores of SF leakage into the aqueous humor were graded subjectively, characterized as grade 0 = none, grade 1 = mild, grade 2 = moderate, and grade 3 = severe (Figure 2). All measurements were performed in duplicate (Christopher G Pirie) and averaged upon completion of the study. Angiographic images were compared between groups, characterizing any noted vascular changes and assessing the degree of dye extravasation.

2.5 | Statistical analysis

The sample size for this study was determined by assuming a time difference of 2 s between angiographic phases when comparing glaucomatous and control eyes, utilizing a power calculation that set for a power of 80%, α of 0.05, and a standard deviation of 1.2 s.

For each dog, mean values were first calculated for parameters involving more than one measurement obtained under anesthesia (pulse, SBP, DBP, MAP). Systolic OPP (SOPP), diastolic OPP (DOPP), and mean OPP (MOPP) were calculated using differences between the mean SBP,

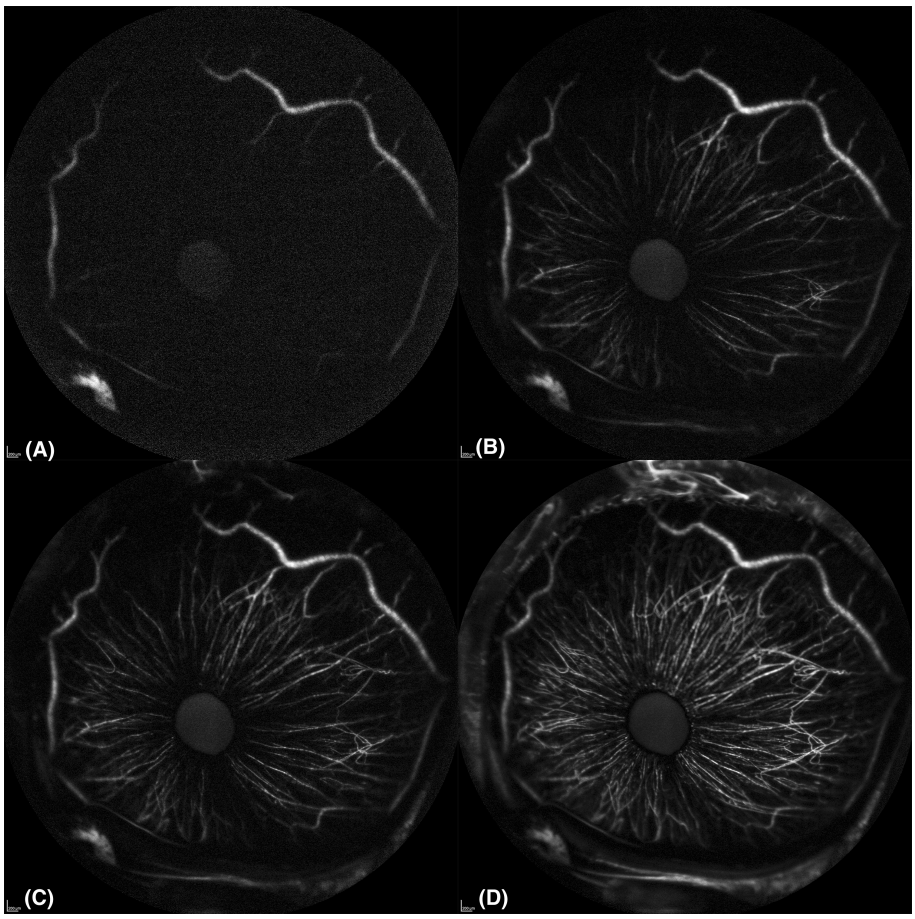

FIGURE 1 Representative anterior segment indocyanine green angiography (ASICGA) images of the left eye from an 8 month-old intact male *wild-type* control dog. After intravenous (IV) injection of indocyanine green (ICG), initial filling of the major arterial circle (A; 4 s) and early filling of radial iris arteries (B; 6 s) is observed during the arterial phase. Progressive filling of radial iris arteries and initial filling of terminal capillary loops within the peri-pupillary region denotes the capillary phase (C; 8 s), and progressive filling of radial iris veins is observed during the venous phase D; 11 s).

