Elastin expression in the conjoint fascial sheath and levator palpebrae superioris muscle of children with unilateral severe congenital ptosis with different muscle strengths

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Abstract. Elastin expression in the conjoint facial sheath (CFS) of patients of different ages with severe ptosis has been extensively studied, but its expression in the CFS of pediatric patients with severe ptosis with different muscle strengths remains poorly understood. The aim of the present study was to investigate the expression of elastin in the CFS and levator palpebrae superioris muscle (LM) of children with severe congenital ptosis with different LM strengths. In total, 20 pediatric patients with unilateral severe congenital ptosis (20 eyes) were included, who underwent CFS + LM complex suspension surgery from June 2020 to February 2022. Among these patients, the LM strength was 0-1 mm in 10 patients and 2-3 mm in the other 10 patients. Excess CFS and LM tissue samples were obtained from the patients during surgery, before the protein expression levels of elastin in the specimens were measured by western blotting. During the 6-month postoperative follow-up period, the good correction rate, the degree of incomplete eyelid closure and the incidence of complications were observed. Western blotting results showed that, compared with that in the 0-1 mm group, elastin expression was not significantly different in the CFS, whereas it was significantly increased (P=0.021) in the LM of the 2-3 mm group. In addition, elastin expression in the CFS was markedly higher compared with that in the LM in both groups (in the 0-1 mm group, P=0.005; in the 2-3 mm group, P=0.009). Additionally, the curative effect evaluation revealed that the good correction rates in the 0-1 and 2-3 mm groups were 90 and 100%, respectively. In total, 3 patients experienced conjunctival prolapse during the follow-up period, including 2 patients in the 0-1 mm group and 1 patient in the 2-3 mm group, but there were no other complications. To conclude, elastin expression in the CFS was found to be higher compared with that in the LM of children with severe congenital ptosis. Although elastin expression in the LM was positively associated with LM strength, its expression in the CFS displayed no clear association with LM function. Therefore, these observations suggested that CFS + LM complex suspension surgery is viable to correct severe congenital ptosis in pediatric patients.

Introduction

Ptosis, a common condition in clinical practice, is characterized by a low-lying upper eyelid margin (1). The conjoint fascial sheath (CFS) is a fibrous connective tissue located in the space between the superior conjunctival levator palpebrae superioris muscle (LM) and the anterior third of the superior rectus muscle (2). Since 2002, CFS suspension surgery has been used to correct ptosis (3). In CFS surgery, the CFS is fixed at the anterior one-third of the tarsus so that the upper eyelid margin of the affected eye is located at the upper edge of the cornea when looking straight ahead in a sitting position to serve as a corrective role (4). This surgery is now recognized in clinical practice due to good efficacy and a low number of complications, such as lagophthalmos, exposure conjunctivitis and hematoma in the eyebrow area (5). However, a number of patients experience upper eyelid retraction after surgery, and Sang *et al* (4) reported that the amount of upper eyelid retraction was 0.21±0.07 mm 3 months after surgery. CFS suspension alone lacks strong attachment points, so it cannot maintain long-term tissue tension. The combination of the CFS and LM to form a CFS + LM compound flap suspension on the tarsus can provide the suspension force and an attachment point for the CFS (5) to maintain long-term postoperative

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Abbreviations: CFS, conjoint facial sheath; LM, levator palpebrae superioris muscle

Key words: elastin, CFS, LM, severe congenital ptosis, complex suspension, children

outcomes, which is called CFS + LM complex suspension surgery (6). A clinical study revealed that the undercorrection and recurrence rates in a CFS + LM complex suspension group were notably lower compared with those in the simple CFS suspension group (7).

In pediatric patients, congenital ptosis not only affects the appearance of the eye but also affects visual function in severe cases because obstructions of the pupillary area can cause visual dysfunction (1). Therefore, the correction of congenital severe ptosis was the focus of the present study. To the best of our knowledge, there have only been a small number of studies documenting the correction of severe congenital ptosis in children with CFS + LM complex suspension (6-9).

