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Surgical Treatment of Nictitans Membrane Eversion in Dogs

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Abstract: The presented study is the first retrospective evaluation of the scrolling of the third eyelid in a total of 44 dogs referred to the Istanbul University-Cerrahpaşa, Faculty of Veterinary, Department of Surgery between 2012 and 2021 with a sudden onset of an ocular mass in the medial canthus with epiphora and conjunctival hyperemia. The clinical appearance of the patients, the treatment procedures applied, and the results were examined. A complete ophthalmological inspection revealed the cartilage eversion of the nictitating membrane in sixteen patients (24 eyes) due to the scrolling of the third eyelid and cartilage eversion accompanied by a prolapsed gland in twenty-eight patients (32 eyes). Cartilage eversion was treated by the resection of the defected cartilage portion. In cases with prolapse of the nictitans gland accompanying cartilage eversion, the Morgan pocket method was applied to reposition the prolapsed gland by resectioning the rotating cartilage. In conclusion, -taking into account the potential effect of breed, age, and gender predispositions- the therapeutic approach followed revealed satisfactory results in maintaining the functional capacity of the third eyelid in dogs with cartilage eversion of the nictitating membrane and hyperplasia of the nictitans gland.
Keywords: *Cartilage eversion, Dog, Scrolling, Third eyelid*.

Köpeklerde Üçüncü Göz Kapağının Dışarı Dönmesinin Cerrahi Yöntemler ile Sağaltımı

Özet: Bu çalışma, 2012-2021 yılları arasında İstanbul Üniversitesi-Cerrahpaşa, Veteriner Fakültesi Cerrahi Anabilim Dalı Kliniği'ne epifora, konjunktival hiperemi ve medial kantusta aniden ortaya çıkan bir kitle varlığı şikâyeti ile getirilen toplam 44 köpeğin değerlendirildiği ilk retrospektif çalışmadır. Getirilen hastaların klinik görünümü, tedavisi ve sonuçları incelenmiştir. Ayrıntılı oftalmolojik muayeneler sonucunda üçüncü göz kapağının kıvrılması ile ilişkili kıkırdağın dışarı dönmesi (16 olgu, 24 göz) ve kıkırdağın dışarı dönmesi ile üçüncü göz kapağı bezinin prolapsusunun (28 olgu, 32 göz) varlığı ortaya çıktı. Kıkırdağın dışarı dönmesi olgularında bozulmuş kıkırdak bölümü uzaklaştırıldı. Kıkırdağın dışarı dönmesine eşlik eden üçüncü göz kapağı bezinin prolapsusu olgularında ise dönen kıkırdağın uzaklaştırılması ile prolabe olan bezin yeniden konumlandırılması için Morgan cep yöntemi uygulandı. Çalışma sonunda elde edilen verilere göre üçüncü göz kapağı ile kıkırdağının dışarı dönmesi ve bu duruma eşlik eden üçüncü göz kapağı bezinin hiperplazisi oluşumunda ırk predispozisyonu, yaş ve cinsiyetin etkisi dikkate alınarak, kullanılan cerrahi yöntemlerin üçüncü göz kapağının fonksiyonunun korunmasında yeterli olduğu belirlendi.
Anahtar Kelimeler*: Kıkırdak eversiyonu, Kıvrılma, Köpek, Üçüncü göz kapağı*

Introduction

The third eyelid scrolling is the rolling out or eversion of the nictitating membrane (Rezaei et al., 2019; Williams and Miller, 2006). The deformity that developed due to the rotation or folding of the T-shaped cartilage of the third eyelid (eversion) toward the lower eyelid clinically manifests itself as the nictitating membrane's partial visibility from outside on the bulbar surface (Çakmakçi, 2019; Rezaei et al., 2019; Williams and Miller, 2006). The condition is a rare ophthalmological disorder in companion animals, more common in dogs than cats (Williams et al., 2012). Although the disorder may develop at any age range, it was most frequently reported in young dogs (Ramani et al., 2010). All canine breeds may be affected; nevertheless, some breeds revealed a higher prevalence rate (Çakmakçi, 2019; Ramani et al., 2010). The etiology of the lesion, which has both unilateral and bilateral involvement in dogs, is still unclear, yet genetic predisposition and some environmental factors such as trauma have been suggested as the underlying cause (Çakmakçi, 2019; Rezaei et al., 2019). Clinical signs include epiphora, blepharospasm with relatively mild severity, sudden onset of a pinkish mass or swelling in the medial canthus (Williams et al., 2012), and even a simultaneously occurring nictitans gland prolapse (Hendrex, 2007; Williams et al., 2012).