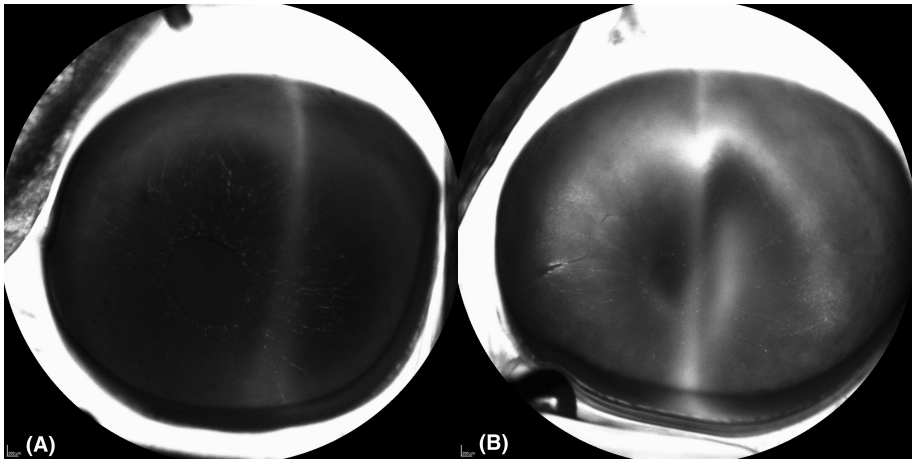

FIGURE 2 Representative anterior segment sodium fluorescein angiography (ASSFA) images of the left eyes of two *ADAMTS10-OAG* affected dogs (A; 4-year-old intact male, B; 4-year-old intact female) to illustrate the subjective grading scheme used to characterize the severity of dye leakage following intravenous (IV) injection of sodium fluorescein (SF). Images were acquired at 2 min after SF injection. Grade 0 corresponds to no SF leakage within the anterior chamber (not shown). Grade 1 corresponds to a mild degree of SF leakage within the anterior chamber (A). Grade 2 corresponds to a moderate amount of SF leakage (B). Grade 3 (not shown) corresponds to severe SF leakage within the anterior chamber.

DBP, and 2/3 MAP and the aIOP of the primary eye imaged, respectively.[13] A Welch two-sample t-test was used to compare differences in age; pulse; pIOP; aIOP; SBP; DBP; MAP; SOPP; DOPP; MOPP; times to onset of arterial, capillary, and venous phases; times to onset of SF leakage into the iris stromal and aqueous humor; and stromal and aqueous humor SF leakage severity scores between the mutant dogs with glaucoma and controls. The same set of comparisons was analyzed utilizing a nonparametric bootstrap test with pooled resampling, which has been suggested to be appropriate for small sample sizes.[14] In addition, multiple linear regression analysis was used to evaluate whether the presence or absence of glaucoma is predictive of the time to onset of arterial, capillary, and venous phases and iris stromal and aqueous humor leakage, when controlling for age, pulse, and aIOP. For all analyses, a value of $p < .05$ was considered significant.

3 | RESULTS

3.1 | Animals

All dogs in the study were beagles. The *wild-type* control dogs were all intact males and 8 months of age. The median weight of the control dogs was 7.75 kg (range, 7.0–9.5 kg). Of the glaucomatous dogs studied, five were intact females, and four were intact males. Their median age and weight were 3.5 years (range, 3.2–5.8 years) and 15.0 kg (range, 9.2–18.4 kg), respectively. Dogs with OAG were significantly ($p < .001$) older than control dogs. Half of the control dogs were subjectively considered to possess heavily pigmented irises (dark brown), whereas the other half had moderately pigmented irises (brown). Six *ADAMTS10-OAG* glaucomatous dogs possessed heavily pigmented irises (dark brown), and the rest had moderately pigmented irises (brown). IOP data for all dogs studied are listed in Table 1. Compared to the *wild-type* controls, the dogs with *ADAMTS10-OAG* had a significantly greater pIOP ($p < .001$) and aIOP ($p < .05$).