Previous anatomical and histological studies have reported that the CFS and LM are rich in collagen and elastic fibers, but lack smooth muscle or skeletal muscle cells (10,11). Elastic fibers and collagen fibers form the key structures that maintain the elasticity of stress-bearing tissues, within which elastin is the most important structural component (12). Furthermore, elastin expression in the CFS has been previously reported to decrease with age (8). Clinically, the grade classification of ptosis depends on LM strength, and doctors also determine the method of surgery based on the LM strength (1). Therefore, the present study followed up on a previous study (8) and continued to investigate the association between elastin expression and LM strength.

The present study aimed to measure the expression of elastin in the CFS and LM tissues of children with unilateral severe congenital ptosis with different LM strengths, and to perform a postoperative evaluation of CFS + LM complex suspension. The results of the present study may be beneficial for clarifying the association between CFS/LM elasticity and LM strength, and may explain why CFS + LM complex suspension surgery has more suspension force compared with simple CFS suspension surgery. This information may in turn be applied to provide a theoretical basis for estimating the surgical volume of CFS + LM complex suspension for the correction of severe congenital ptosis in children.

Materials and methods

General information. A total of 20 patients (20 eyes) with unilateral severe congenital ptosis, aged 4-12 years, 15 males and 5 females, underwent CFS + LM complex suspension surgery in Hebei Eye Hospital (Xingtai, China) from June 2020 to February 2022. The average age of the participants was 7.60±2.44 years. According to LM strength, the patients were divided into the 0-1 mm group and the 2-3 mm group (n=10/group). The LM strength was measured as follows: The eyebrow arch was pressed while both eyes of the patient were looking down as far as possible, then the patient was instructed to look upwards, the distance that the upper eyelid margin moved was observed and the value was recorded as the LM strength.

The present study was reviewed and approved by the Ethics Committee of Hebei Eye Hospital (approval no. 2020KY013; Xingtai, China). Written informed consent for participation was obtained from the participant and the minor(s)' legal guardian, for the publication of any potentially identifiable images or data included.

Inclusion and exclusion criteria. Inclusion criteria: i) Patients with unilateral severe congenital ptosis; ii) patients aged <14 years of age; iii) patients with Bell's phenomenon before surgery; and iv) patients without a history of eyelid surgery.

Exclusion criteria: i) Patients with genetic syndromes, mainly including blepharophimosis-ptosis-epicanthus inversus syndrome and Marcus Gunn jaw winking syndrome; ii) acquired ptosis caused by trauma, oculomotor nerve palsy and myasthenia gravis; and iii) other ocular and systemic diseases that may affect the outcome of surgery, such as ocular inflammation, ocular cyst, ocular tumor, coagulation dysfunction, immune system disorders and infectious diseases.

Surgical technique. All the CFS + LM complex suspension surgeries were performed under general anesthesia and by the same surgeon. According to the LM strength, different surgical volumes were used during the operation between the two groups: i) In the 0-1 mm group, the separation height of the CFS + LM composite flap was 5-6 mm, where the upper eyelid margin was flat at the level of the upper edge of the cornea; and ii) In the 2-3 mm group, the separation height of the composite flap was 3-4 mm, such that the upper eyelid margin covered the cornea by 0.5-1 mm.

The surgery was performed as follows: i) The surgical incision was designed as a double eyelid line incision and was marked in advance, and local anesthesia was administered to the upper eyelid; ii) the skin was incised along the marked line, before the tarsal plate and LM were separated and exposed; iii) the orbicularis oculi and the LM aponeurosis were cut at a distance of 2 mm above the margin of the tarsal plate, and the LM aponeurosis was separated from the Müller muscle and pulled ~5 mm over the fornix to expose the CFS; iv) the CFS + LM composite flap was fixed at the outer, intermediate and inner positions of the tarsal plate with 5-0 absorbable thread, and the upper eyelid margin was flat at the level of the upper edge of the cornea in the 0-1 mm group or covered the cornea by 0.5-1 mm in the 2-3 mm group (any excess CFS and LM tissues that were resected during surgery were collected, cleaned and stored at -80˚C); and v) a 5-0 silk thread was used to intermittently suture the skin incision and shape the double eyelid.

