Analysis of Facial Features of Patients With Sagging Eye Syndrome and Intermittent Exotropia Compared to Controls

KEIKO KUNIMI, TOSHIAKI GOSEKI, KYO FUKAYA, SHINYA TAKAHASHI, AND ERI ISHIKAWA

• PURPOSE: To compare the facial features of patients with sagging eye syndrome (SES) and other ophthalmic diseases, and to evaluate the diagnostic usefulness of facial features for SES.

• DESIGN: Retrospective cross-section study.

• METHODS: We evaluated frontal facial photographs of patients >60 years of age with SES and intermittent exotropia (IXT), and control patients who visited the ophthalmology outpatient clinics of 2 institutions between June 2020 and December 2021. Three ophthalmologists evaluated each eye for sunken upper eyelid, blepharoptosis, and baggy lower eyelid, using a scoring scale. The average scores for each parameter among the 3 groups were analyzed. Patients with glaucoma, visual acuity <16/20, SES with a vertical strabismus angle of ≥6 Δ, IXT that could not be maintained in the phoria position during photography, a history of previous oculoplastic or ophthalmic surgery, and use prostaglandin analogs for cosmetic purposes were excluded.

• RESULTS: A total of 86 patients were included: 23 with SES, 28 with IXT, and 35 in the control group. All were Japanese. In all, 45 patients were male and 41 were female. The mean age was 72.7 ± 7.4 years. The sunken upper eyelid scores were significantly higher in the SES group than in the control and IXT groups ($P < .001$), whereas the baggy lower eyelid scores were significantly higher in the IXT group than in the control group ($P < .05$).

• CONCLUSIONS: Age-related orbital connective tissue degeneration may manifest as SES in the upper eyelid and as IXT in the lower eyelid. (Am J Ophthalmol 2023;246: 51–57. © 2022 Elsevier Inc. All rights reserved.)

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Sagging eye syndrome (SES) is a strabismus condition caused by the degeneration of the orbital pulley.[1,2] It has a prevalence of 33.3% in the United States[3] and 24.2% in Japan in patients with adult-onset diplopia,[4] and is the number 1 acquired strabismus condition in both countries. Chaudhuri and Demer expected that age-related degeneration of the orbital connective tissue would involve not only the pulley but also external signs of adnexal laxity, and reported sagging of the levator aponeurosis (LA), resulting in a sunken upper eyelid, blepharoptosis, or a baggy lower eyelid, by essentially the same mechanism as the degeneration of the lateral rectus muscle-superior rectus muscle (LR-SR) band.[5] A statistical study of facial changes in SES revealed that sunken upper eyelid was present in 64%, blepharoptosis in 29%, and a history of ophthalmoplasty in 29% of patients with SES.[5] However, after reviewing PubMed and Embase databases, no reports have investigated whether facial features are significantly more useful for diagnosis of SES than other diseases. Therefore, we compared the facial features of SES patients with those of patients with other ophthalmic diseases, such as intermittent exotropia (IXT), to evaluate the usefulness of facial features in diagnosing patients with SES and other ophthalmic disorders.

METHODS

• PARTICIPANTS: In this retrospective study, we included patients >60 years of age with SES or IXT, and control patients who visited the ophthalmology outpatient clinics of 2 institutions between June 2020 and December 2021. Patients with glaucoma, visual acuity (VA) of <16/20, SES with a vertical strabismus angle of ≥6 Δ, IXT that could not be maintained in the phoria position during photography, a history of previous oculoplastic or ophthalmic surgery, and use of prostaglandin analogs for cosmetic purposes were excluded. This study was approved by the Institutional Review Board of the International University of Health and Welfare, Atami Hospital, Shizuoka, Japan (22-A-210), and followed the tenets of the Declaration of Helsinki.