Several surgical procedures such as application of a temporary third eyelid flap, resection of the eyelid, resection of the eyelid margin and cartilage, removal of the deformed or bent portion of cartilage, total cartilage resection, and cartilage homograft application, thermal cautery of the nictitating membrane (Allbaugh and Stuhr, 2013; Crispin, 1986; Rezaei et al., 2019), and resection of the gland and cartilage in cases with a concurrent prolapsed gland

(Allbaugh and Stuhr, 2013; Michel et al., 2020) are proposed for the surgical correction of outwardly rotated/everted nictitating membrane.

The present study aims to investigate the clinical outcomes and potential complications of the preferred surgical approach to correct the third eyelid eversion in dogs by also demonstrating the most frequently affected dog breeds with the age and gender distribution.

Materials and Methods

Dogs Involved in the Study: The study was conducted with fifty-six eyes of a total of 44 dogs, which were referred to the surgery clinics of the Istanbul University-Cerrahpaşa, Faculty of Veterinary Medicine between 2012 and 2021, with the complaints of a sudden onset of a pinkish-colored ocular swelling, blepharospasm, conjunctival hypermia, and epiphora (Figure 1a). This study is not subject to HADYEK's permission under Article 8(k) of the "Regulation on Working Procedures and Principles of Animal Experiments Ethics Committees".

Ophthalmologic Examination and Preoperative Process: All patients underwent detailed eye examinations. Five to 10 min after applying a topical anesthetic agent, proparacaine HCl (Alcaine 0.5%, Alcon, Belgium), the rolled-out nictitating membrane was carefully examined. The everted cartilage and gland prolapse accompanying the eversion of the nictitating membrane was distinguished (Figures 1b, c,d).

All surgical procedures were performed under general anesthesia. An informed consent document was obtained from each owner, showing that they accepted all complications that may occur during and after the operation. Premedication was achieved by intravenous (IV) injection administration of xylazine hydrochloride (Rompun® 2%, Bayer, Turkey) at a dose of 0.5-1 mg/kg. Anesthesia was induced by the IV injection of 4-6 mg/kg of propofol (Propofol® 200 mg/20mL, Abbott, Turkey) and maintained by an inhalation anesthetic, isoflurane at a concentration of 2-3% (Forane®, liquid, Abbott, England) in %100 oxygen.

Figure 1. a) Conjunctival swelling and hyperemia in the right eye for 1 month in a one-year-old Alabai b) The appearance of cartilage eversion in a 3-months-old Alabay in case 43 c) Cartilage eversion and nictitans gland prolapse in the right eye in a 10-years-old German Shepherd d) Bilateral cartilage eversion in a 5-months-old Anatolian Shepherd.

Surgical Procedures

Resection of Cartilage: The procedure was performed in accordance with the method previously described by Ramani et al. (2010) for dogs. The surgical approach for cartilage resection was directed at the bulbar surface of the nictitating membrane. The loose end of the nictitating membrane was stabilized by two mosquito forceps. Initially, two small transverse incisions were made parallel to the long arm of the scrolled cartilage to excise the everted cartilage portion using a Stevens sharp pointed scissors. Then, a small tunnel was created by inserting the scissors into the initial incision site directed toward the latter to separate the everted cartilage portion away from the adjacent palpebral conjunctiva. Thus, the long arm of the cartilage was released from the third eyelid's palpebral conjunctiva by blunt dissection, and the scrolled cartilage was cut out. The incised conjunctival tissue was not sutured and left intact for secondary wound healing.