The patients and their parents or guardians were consulted preoperatively about the need for double eyelid reconstruction of the other eye to maintain bilateral symmetry.

Western blotting. The CFS and LM specimens were removed from the freezer, homogenized and lysed in RIPA buffer with protease and phosphatase inhibitors (Beijing Solarbio Science & Technology Co., Ltd.). The protein concentrations were measured using a BCA protein assay (Beijing Solarbio Science & Technology Co., Ltd.). The protein samples (15 μg of protein per lane) were separated by SDS-PAGE on 10% gels and were transferred onto PVDF membranes, which were then blocked with 5% skimmed milk blocking solution at room temperature for 1 h. The membranes were cut between 63 and 48 kDa, and probed with rabbit anti-elastin (1:1,000; Abcam; cat. no. ab23747) and mouse anti-β-actin (1:5,000; Hangzhou Lianke Biotechnology, Co., Ltd.; cat. no. ab008-40) antibodies and incubated overnight at 4˚C. The membranes were then washed with TBST solution (0.05% Tween-20

used) and incubated with HRP-conjugated goat anti-rabbit (cat. no. BA1054) and anti-mouse (cat. no. BA1050) IgG secondary antibodies (1:5,000; Wuhan Boster Biological Technology, Ltd.) at room temperature for 1 h. A Superstar Enhanced Chemiluminescence (ECL) Reagent kit (Wuhan Boster Biological Technology, Ltd.; cat. no. AR1170) was used to detect the signals by X-ray film exposure. The gray values of the protein bands were analyzed using ImageJ software (version 1.7.0; National Institutes of Health) to determine the difference between the target protein expression and the internal reference protein expression. The ratio of the grayscale values of the bands was used to indicate the relative expression level of the proteins.

Postoperative evaluation of curative effects. The parameters of surgical outcomes included the postoperative good correction rate, the degree of incomplete eyelid closure and the incidence of complications. The patients returned for follow-up at 1, 3 and 6 months postoperatively. The same physician conducted the examination and analyzed the data.

Therapeutic effect indices: i) If the upper eyelid covered the upper limbus of the cornea by 1-2 mm, it was considered a 'good correction'; ii) if the upper eyelid covered the upper corneal limbus by >2 mm, it was considered an 'undercorrection'; iii) if the upper eyelid was located above the upper corneal limbus, it was considered an 'overcorrection'; iv) the upper eyelid margin located at the preoperative level was considered a 'relapse'. The postoperative good correction rate was then calculated as the ratio of the number of patients with good correction to the total number of patients.

For assessing the degree of incomplete eyelid closure, the patient was instructed to close their eyes naturally, before the unclosed distance between the upper and lower eyelid margins was measured with a ruler to determine the degree of incomplete eyelid closure.

For assessing the incidence of complications, complications such as exposure keratitis, eyelid hematoma, conjunctival prolapse, trichiasis and eyelid-ball separation, were all recorded.

Statistical analysis. The data were analyzed using SPSS 20.0 statistical software (IBM Corp.) and are presented as the means ± standard deviation. Comparisons between two groups were performed using an independent t-test. Comparisons between two tissues from the same individual were determined by paired t-test. Categorical variables were summarized as numbers and compared by Fisher exact probability method. P<0.05 was considered to indicate a statistically significant difference. Illustrator CS6 software (version 16.0.0; Adobe Systems, Inc.) was used for assembling the figures.

Results

Comparison of elastin expression in the CFS and LM between the groups. There were no significant differences in sex or age between the two groups (Tables I and II). Western blotting results (Fig. 1; Table III) showed that compared with that of the 0-1 mm group, the expression of elastin in the CFS of the 2-3 mm group was increased, but the difference was not statistically significant (P=0.125); however, the expression of elastin in the LM of the 2-3 mm group was significantly increased compared with that in the 0-1 mm group (P=0.021).