3.2 | Vital parameter findings

Vital parameter data for all dogs studied are listed in Table 1. Average pulse was found to be significantly higher ($p < .05$) in the *wild-type* control group compared to the *ADAMTS10*-OAG group. The average SBP, DBP, MAP, SOPP, DOPP, and MOPP were not significantly different between the two groups.

TABLE 1 Summary of vital parameters for *ADAMTS10*-OAG-affected and wild-type dogs during peri-anesthetic period.

	Pulse (beats/minute)	(mmHg)							
		pIOP	aIOP	SBP	DBP	MAP	SOPP	DOPP	MOPP
ADAMTS10-OAG									
1	120.6	43	23	106.6	45.9	74.3	83.6	22.9	28.8
2	120.6	34	35	118.6	49.6	80.8	83.6	14.6	25.1
3	99.5	44	20	114.2	48.5	80.8	94.2	28.5	33.6
4	104.2	23	41	97.8	44.3	63.5	56.8	3.3	14.1
5	87	40	21	92.8	37	60.5	71.8	16	23.1
6	109.4	31	29	109.5	38.7	70.1	80.5	9.7	22.2
7	99.4	51	39	91.1	36.1	60	52.1	−2.9	10.3
8	114.4	21	24	120.4	57.8	86.6	96.4	33.8	36.4
9	95.1	27	20	86.6	31.6	56	66.6	11.6	20
Median	104.2	34	24	106.6	44.3	70.1	80.5	14.6	23.1
Wild-type									
10	126	20	17	119.6	50.2	83.2	102.6	33.2	37.6
11	165.4	18	12	97.7	36.4	57.9	85.7	24.4	29.9
12	137.5	18	15	73.2	35.2	51	58.2	20.2	21.9
13	154.9	22	20	104.6	40.4	68.5	84.6	20.4	27.9
Median	146.2	19	16	101.15	38.4	63.2	85.15	22.4	28.9

Abbreviations: aIOP, anesthetic intraocular pressure; DBP, diastolic blood pressure; DOPP, diastolic ocular perfusion pressure; MAP, mean arterial pressure; MOPP, mean ocular perfusion pressure; pIOP, pre-sedation intraocular pressure; SBP, systolic blood pressure; SOPP, systolic ocular perfusion pressure.

TABLE 2 Summary of times to onset of angiographic events for *ADAMTS10*-OAG-affected and wild-type dogs.

	Indocyanine green angiography (s)			Sodium fluorescein angiography (s)	
	Arterial phase	Capillary phase	Venous phase	Stromal leakage	Aqueous humor leakage
ADAMTS10-OAG					
1	3.1	3.9	4.6	5.9	30
2	2.5	4.4	5.2	6.2	20
3	2.5	3.4	4.7	5.3	21
4	3.8	7	8.5	18.3	30
5	3.6	5.5	6.4	7	20
6	3.4	9.7	10.8	12.5	30
7	7	15.5	17.4	14.7	25
8	4	8	8.8	4.6	20
9	3.8	7.3	8.1	10.4	25
Median	3.6	7	8.1	7	25
Wild-type					
10	2.3	3.6	4.1	No leakage	60
11	1.8	4	4.8	No leakage	120
12	2.1	3.1	3.6	No leakage	60
13	3	4.9	5.6	No leakage	120
Median	2.2	3.8	4.45	Not applicable	90