Resection of Cartilage and Applying Morgan Pocket Technique: When the glands prolapse accompanied the eversion of the third eyelid cartilage, the Morgan pocket technique was applied as a further intervention. The surgical procedure was performed in accordance with the combined method previously described by Georgescu et al. (2015) in a Basset Hound dog diagnosed with the relevant two conditions. Likewise, the bulbar surface of the nictitating membrane was targeted for the surgical approach. Two parallel incisions were made on the dorsal (close to the loose end of the third eyelid) (Figure 2a) and ventral (close to the cornea) (Figure 2b) aspects of the prolapsed gland on the bulbar aspect of the third eyelid. The bulbar and palpebral conjunctiva that was adjacent to and bilaterally surrounding the cartilage was bluntly dissected by Stevens scissors (Figures 2c, d) along the dorsal incision line, which was situated 2-3 mm behind the eyelid's loose end, and the bent portion of the cartilage was removed (Figures 3a, b). After resectioning the defected cartilage portion, the ventral incision line parallel to the dorsal incision was further dissected to allow the subconjunctival repositioning of the prolapsed gland (Figure 3c). Then, the prolapsed gland was inserted within the subconjunctival tissue by the Morgan pocket technique and stabilized. The incision line was closed with a continuous suture (Vicryl® 4-0, polyglactin 910, Belgium), assuring that the knots remained on the palpebral aspect of the nictitating membrane (Figure 3d).

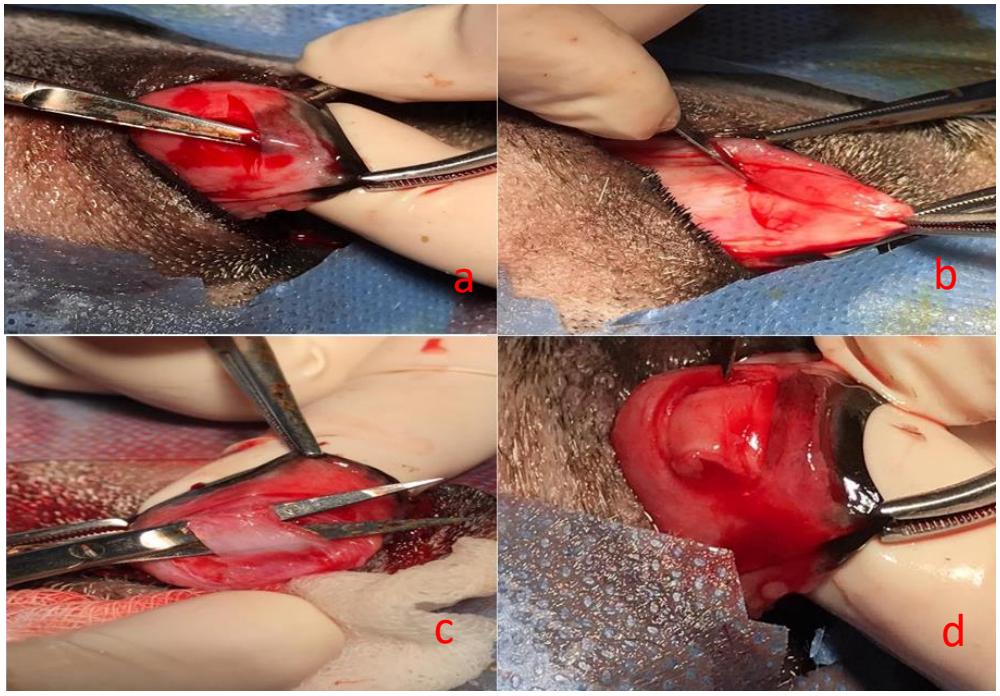

Figure 2. a) First incision close to the free edge of the third eyelid and dissection with scissors b) Second incision close to the cornea c) Blunt dissection of the scrolled cartilage portion using a Stevens pointed scissors d) Appearance of the rotating cartilage after blunt dissection from the palpebral conjunctiva.