Table I. Comparison of the sex of the groups of patients with different LM strengths (n=10).

	Sex	
Group	Male	Female
0-1 mm	7	3
2-3 mm	8	2
P-value[a]	1.000	

[a]vs. 0-1 mm.

Table II. Comparison of the age of the groups of patients with different LM strengths (n=10).

Group	Age, years
0-1 mm	8.20±2.25
2-3 mm	7.00±2.58[a]
t-value	1.108
P-value[a]	0.283

[a]vs. 0-1 mm.

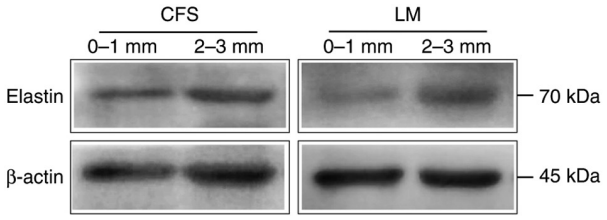

Figure 1. Comparison of elastin expression in the CFS and LM from the two groups of patients with different LM strengths. CFS, conjoint facial sheath; LM, levator palpebrae superioris muscle.

Comparison of elastin expression in the CFS and LM within the groups. In both the 0-1 (P=0.005) and 2-3 mm (P=0.009) groups, the expression level of elastin in the CFS was significantly higher compared with that in the LM tissues (Fig. 2; Table IV).

Therapeutic effects. Within 6 months after surgery, there were 9 patients (9 eyes) exhibiting good correction and 1 patient (1 eye) with undercorrection in the 0-1 mm CFS + LM group, yielding a 90% correction rate (Table V). In the 2-3 mm group, the good correction rate of CFS + LM complex suspension surgery was 100% (Table V). In addition, there were no overcorrections or relapses in the two groups at the end of follow-up (Table V).

Degree of incomplete eyelid closure. A total of 6 months after surgery, the degree of incomplete eyelid closure in the 2-3 mm group was significantly lower compared with that in the 0-1 mm group (P=0.048; Table VI), indicating that

Table III. Comparison of the expression of elastin in the CFS and LM of the groups of patients with different LM strengths (n=10).

Group	CFS	LM
0-1 mm	0.95±0.43	0.69±0.32
2-3 mm	1.23±0.35[a]	1.13±0.45[a]
t-value	-1.611	-2.537
P-value[a]	0.125	0.021

[a]vs. 0-1 mm. CFS, conjoint fascial sheath; LM, levator palpebrae superioris muscle.

Table IV. Comparison of the expression of elastin in the CFS and LM of patients with the same LM strength (n=10).

Group	In 0-1 mm	In 2-3 mm
CFS	1.33±0.41	1.54±0.62
LM	0.70±0.39[a]	0.95±0.34[a]
t-value	3.656	3.305
P-value[a]	0.005	0.009

[a]vs. CFS. CFS, conjoint fascial sheath; LM, levator palpebrae superioris muscle.

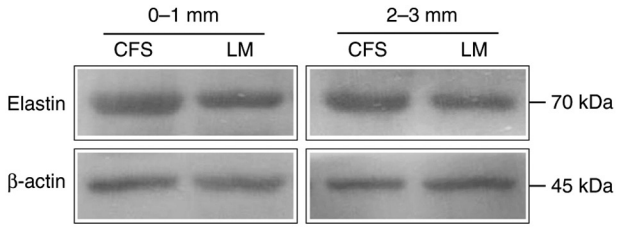

Figure 2. Comparison of elastin expression in the CFS and LM from the two groups patients with the same LM strength. CFS, conjoint facial sheath; LM, levator palpebrae superioris muscle.

patients with an LM strength of 2-3 mm, but not 0-1 mm, have improved closing function of the eyelid after surgery.