• DIAGNOSTIC CRITERIA FOR SES, IXT, AND CONTROL GROUP: For SES, we included 2 types of SES strabismus:

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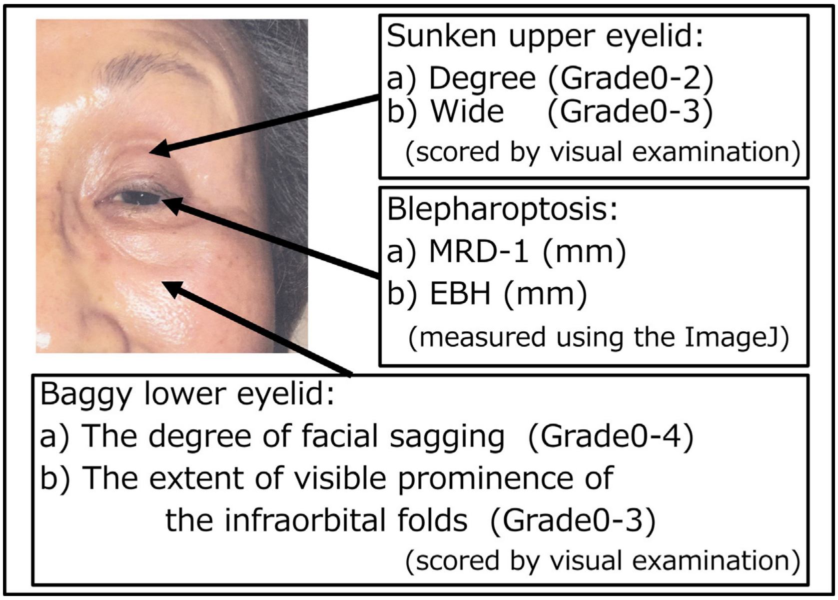

FIGURE 1. Overview of scoring. Sunken upper eyelid was scored for the (a) degree and (b) width of the sulcus by visual examination. Blepharoptosis was measured using ImageJ software (National Institutes of Health) for MRD-1 and eyebrow height, and baggy lower eyelid was scored for (a) the degree of facial sagging and (b) the extent of visible prominence of the infraorbital folds by visual examination. EBH = eyeblow height, MRD = margin reflex distance.

age-related distance esotropia (ARDE) with a deviation angle of esotropia at distance but orthophoria or <10 Δ at near esophoria, and small-angle cyclovertical strabismus (CVS). For CVS, strabismus with <5 Δ vertical deviation was included.[3,5,6]

For IXT, we included patients with horizontal lateral ocular misalignment and noted intermittent outward deviation in 1 or both eyes.

For a control group, we included preoperative patients with good VA without a history of orthoplastic or ophthalmic surgery were included.

• **DATA AND MAIN OUTCOME MEASURES:** We recorded clinical factors, including age, sex, diagnosis, and binocular alignments at distance (5 m) and near (1/3 m) using the alternate prism cover test in the primary position. For all patients included in this study, frontal facial photographs were obtained using a flash camera. Using a scoring scale based on previous reports,[7-13] three ophthalmologists evaluated each eye for sunken upper eyelid, blepharoptosis, and baggy lower eyelid after randomizing the photographs (Figure 1). Randomization was performed by assigning recognition numbers matched to photographs and diagnoses, hiding the diagnosis so that photographs could not be matched, and then distributing all photographs shuffled by a non-ophthalmologist to 3 ophthalmologists, each of whom was asked to evaluate them using scoring criteria. Statistical analysis was performed to compare the scores of the groups.

• **SCORING CRITERIA FOR SUNKEN UPPER EYELID, BLEPHAROPTOSIS, AND BAGGY LOWER EYELID:** All scoring was based on previous reports on the scoring of facial features.

Scoring for sunken upper eyelid

The sunken upper eyelid score was based on the facial evaluation criteria in a previous report on the association between ocular surface diseases, such as dry eye or prostaglandin-associated periorbitopathy, and the severity of the sunken upper eyelid. Grade a was assigned for the presence of a sunken upper eyelid and orbital rim, and grade b was assigned according to the presence of an enlarged invaginated skin space between the brow bone and upper eyelid by visual examination[7,8] (Figure 2, I-a,b).