In the postoperative period, all dogs had to wear an Elizabethan collar for two weeks to avoid self-trauma. Ofloxacin (Exocin®, Alcon, Ireland), dextran 70 and hypromellose (Tears natural II® free, Alcon, France), and diclofenac sodium (Inflased®, Bilim, Turkey) eye drops were prescribed for one

drop TID for two weeks, while carbomer gel (Thilo – Tears®, Alcon, Belgium) was topically applied twice a day. The follow-up inspections were performed on days 7, 14, 30, 45, and 90 in the postoperative period to monitor potential recurrence and complications, such as ocular surface disorders manifested by corneal injury and keratoconjunctivitis sicca.

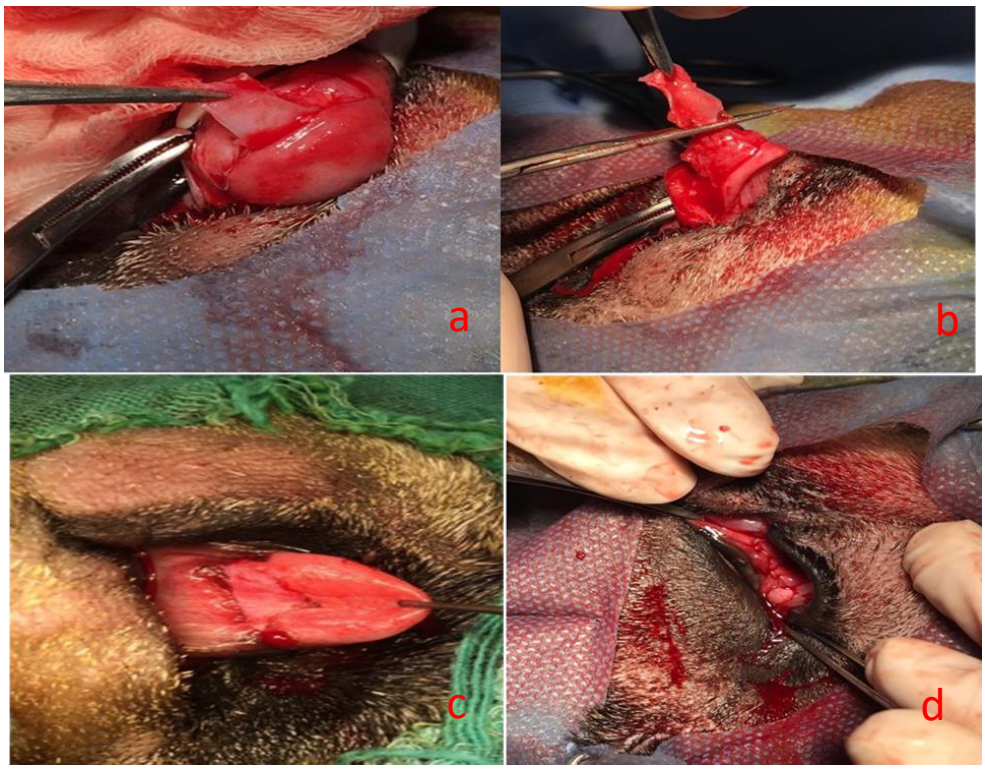

Figure 3. a) The first incision of the everted cartilage close to the nictitans gland b) Removing the rotating part of the cartilage c) Subconjunctival repositioning of the prolapsed gland through the ventral incision line after resection of the defective part of the cartilage d) Closing the incision line using of 4/0 polyglycolic acid with simple continuous suture.

Results

The distribution of the age of the dogs with the nictitating membrane eversion was as follows: Twenty (45.4%) dogs were younger than one year old, nineteen (48.1%) were between 1- 7 years old, and five (11.3%) were older than seven years, (age range from 3.5 months to 10 years, the average age was 2.5 years). The lesion showed bilateral involvement in 12 (27.2%) while unilateral in 32 (72.7%) dogs. The distribution of dogs with cartilage eversion by sex, affected eyes, and accompanying gland prolapse was shown in figure 4 and the breed distribution of dogs with cartilage eversion in figure 5.