Incidence of complications. During the 6-month follow-up period, conjunctival prolapse was observed in 3 patients (3 eyes), including 2 patients in the 0-1 mm group and 1 patient in the 2-3 mm group (Table VII). Those patients recovered after fixation of the prolapsed conjunctiva to the corresponding eyelid with a vertical mattress suture using 3-0 silk threads, which were removed after 14 days. Other postoperative complications, such as exposure keratitis, eyelid hematoma, trichiasis, and separation of the eyelid from the eyeball, did not occur after CFS + LM complex suspension surgery, as shown in Table VII.

Presentation of representative patients. In order to observe the postoperative effect of CFS + LM complex suspension for correction of severe congenital ptosis, two patients are presented.

Case presentation from the 0-1 mm group. An 8-year-old male patient was diagnosed with severe congenital ptosis of the right eye. The LM strength was 0 mm in the right eye and 11 mm in the left eye. The superior rectus muscles of both eyes were functional and Bell's sign was positive. CFS + LM complex suspension of the right eye and double eyelid reconstruction of the left eye were performed. Based on the evaluation of the height of the palpebral fissure, the contour of the eyelid margin and the formation of the double eyelid crease, it was concluded that the postoperative appearance was satisfactory (Fig. 3).

Case presentation from the 2-3 mm group. A 5-year-old female patient was diagnosed with severe congenital ptosis of the left eye. The LM strength was 2 mm in the left eye and 12 mm in the right eye. The superior rectus muscles of both eyes were functional and Bell's sign was positive. CFS + LM complex suspension of the left eye was performed and the effect of postoperative correction was satisfactory (Fig. 4). The results demonstrated that both patients with severe congenital ptosis with different LM strength were corrected by surgery without complications.

Discussion

Ptosis is a common ophthalmic condition in which the upper eyelid cannot be lifted, which can be due to congenital, acquired LM dysfunction or loss of function (13,14). Clinically, ptosis can be divided into three grades, namely mild, moderate and severe, according to LM strength and position of the upper eyelid margin (15). Severe ptosis means that LM strength is <4 mm and the upper eyelid margin covers the pupil by ≥50% (16). Due to the abnormal obscuration of the optical axis by the upper eyelid at birth, children with severe congenital ptosis are at serious risk of form-deprivation amblyopia and refractive errors, especially in unilateral cases (17-19).

At present, severe congenital ptosis is typically corrected with frontalis muscle suspension surgery (20). The method is to connect the frontalis muscle with the tarsus, and use the strength of the frontalis muscle to lift up the eyelids (21). However, certain complications, such as incomplete eyelid closure, undercorrection and postoperative keratitis, are common (21). The main reason for these is that the direction of the traction force of the frontal muscle during the correction of ptosis is vertical upward, which changes the direction of the physiological force of the upper eyelids (6,22). Over the past decade, CFS suspension surgery has attracted considerable attention (23,24). The safety, therapeutic and cosmetic effects of CFS suspension surgery have been reported to be significantly superior compared with those of traditional frontalis muscle suspension (4,25-26). In addition, these results have been found to be closely associated with the anatomical characteristics of the CFS. Previous anatomical studies have shown that the CFS is attached to the superior conjunctival fornix and is comprised of the fascia between the LM and the superior rectus muscle (2,27). When the eyeball looks upward and the upper eyelid is lifted, the CFS, LM and superior rectus muscle exert a synergistic effect (28). Therefore, the CFS is a dynamic structure that is involved in lifting the upper eyelid. This anatomical advantage of the CFS reduces the resistance during eye closure after CFS suspension surgery, and therefore reduces postoperative upper eyelid hysteresis to achieve

Table V. Curative effect within 6 months after surgery (n=10).

Group	Good correction	Undercorrection	Overcorrection	Relapse	Correction rate
0-1 mm	9	1	0	0	90%
2-3 mm	10	0	0	0	100%

Table VI. Unclosed distance between the upper and lower eyelid margins in the two groups at 6 months after surgery (n=10).

Group	Distance, mm
0-1 mm	1.80±0.63
2-3 mm	1.20±0.63[a]
t-value	2.121
P-value[a]	0.048

[a]vs. 0-1 mm.

good therapeutic and cosmetic effects (22). Furthermore, the correction of ptosis by CFS suspension is proposed to be more effective at aligning with the physiological lifting of the upper eyelid and is therefore safer, which to some extent compensates for the shortcomings of frontalis muscle suspension (29).