Scoring for blepharoptosis

Blepharoptosis was defined by the corneal width (11.77 mm for men and 11.64 mm for women) for each image, and marginal reflex distance 1 (MRD-1) (distance from the corneal reflectance to the upper eyelid margin) and eyebrow height (EBH) (distance from the corneal apex to the center of the eyebrow directly above) were measured using the ImageJ software (National Institute of Health; https://imagej.nih.gov/ij/index.html) in the same manner as in a previous report (Figure 2, II-a,b).[9-11]

Scoring for baggy lower eyelid

The score for baggy lower eyelid was based on a previous report that attempted to classify the severity of baggy lower

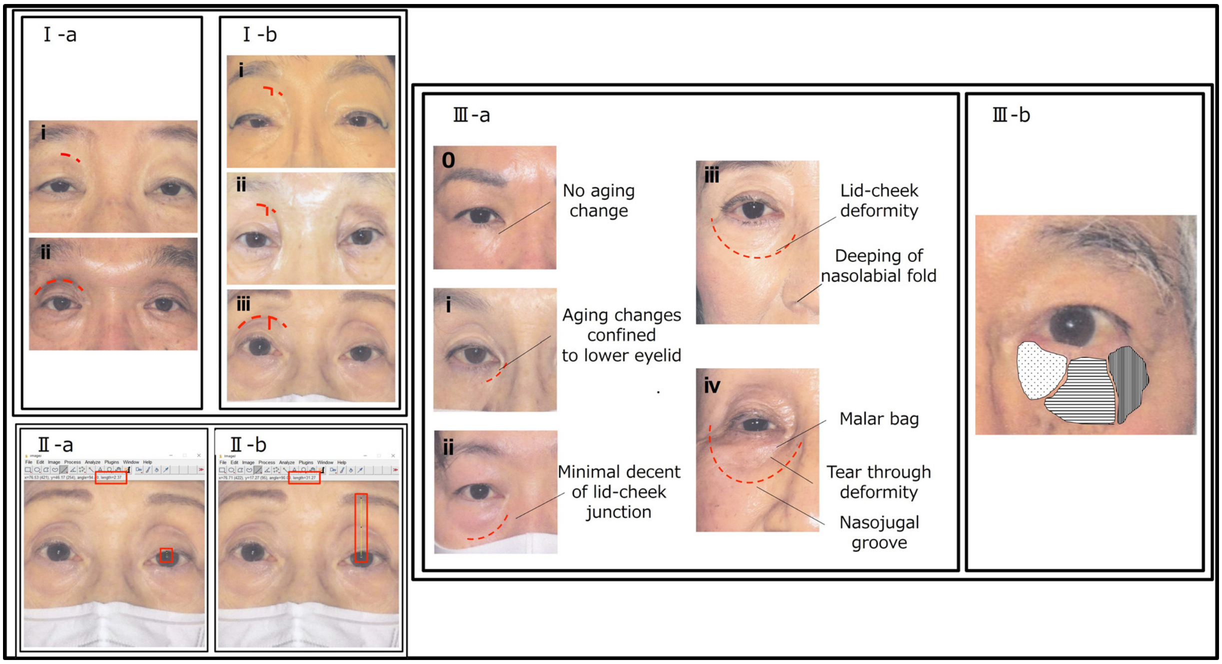

FIGURE 2. Details of the scoring. I-a: Zero indicates no sunken upper eyelid; (i) is an early sunken upper eyelid in which the skin of the superior sulcus is involuted but remains at the superior orbital rim; and (ii) is the most severely sunken upper eyelid in which the sulcus rests posterior to the orbital rim in the sagittal plane. I-b: Zero indicates no sunken upper eyelid; (i) is "mild," a space of 1 mm mostly in the nasal aspect; (ii) is "moderate," a space of 3 mm mostly in the nasal aspect but not the entire superior sulcus; and (iii) is "severe," a space of 3 mm involving the entire superior sulcus. Blepharoptosis was defined as the corneal width for each image, and (II-a) margin reflex distance−1 and (II-b) eyebrow height was measured using ImageJ software (National Institutes of Health). III-a: Zero indicates no baggy lower eyelid; (i) includes aging changes confined to the lower eyelid; (ii) includes minimal descent of the lid−cheek junction, (iii) includes lid−cheek deformity and deepening of the nasolabial fold; and (iv) includes malar bag, tear through deformity, and nasojugal groove. III-b: Only the medial (M) type, in which only the M part (dots) of the lower eyelid protrudes prominently; medial and central (MC) type, in which the MC parts, colored dots and horizontal lines, protrude prominently; medial to lateral (MCL) type, in which the whole lower eyelid protrudes, colored dots, horizontal lines, and vertical lines.