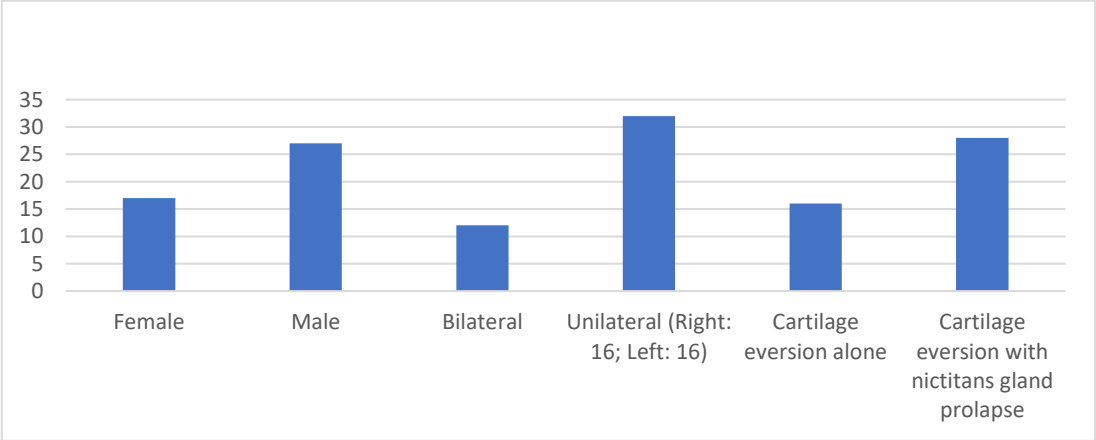

Figure 4. Distribution of cartilage eversion in dogs by sex, affected eyes, and accompanying gland prolapse.