With the development of surgery, CFS + LM complex suspension surgery is becoming increasingly common for correcting severe congenital ptosis in children, since this surgical method has been documented to achieve superior therapeutic effects compared with those exerted by simple CFS suspension and frontalis muscle suspension (7,9). Previous histological studies have revealed that the CFS and LM are rich in collagen fibers and elastic fibers, which may explain why the CFS and LM are elastic and why CFS + LM complex suspension surgery can be used for severe blepharoptosis (8,10,11). Furthermore, the CFS tissue of children has significantly higher elastin expression compared with that of adolescents and adults (8). Higher elastin content indicates an improved elasticity of the CFS and CFS + LM complex, providing structural support for the use of CFS + LM complex in pediatric patients. However, elastin expression in the CFS and LM of pediatric patients with severe ptosis with different LM strengths requires further exploration. To address this issue, the present study measured and analyzed the relationship between the expression levels of elastin and the surgical volume necessary to accurately implement CFS + LM complex suspension surgery in children with severe congenital ptosis.

It was found that in the 2-3 mm group, elastin expression in the LM was significantly higher compared with that in the 0-1 mm group, suggesting that the function of the LM is superior in this group, due to higher elastin content, where the two factors are positively associated. However, there was no significant difference in the expression levels of elastin in the CFS between the two groups. These results potentially provide a theoretical basis for choosing the appropriate volume for ptosis correction surgery according to LM strength. In the present study, the standard surgical volume used for patients with LM strengths in the range of 0-1 mm was a separation height of the CFS + LM complex of 5-6 mm, and the upper eyelid margin was flat at the level of the upper edge of the cornea. For patients with LM strengths in the range of 2-3 mm, the surgical volume was a separation height of the composite flap of 3-4 mm, and the upper eyelid margin covered the cornea by 0.5-1 mm.

Furthermore, elastin expression in the CFS was found to be significantly higher compared with that in the LM in both the 1-2 and 2-3 mm groups, suggesting that the elasticity of the CFS was superior compared with that of the LM, especially in patients with severe ptosis with higher LM strength. Elastin is the most important structural component of elastic fibers, and its content can reflect the elasticity of the tissue (30). It is therefore possible that the CFS has a high content of elastin, whereas the LM may also contain a certain degree of elastin that is superimposed with the CFS in pediatric patients with severe congenital ptosis, consistent with the findings of a previous study (11). The LM firmly adheres to the orbital apex, towards which it exerts strong suspending force and traction (31). Combined with the histological evidence, the CFS + LM complex had good elasticity, flexibility and traction, which rendered the postoperative upper eyelid position more stable.

In the present study, the postoperative follow-up duration was 6 months. The good correction rate, the degree of incomplete eyelid closure and the incidence of complications were then recorded. Within 6 months after surgery, the correction rate of the 2-3 mm group was 100%. In the 0-1 mm group, 1 patient (1 eye) experienced mild undercorrection, yielding a 90% correction rate. The reason for this undercorrection may be excessive retraction caused by early postoperative eye movement or suture loosening. In terms of incomplete closure, the degree of eyelid closure in the 2-3 mm group was higher compared with that in the 1-2 mm group, suggesting that the increased LM strength is conducive to eyelid closure. In terms of surgical complications, conjunctival prolapse is a common complication of CFS + LM complex suspension surgery (6). Of the 20 patients enrolled to the present study, 3 patients (3 eyes) experienced upper fornix conjunctival prolapse within 1 week after surgery. The main cause was that the upper fornix conjunctival tissue developed edema postoperatively and detached from the suspensory ligament due to gravity. However, these patients recovered after the fixation of the prolapsed conjunctiva to the corresponding eyelid. Other postoperative complications, such as exposure keratitis, eyelid hematoma, trichiasis, and eyelid-ball separation, did not occur. The clinical observation results of this study suggest that CFS + LM complex suspension surgery is safe and effective.