TABLE 1. Distribution of Study Patients

	SES	IXT	Control	*P* Value
Patients, n	23	28	35	—
Sex, male/female	7/16	22/6	16/19	<.001[a]
Mean age, yr	71.2 ± 6.0	73.0 ± 7.2	73.5 ± 8.3	.61[b]

IXT = intermittent exotropia; SES = sagging eye syndrome.
[a] Fisher exact test.
[b] Kruskal−Wallis test.

eyelid to determine a treatment plan in the field of blepharoplasty and the severity of laxity of the entire face. Grade a was assigned according to facial sagging from the lower orbital tissue to the nasolabial sulcus, and grade b was assigned according to the visible prominence of the infraorbital folds[12,13] (Figure 2, III-a,b).

• **STATISTICAL ANALYSES:** Statistical analyses were performed using SPSS software (IBM SPSS Statistics for Windows, version 28.0; IBM Corporation). After parametric testing, an intraclass correlation coefficient was used to confirm that the results for each individual measurement were correlated. The Fisher exact test was used to compare the male-to-female ratio among the 3 groups. The Kruskal–Wallis test was used to compare age and score for each parameter. Statistical significance was set at $P < .05$.

RESULTS

A total of 86 patients were included: 23 in the SES group, 28 in the IXT group, and 35 in the control group. All patients were Japanese. There were 45 male and 41 female patients, with a significant difference in the sex ratio among the 3 groups: there were 7 male and 16 female patients in the SES group, 22 male and 6 female patients in the IXT group, and 16 male and 19 female individuals in the control group ($P < .001$). The average age of all patients was 72.7 ± 7.4 years, with no difference among groups: 71.2 ±

6.0 years for the SES group, 73.0 ± 7.2 years for the IXT group, and 73.5 ± 8.3 years for the control group (*P* = .61) (Table 1).

• **AVERAGE SCORE FOR EACH PARAMETER:** For sunken upper eyelid, grade a and b scores were 1.2 ± 0.7 and 1.8 ± 1.0 in the SES group, 0.6 ± 0.3 and 0.6 ± 0.4 in the IXT group, and 0.5 ± 0.4 and 0.6 ± 0.6 in the control group, respectively. The SES group scored significantly higher than the other 2 groups (*P* < .001). For blepharoptosis, MRD-1 and EBH were 2.8 ± 1.1 mm and 26.4 ± 5.8 mm in the SES group, 3.3 ± 4.6 mm and 26.0 ± 3.7 mm in the IXT group, and 3.0 ± 2.8 mm and 26.1 ± 4.7 mm in the control group, respectively. No significant differ-