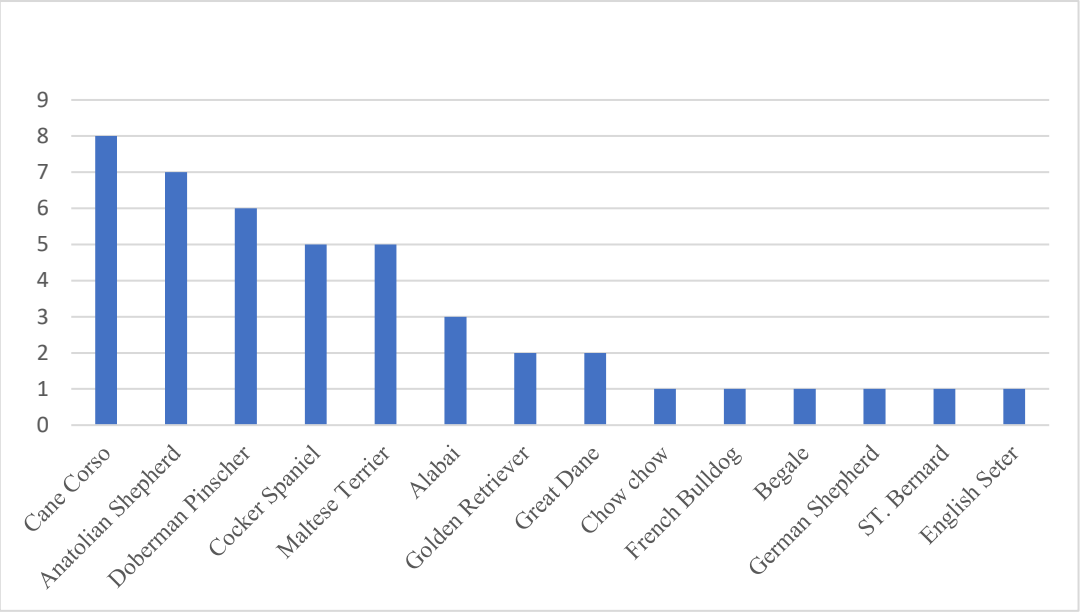

Figure 5. The breed distrubution of dogs with cartilage eversion

The period between the onset of the condition and the referral for treatment ranged from 3 days to two years (Average: 41.7 days). Seven (15.9%) dogs had an acute condition, while the disorder revealed a chronic course in thirty-seven (84.1%) patients. In 21.4% (n=12) of the cases, the eversion had developed as bending at the junction of the vertical and horizontal portions of the T-cartilage, while in a horizontal pattern overlapping the cartilage's shaft, which provides structural support for the nictitating membrane, in 78.6% (n=6, cartilage eversion per se; n=38 cartilage eversion and comorbid gland prolapse). Comorbid ocular disorders, such as keratoconjunctivitis sicca (n=4, Figure 6a), reduced tear quality and quantity (n=5), eyelid abnormalities (entropion, n=2; lagophthalmos, n=3; eyelash disorders, n=3, bulbar and orbital diseases (proptosis, n=1; enophthalmos, n=1), chronic follicular conjunctivitis (n=5), and corneal diseases (n=6) were also noted in some patients. The nictitans gland cyst that developed due to the Morgan pocket method was shown in Figure 6b. Postoperative complications were shown in figure 7.

Figure 6. a) Keratoconjunctivitis sicca, mucoprulent discharge, conjunctival hyperemia and pigmentation accompanying third eyelid diseases in one year old Anatolian Shepherd dog (Case No. 36) b) The development of nictitans gland cyst as a postoperative complication in a 6-month-old French Bulldog.

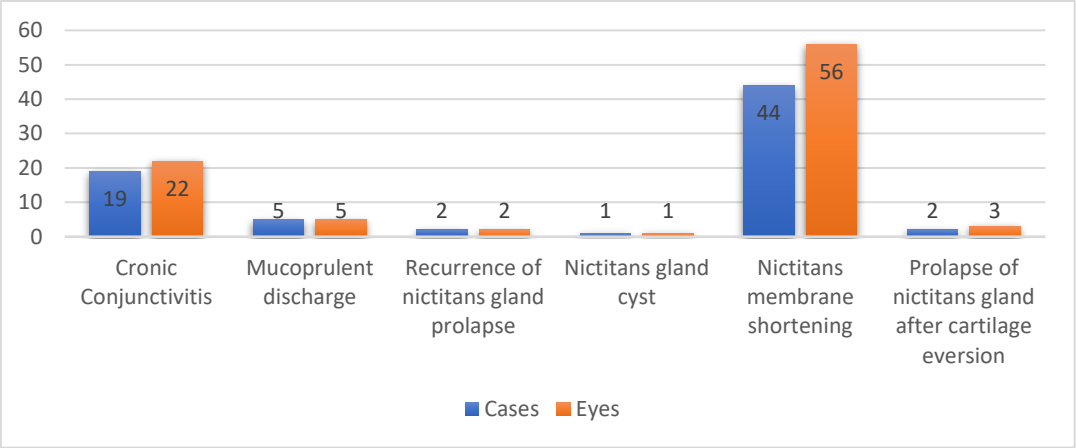

Figure 7. The observed complications after cartilage resection and/or nictitans gland replacement.