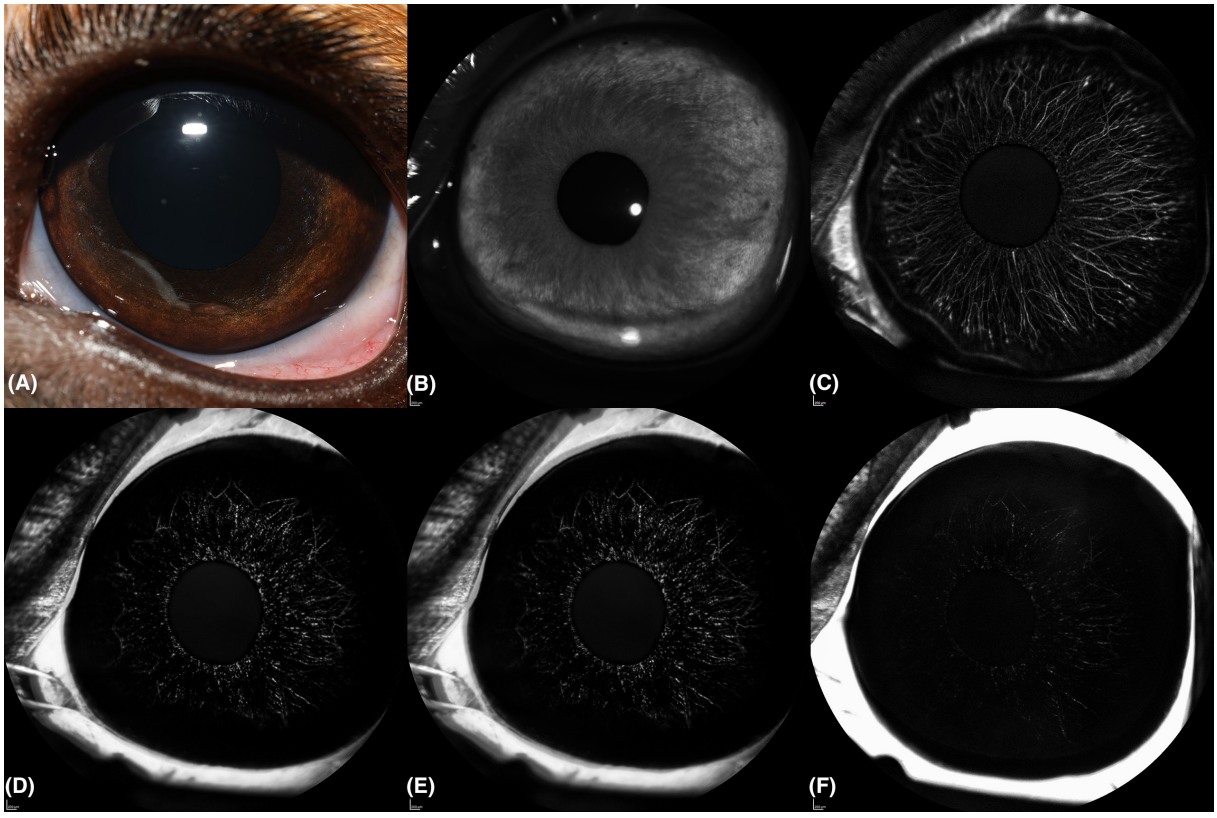

FIGURE 3 Representative standard color (A), near-infrared (B), anterior segment indocyanine green angiography (ASICGA) (C), and anterior segment sodium fluorescein angiography (ASSFA) (D–F) images of the left eye of an 8-month-old intact male *wild-type* control beagle dog. Angiographic images were obtained at 20 s (C and D), 30 s (E), and 60 s (F) after intravenous (IV) injection of dye. There is no evidence of leakage of indocyanine green (ICG) (C) or SF (D–F).

3.3 | Angiographic imaging

Quantitative angiographic imaging data are listed in Table 2. Time of onset for the arterial, capillary, and venous phases was significantly shorter ($p < .05$) in *wild-type* control eyes compared to *ADAMTS10*-OAG eyes.

No leakage of SF dye into the iris stroma was detected in *wild-type* control eyes (Figure 3; grade 0); however, leakage was observed in all *ADAMTS10*-OAG eyes imaged (Figure 4). Leakage of SF into the iris stroma was significantly greater ($p < .001$) in *ADAMTS10*-OAG eyes versus *wild-type* control eyes. The leakage severity score in all *ADAMTS10*-OAG eyes imaged was graded as 2 (Figure 5).

The time to onset of leakage of SF into the aqueous humor was found to be significantly longer ($p < .05$) in *wild-type* control eyes as compared to *ADAMTS10*-OAG eyes (Table 2). The aqueous humor SF leakage severity score median values in *wild-type* control and *ADAMTS10*-OAG eyes were 1 (range, 1–2) and 2 (range, 1–2), respectively. This difference between groups was not found to be statistically significant ($p > .3$).