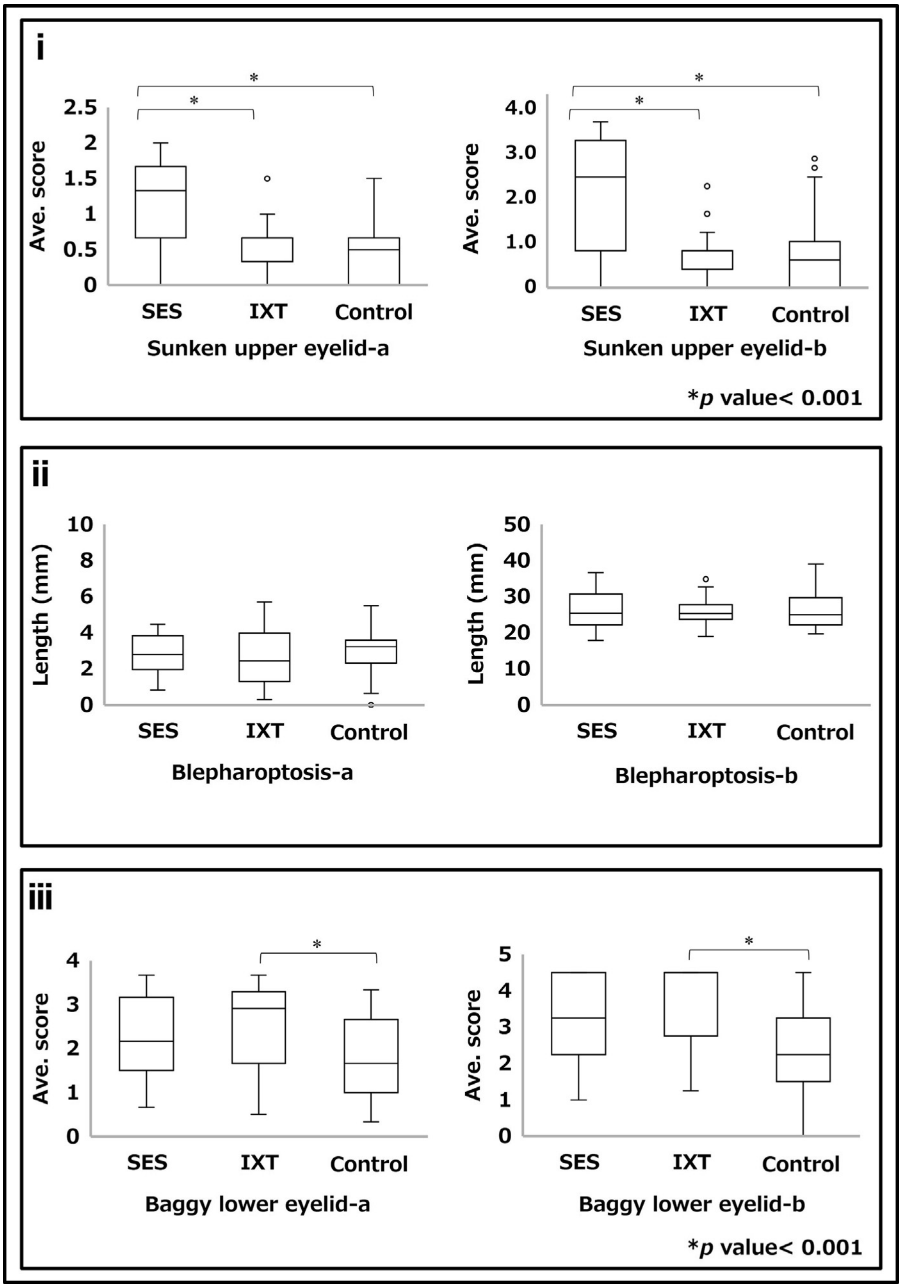

FIGURE 3. Average scores for each parameter. (i) The score for sunken upper eye lid grades a and b; the SES group scored significantly higher than the other 2 groups (*P* < .001).
(ii) Measurements of blepharoptosis for margin reflex distance—1 (a) and eyebrow height (b); no significant differences were observed among the 3 groups (margin reflex distance—1: *P* .56, eyebrow height: 1.00). (iii) Scores for baggy lower eyelid grades a and b; the intermittent exotropia group scored significantly higher for grade a and grade b than the control group, whereas it did not differ from that of the SES group (*P* < .05). SES = sagging eye syndrome.