Discussion and Conclusion

The eversion of the nictitating membrane, also known as the rotation or scrolling of the third eyelid, mainly results from the rolling out of the T-shaped hyaline cartilage at the junction of its short and long arms (Allbaugh and Stuhr, 2013). The cartilaginous tissue holds the weakest consistency or rarely from the bending of the cartilage's long arm over its shaft generating a U-shaped folding, which forces the third eyelid to move outwards away from the cornea in the affected animals (Allbaugh and Stuhr, 2013; Şaroğlu, 2010). The deformed cartilage, which might be easily distinguished beneath the conjunctival surface in the clinical inspections, exhibits a varying clinical course. Even though the bent or scrolled cartilage does not directly threaten corneal health or vision quality, malposition of the third eyelid's edge discordant with the corneal surface leads to uneven tear film distribution and impairment in its drainage. Furthermore, apart from the everted cartilage, partial or complete protrusion of the nictitans gland (Cherry eye) is one of the ocular conditions associated with the eversion of the third eyelid (Esson, 2015). In the present study, the scrolled cartilage revealed a U-shaped appearance, as was reported in previous studies (Allbaugh and Stuhr, 2013, Şaroğlu, 2010). The eversion site involved the junction of the cartilage's vertical and horizontal arms or the portion close to the junction in the dogs with cartilage eversion per se, as was previously indicated (Dehghan et al., 2012; Michel et al., 2020; White and Brennan, 2018). In contrast, the eversion occurred at the cartilage's shaft in the patients with comorbid partial or complete gland prolapses due to the localization of the gland enveloping the cartilage base, which was directly associated with the repulsive force of the protruded gland. Cartilage eversion was the sole condition in 42.8% (n=16) of the eyes that underwent the surgical procedure for repositioning the nictitating membrane. In comparison, cartilage eversion was accompanied by the nictitans gland's partial or complete prolapse in 57.2% (n=28).

Although the underlying causes of the eversion of the third eyelid are not fully understood (Allbaugh and Stuhr, 2013), several authors pointed out a genetic predisposition concerning large dog breeds, such as Great Dane, Golden Retriever, English Bulldog, St. Bernard, Weimaraner, Doberman, German Shepherd Dog, Newfoundland Dog, and Irish Setter due to the relatively increased prevalence in these breeds (Allbaugh and Stuhr, 2013; Esson, 2015; Rezaei et al., 2019). Acquired factors such as traumatic injuries, chronic conjunctivitis, and improper suturing of the conjunctival surface of the nictitating membrane during ophthalmological surgical interventions were also suggested (Hadži-Milic, 2006). Moreover, a non-equivalent growth rate of the two conjunctival surfaces or primary cartilage deformities (more rapid growth of the posterior aspect than the anterior) were hypothetically associated with the condition (Gelatt, 1972; Martin,1970; Ramani et al., 2010). Gelatt (1972) assumed that uneven forces applied on the third eyelid due to the unique orbital conformation in morphologically enophthalmic large dog breeds gave rise to the disorder. The most frequently affected dog breeds in the present study were Cane Corso (18.18%), Anatolian Shepherd (15.89%), and Doberman Pinscher (13.62%). It was considered that -apart from a genetic predisposition- the varying popularity of some dog breeds in different countries or geographical regions played a significant role in the breed-wise prevalence of the eversion of the nictitating membrane/cartilage eversion. The overall data were compatible with those of Şaroğlu (2012), indicating that the condition was relatively more prevalent in Doberman Pinschers and Anatolian Shepherd dogs, occurring as an occasional and

sporadic lesion in these breeds. Furthermore, cartilage eversion was found to have developed due to Horner Syndrome-associated secondary enophthalmos, which might be considered to have supported Gelatt's (1972) assumptions.

Unilateral/bilateral eversion of the third eyelid and cartilage eversion occurred more frequently, particularly in young animals during adolescence (most specifically in the early period of life like within the first two years) as a primary condition, while secondary to other ocular lesions in the middle-aged or older dogs (Allbaugh and Stuhr, 2013; Hadži-Milic, 2006). Allbaugh and Stuhr (2013) reported that cartilage eversion developed unilaterally in eight out of 10 dogs aged between six months and 1.7 years, while two dogs had bilateral involvement. Şaroğlu (2012) indicated an age range of three to six months. No statistically significant data is available concerning gender predisposition (Allbaugh and Stuhr, 2013). The present study comprising retrospective evaluations over nine years revealed that cartilage eversion occurred as a primary condition in 28 cases (8 dogs with bilateral involvement and 20 with unilateral involvement) between three months and nine years of age, with an average of 1.2 years. The lesion was found to have developed secondary to other ocular lesions such as corneal disorders, eyelid abnormalities, chronic keratoconjunctivitis sicca, eye globe abnormalities, and as a complication to ocular surgery in sixteen dogs (2 dogs bilaterally affected and 14 dogs unilaterally). The age range for the eversion that occurred as a secondary lesion was 3.5 months to ten years, with an average of 4.4 years. The data were consistent with the previous reports (Georgescu et al., 2015; Hadži-Milic, 2006), indicating that primary lesions were mainly encountered in young dogs, while secondary lesions more frequently affected middle-aged dogs. The gender-based evaluations revealed that 27 (61.36%) out of forty-four dogs diagnosed with the eversion of the nictitating membrane were male, while seventeen (38.63%) were female. It might be deduced that the condition was more prevalent in males.