The presence or absence of OAG, when controlling for age, pulse, and aIOP, was not predictive of the time to onset of arterial, capillary, and venous phases or iris stromal and aqueous humor leakage based on the linear regression model. However, the overall model was significant (adjusted $R^2 = 79.96\%$, $F = 12.97$, $p < .001$), indicating pulse significantly predicted the severity of aqueous humor leakage ($p < .05$).

4 | DISCUSSION

To our knowledge, this pilot study is the first in the veterinary literature to examine the relationship between OAG and ocular perfusion involving the anterior segment, notably the iridal and ciliary body vasculature. The study results suggest potential hindrance to perfusion of the iris vasculature in dogs with *ADAMTS10-OAG*, as indicated by the statistically significant prolongation in times to onset of the arterial, capillary, and venous phases in dogs with OAG compared to dogs without glaucoma.

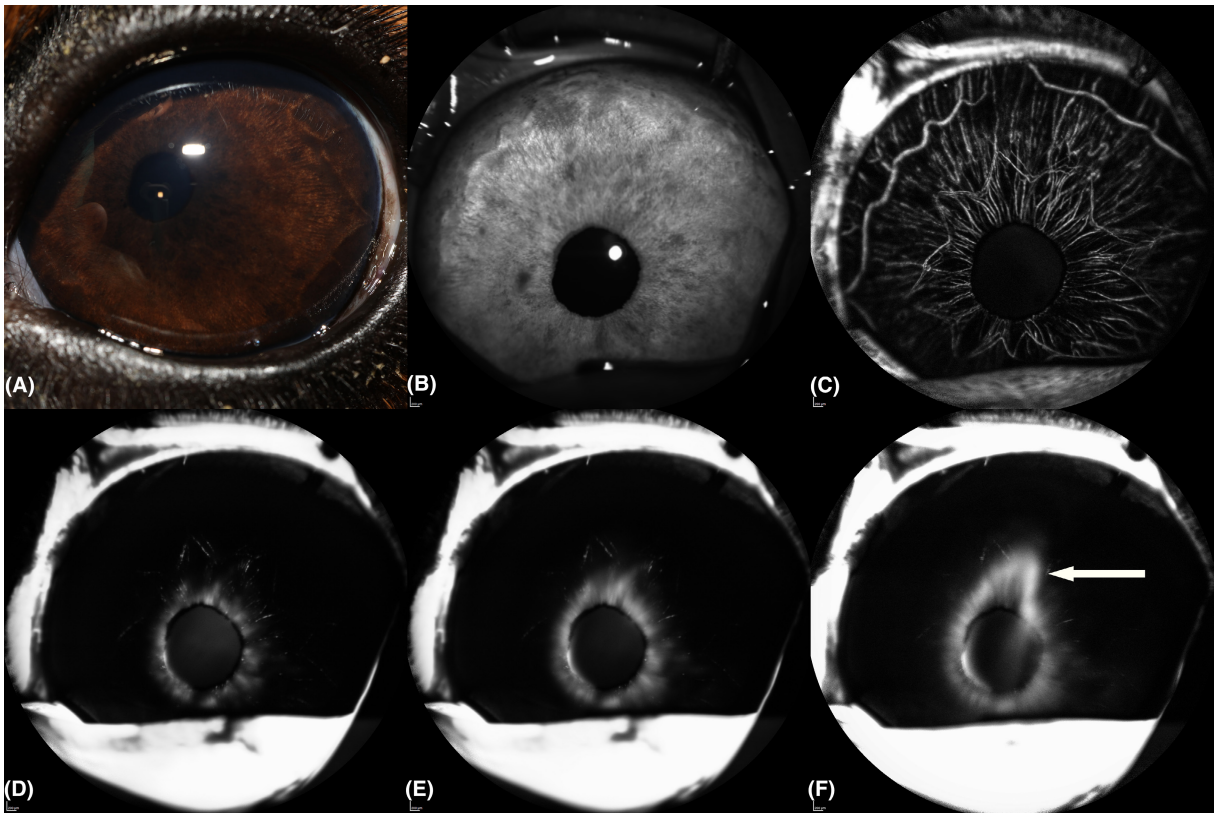

FIGURE 4 Representative standard color (A), near-infrared (B), anterior segment indocyanine green angiography (ASICGA) (C), and anterior segment sodium fluorescein angiography (ASSFA) (D–F) images of the left eye of a 4-year-old intact female *ADAMTS10*-OAG-affected beagle dog. Angiographic images were obtained at 20 s (C and D), 30 s (E), and 60 s (F) after intravenous (IV) injection of dye. There is no evidence of leakage of indocyanine green (ICG) (C). After IV injection of sodium fluorescein (SF), progressive leakage within the peripupillary region is apparent at 20 s (D), 30 s (E), and 60 s (F). Leakage of SF is evident in 4 quadrants of the peripupillary border (grade 2). There is marked leakage of SF into the aqueous humor (F; arrow). Extravasation of SF within the lower palpebral conjunctiva, due to outward rolling of the lower eyelid margin, is also noted (D–F).

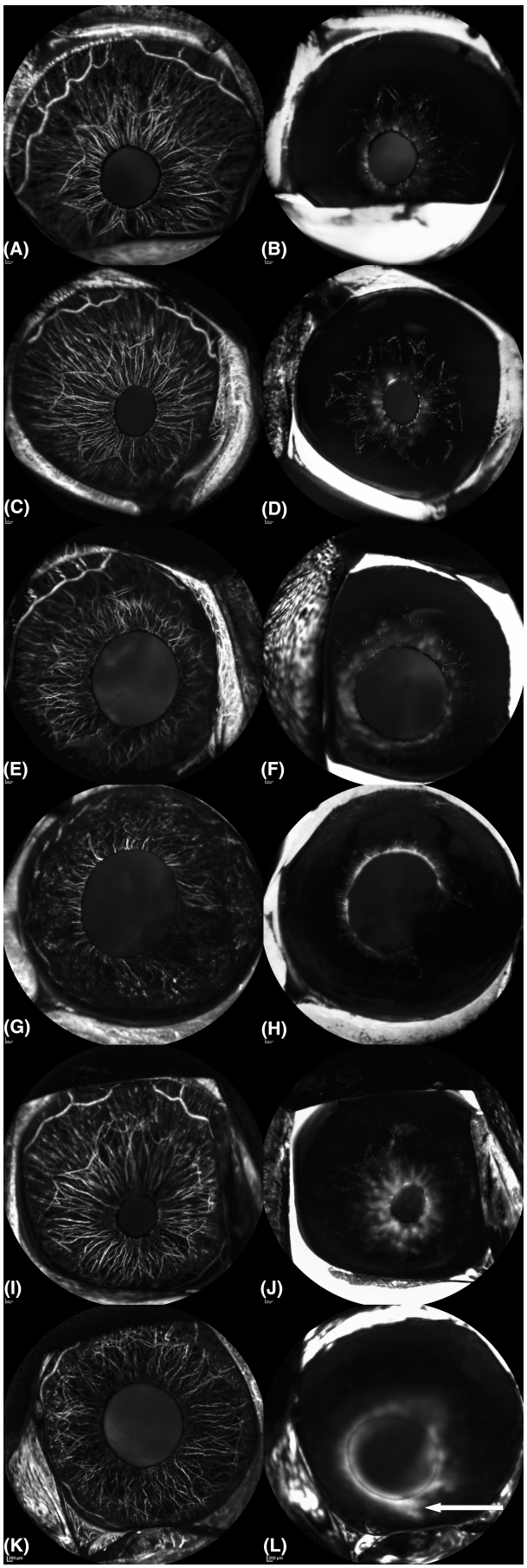

FIGURE 5 Representative anterior segment indocyanine green angiography (ASICGA) (A, C, E, G, I, and K), and anterior segment sodium fluorescein angiography (ASSFA) (B, D, F, H, J, and L) images from 6 *ADAMTS10*-OAG-affected beagle dogs. All images were obtained 20 s following intravenous (IV) dye injection. Images represent the left eye of a 4-year-old intact male (A and B), the right eye of a 3.3-year-old female (C and D), the right eye of a 5.5-year-old female (E and F), the left eye of a 4-year-old intact male (G and H), the right eye of a 3.3-year-old intact male (I and J), and the left eye of a 3.3-year-old female (K and L). No stromal leakage of indocyanine green (ICG) was observed (A, C, E, G, I, and K) Note that peripupillary leakage of SF in 3–4 quadrants (grade 2) of the iris stroma is readily apparent (B, D, F, H, J, and L). Early leakage of sodium fluorescein (SF) into the aqueous humor (L; arrow) is also noted 20 s following dye injection.