TABLE 2. Summary of Age-Related Degeneration in Pulley and Orbital Connective Tissue

	Upper Eyelid	Lower Eyelid
Degeneration of orbital pulley	LR−SR band	IPPM (MR−IR band)
Main comportment of pulley	Collagen	Smooth muscle
Degeneration of orbital connective tissue	Displacement of LA from tarsus and LA and OS retraction by LPS	Extension of fat pad compartments
Facial feature	Sunken upper eyelid	Baggy lower eyelid
Diagnosis	Sagging eye syndrome	Intermittent exotropia

IPPM = inframedial peribulbar muscle; IR = inferior rectus muscle; LA = levator aponeurosis; LR = lateral rectus muscle; LPS = levator palpebral superioris; MR = medial rectus muscle; OS = orbital septum; SR = superior rectus muscle.

ences were observed among the 3 groups (MRD-1: $P = .56$; EBH: $P= 1.00$). For baggy lower eyelid, grades a and b were 2.2 ± 0.9 and 3.1 ± 1.2 in the SES group, 2.5 ± 1.0 and 3.6 ± 1.1 in the IXT group, and 1.8 ± 0.9 and 2.4 ± 1.3 in the control group, respectively. The IXT group scored significantly higher than the control group ($P < .05$), whereas no significant differences were found between the SES and IXT groups (Figure 3).

• **CORRELATION BETWEEN BINOCULAR ALIGNMENT AND EVALUATION SCORES:** The mean binocular alignment at distance was +13.8 ± 10.7Δ for the SES group and −31.1 ± 15.3Δ for the IXT group, with no correlation between binocular alignment and any of the evaluation parameters in either group.

DISCUSSION

In a previous report, Rutar and Demer anticipated that orbital connective tissue degeneration due to aging would not be limited to the pulley connective tissues but would also involve the adnexal connective tissues.[1] However, in this study, age-related orbital tissue degeneration, which causes SES, was significantly more associated with sunken upper eyelid than with other ophthalmologic diseases, but not with blepharoptosis or baggy lower eyelid, which are considered characteristics of SES. Based on previous reports, we reviewed the literature on the pathophysiology and causes of sunken upper eyelid, blepharoptosis, and baggy lower eyelid in this study.

The orbital pulley comprises collagen, elastin, and smooth muscle (SM), and the distribution of these elements varies depending on the location of the orbital pulley.[14] In addition, the LR−SR band and the LR pulley in the upper orbit contain collagen tissue, and collagen degenerates with age. Therefore, aging causes an inferior shift in LR and degeneration of the LR−SR band. These cause development of ARDE and CVS, which are clinical manifestations of SES.[1,3,14] Regarding the cause of sunken upper eyelid or blepharoptosis developing in patients with SES, Rutar and Demer reported that this is because of a dehiscence of the levator muscle associated with the orbital pulley.[1] However, in the current study, only sunken upper eyelid scored significantly higher than other ophthalmologic conditions, whereas blepharoptosis and baggy lower eyelid were not specific to SES. As previously reported, if the levator muscle contributes to the development of a sunken upper eyelid, it is important to understand the anatomy of the upper eyelid in order to consider the cause. During eyelid opening, the anterior layer of the LA pulls the orbital septum (OS) and the submuscular fibro-adipose tissue, whereas the posterior layer pulls the anterior aspect of the tarsus, the orbicularis oculi muscle, and the skin.[15] Considering the previous reports of sunken upper eyelid improvement with levator advancement,[16] we considered that the LA is displaced and extended from the tarsus, which causes the LA to retract, pulled by the levator palpebral superioris (LPS), and, at the same time, the confluence of the anterior layer of LA and OS also retracts, which may worsen the sunken upper eyelid. The ptotic eyelid causes the LPS to pull strongly on the tarsus, resulting in pulling on the OS where the anterior layer of the LA is attached, possibly deepening the sulcus. It seems clear from our study as well as previous reports that SES substantially worsens sunken upper eyelid. This may be because the pathogenesis of age-related sunken upper eyelid is caused by changes in the orbital connective tissue, especially collagen, whereas SES develops because of atrophy of the pulley, which also exhibits age-related changes.