Different techniques of varying success rates were applied in veterinary surgery for repositioning the rotated nictitating membrane, including 10 to 14 days of efficient third eyelid flapping, resection of the nictitating membrane margin and cartilage, radical excision of the nictitans gland and cartilage, excision of cartilage, and homotransplantations (Rezaei et al., 2013; Williams et al., 2012). Most of the techniques were far from offering satisfactory outcomes. Recently, thermal cautery, considered a novel, rapid and efficient technique, has been suggested to surgically correct the everted cartilage without the necessity of the defected cartilage portion's excision. However, it is inefficacious in repositioning the prolapsed gland in patients with comorbid gland protrusion (Allbaugh and Stuhr, 2013). Therefore, submucosal excision of the deformed or bent cartilage portion near the nictitating membrane's loose edge or total resection of the U-shaped cartilage and cartilage extensions (curled/scrolled portion) is most frequently preferred in the surgical management of the eversion of the nictitating membrane in dogs (Rezaei et al., 2019; Williams et al., 2012). The surgical approach is directed at the bulbar and palpebral aspects to remove the bent cartilage portion (Deveci et al., 2020; Williams et al., 2012). Some authors favor the bulbar approach due to the less potential risk for tissue adhesions, facilitating a more convenient dissection in dogs (Williams et al., 2012). Some others supported the palpebral approach to avoid potential surgical trauma-associated bulbar conjunctival injury and corneal damage due to the scarring of the dissected conjunctival tissue because of secondary healing (Deveci et al., 2020; Ramani et al., 2010; Williams et al., 2012). Redundant or insufficient cartilage resection might cause the nictitans glands to prolapse or recurrence in the third eyelid eversion (Deveci et al., 2020). In contrast, the excision of merely the bent cartilage portion might lead to a shortened or a contracted third eyelid, creating a tension force on the cartilage margins and -as a result- might cause marginal necrosis (Allbaugh and Stuhr, 2013). In the present study, the surgical correction of the everted nictitating membrane was achieved by removing the defected cartilage portion using the bulbar approach in all dogs with solely cartilage eversion due to the feasibility of the technique, allowing the gland's stabilization in terms of avoiding a potential gland prolapse, as reported in previous studies. Despite inflammation, the bulbar approach was preferred in all cases, and no complications such as corneal damage due to scarring were encountered, as reported previous study (Ramani et al., 2010). Considering the significant role of the nictitans gland in tear production removing the prolapsed gland was not considered an option; instead, the gland was inserted and repositioned by the Morgan pocket technique after resectioning the defected cartilage.

In conclusion, the overall data revealed satisfactory results in terms of feasibility and efficiency of the surgical treatment method followed in the study, which was applied as the resection of the scrolled cartilage portion accompanied by the Morgan pocket technique in the patients with a comorbid prolapsed gland in the surgical management of the eversion of the nictitating membrane in dogs. Furthermore, it might be deduced that partial or total resection of the third

eyelid cartilage, which provides structural support to the nictitating membrane, barely revealed an adverse impact on the animal's ocular health, and potentially, only a minimal decline was noted in tear drainage.

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Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

Ethical Approval

This study is not subject to HADYEK's permission in accordance with Article 8 (k) of the "Regulation on Working Procedures and Principles of Animal Experiments Ethics Committees".

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