This hindrance was also evident by the slower onset of leakage and greater severity score of SF within the aqueous humor in dogs with OAG. While SF dye leakage into the aqueous humor has previously been noted to occur in 6/10 (60%) of normal canine eyes,[10] results of this study demonstrated a decreased time to onset and greater severity of SF leakage into the aqueous humor of *ADAMTS10-OAG* eyes, as compared to *wild-type* controls, suggesting pressure-related ischemic damage to iris vasculature may occur. This notion is further supported by only observing SF leakage into the iris stroma of *ADAMTS10-OAG* eyes.

In humans with POAG, posterior segment vascular defects have been reported.[15–17] However, studies examining the effects of ocular hypertension and glaucoma involving the anterior uveal vasculature in humans are lacking. Unlike the reported relationship between blood pressure, OPP, and glaucoma in humans,[7] such a relationship was not established in the present study.

We found that pulse was significantly higher in *wild-type* controls than in *ADAMTS10*-OAG dogs, which is likely related to the fact that *wild-type* controls were considerably younger than *ADAMTS10*-OAG dogs. Other studies have suggested that dogs less than 12 months of age have a higher average pulse compared to adult dogs.[18,19] The pIOP and aIOP were higher in *ADAMTS10*-OAG dogs than in *wild-type* controls. When age, pulse, and aIOP were controlled, multiple linear regression analysis revealed that the presence of OAG was not predictive of the time to onset of the arterial, capillary, and venous phases or of the time to onset of stromal and/or aqueous humor leakage. However, pulse was a significant variable contributing to the severity of aqueous humor leakage.

The present study's small sample size represents a potential limitation; a larger sample size may have revealed a potential relationship between elevated IOP, OPP, and blood pressure. Due to the small sample size,

regression analysis is not likely to produce unbiased results. The erroneous DOPP value obtained, −2 mmHg, in one *ADAMTS10*-OAG dog indicates potential errors in the measurements of anesthetic blood pressure. In addition, because of the study's use of dogs with OAG, the findings do not necessarily translate to dogs with PACG due to the differences in pathophysiology. Further studies to include dogs with PACG are needed to discern if similar findings are present in members of this more common form of primary glaucoma. The absence of age-matched control dogs limited the study's ability to elucidate the effect of age on anterior segment vascular integrity and perfusion.

Despite the aforementioned limitations, the current study findings suggest that dogs with ADAMTS10-OAG have compromised vascular integrity within the anterior segment due to an elevated IOP. The demonstrated delayed perfusion and disruption to the blood–aqueous barrier may be indicative of ischemic damage to the tissues of the anterior uvea, as a direct result of OAG and IOP elevations. This, in turn, may lead to the development of low-grade uveitis. These changes could potentiate elevations in IOP with chronicity through the development of phenomena such as preiridal fibrovascular membranes and synechiae. This vicious cycle of intraocular inflammation and pressure elevation would warrant the use of topical and systemic anti-inflammatory medications as a core component of the treatment regime for dogs with primary glaucoma. This notion is supported by previous studies[20–23] that outline the potential role that inflammation plays in the progression of primary glaucoma. Further studies are warranted to investigate whether such medications benefit to anterior segment perfusion and/or controlling elevations in IOP in dogs with OAG.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts related to this study. Dr. Komáromy received research funding from PolyActiva Pty. Ltd. and CRISPR Therapeutics while the presented work was conducted. He also serves as a consultant for Reichert Technologies and Editor-in-Chief of Veterinary Ophthalmology.

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