Rutar and Demer reported that blepharoptosis is more common in SES because blepharoptosis is caused by dehiscence of the LA and is pathologically similar to age-related changes of the pulley.[1] However, in our study, blepharoptosis scores were not significantly different among the 3 groups. The pathogenesis of blepharoptosis has been reported not only to be due to aponeurotic means (disinsertion or dehiscence of the LA from its normal position on the anterior surface of the tarsus) but also may include myogenic, neurogenic, mechanical, or traumatic causes.[17] Although the current sample is thought to exclude myogenic and traumatic ptosis because of the use of questionnaires and other factors, our sample may not consist solely of patients with true aponeurotic ptosis. In addition, an individual with severely sagging eyelids is more likely to forcefully open their eyes and may have been graded as having moderate or mild severity.[18] In our study, EBH was measured to differentiate eyelid elevation by the frontalis.[10] In other words, if the MRD was equal but the EBH was longer, the frontalis was more likely to be used to lift the eyelid. Thus, we could have considered more severe ptosis by measuring EBH; however, blepharoptosis scores were not characteristic of SES, and ptosis may occur regardless of the disease as an age-related change.

Regarding the baggy lower eyelid, our results were not significantly different for the SES group, but there was a significant difference between the IXT and control groups. Considering the anatomy of the fat pad in the lower eyelid, the fat pad compartments of the lower eyelid were originally divided into 3 parts: medial, central, and lateral. The medial and central fat pads were divided by the inferior oblique muscle (IO), and the boundaries of the middle and lateral fat pads were defined by the arcuate expansion of the Lockwood ligament.[19] Baggy lower eyelid reportedly develops more severely from the nasal to the lateral side.[13] In addition, under the inferolateral part of the OS, on the facial aspect of the zygoma, lies a potential space known as the "recess of Eisler." As a result of this anatomic feature, together with the diminished ligamentous support described above, the periorbital fat tends to sit beyond the orbital rim, concealing the inferolateral orbital rim.[19] However, regarding the tissues of the lower eyelid pulley, previous reports indicate that the MR—SR band contains more collagen, the MR pulley contains more elastin, and the MR—IR band contains more SM.[14] Moreover, there is a mass of pulley array, called the inframedial peribulbar muscle (IPPM), which leads from the MR pulley, via the MR—IR band, to the IR pulley and the IO—IR junction, and reportedly contains a large amount of SM.[20] Considering the anatomy of the lower eyelid and the pathology of the lower eyelid pulley, age-related extension of the IPPM may affect nasal baggy lower eyelid, whereas a severe form of baggy lower eyelid, lateral baggy lower eyelid, may appear with extension of the OS. In addition, the more severe baggy lower eyelid may have a different pathogenesis from age-related degeneration in the pulley due to collagen loss, the pathology of SES. In a previous report, it was observed that the pulley array rotates extensively during convergence, and it is hypothesized that the contraction of the MR—IR band leading to the MR pulley and the IR-IO junction is responsible for the convergence.[14] Considering previous reports, and also considering that over 60% of Japanese adult exotropia[21] is reportedly radial insufficiency, the MR—IR band, which is composed of a large amount of SM, may develop IXT because of diminished convergence with the age-related degeneration of SM. We have summarized our opinion in Table 2.

This study has some limitations. First, the sample size is small. An increase in the number of patients is necessary to obtain more accurate results. Second, there are various other reports on the scoring of each parameter measured here, and the results may vary depending on the measurement conditions. However, this study was conducted using the most widely used scoring measures based on many previous reports, and we expect that the results will be similar to ours, even if other scoring systems are used. Third, all patients were Japanese. Similarity in eyelid involvement (upper and lower), as well as ethnic distribution of both epiblepharon and involutional entropion, may be factors affecting the unique anatomy of the oriental eyelid.[22] It is necessary to conduct a multinational survey in the future to investigate racial differences.

In conclusion, sunken upper eyelid is caused by age-related degeneration of the LPS and LA, which are histologically similar to the LR-SR band. Sunken upper eyelid is likely to be associated with SES; however, because baggy lower eyelid is caused by age-related degeneration of the MR—IR band as a part of the IPPM, which is highly associated with SM, it is more likely to be correlated with IXT.

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