Congenital ptosis is mainly caused by the lack of LM development, resulting in difficulty lifting the upper eyelid (14). It

Table VII. Complications in the two groups during the whole follow-up period (n=10).

Group	Exposure keratitis	Eyelid hematoma	Conjunctival prolapse	Trichiasis	Eyelid-ball separation	Total complications
0-1 mm	0	0	2	0	0	2
2-3 mm	0	0	1	0	0	1

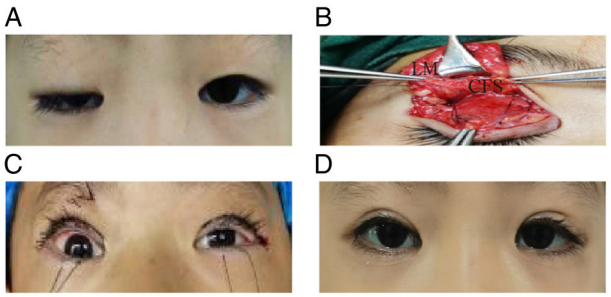

Figure 3. CFS + LM complex suspension to correct severe congenital ptosis with 0-1 mm LM strength. (A) Preoperative image of an 8-year-old boy with congenital ptosis of the right eye. (B) Exposure of the CFS and LM. (C) Postoperative image of the position of the upper eyelid margin, flat at the level of the upper edge of the cornea in the right eye and located at the normal position in the left eye. (D) Image of the patient 6 months after surgery. CFS, conjoint facial sheath; LM, levator palpebrae superioris muscle.

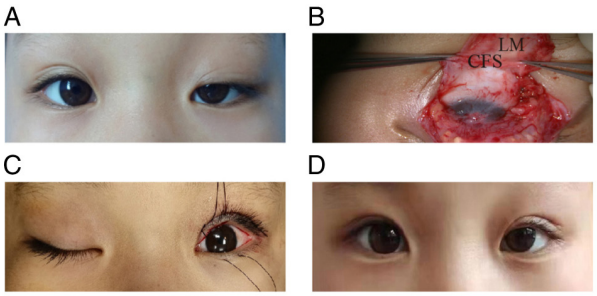

Figure 4 CFS + LM complex suspension to correct severe congenital ptosis with 2-3 mm LM strength. (A) Preoperative image of a 5-year-old girl with congenital ptosis of the left eye. (B) Exposure of the CFS and LM. (C) Postoperative image of the position of the upper eyelid margin, located at the position of 1 mm covering the upper edge of the cornea in the right eye. (D) Image of the patient 6 months after surgery. CFS, conjoint facial sheath; LM, levator palpebrae superioris muscle.

has previously been proposed that LM strength represents LM function and its damage degree (32,33). Consistent with this hypothesis, in the present study LM strength and its elastin content were found to be positively associated. From a clinical point of view, when the muscle strength of LM is 2-3 mm in patients with severe ptosis, it indicates that the elastic fibers are functioning adequately, since the expression level of elastin is high. By contrast, when the muscle strength is 0-1 mm, the expression level of elastin is low. However, from the perspective of molecular mechanisms, additional evidence is needed. In subsequent studies, morphological staining and structural analysis of the tissues is required.

In conclusion, the results of the present study suggested that elastin expression in the CFS was higher compared with that in the LM of children with severe congenital ptosis and that elastin expression in the LM may be positively associated with LM strength. However, elastin expression in the CFS had no clear association with LM function. Therefore, adjusting the operation volume in CFS + LM complex suspension surgery according to LM strength appears feasible, which can achieve satisfactory postoperative results in the correction of severe congenital ptosis in children.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

PB was responsible for the study conceptualization, the surgical operation and manuscript review. XJ was responsible for designing and performing experiments, and for the writing and editing of the manuscript. ZL was responsible for the methodology and data analysis. JS was responsible for the follow-up examination and data acquisition. RP and MW were responsible for the literature search and data interpretation. HW, HZ and SL were responsible for data collection. PB and XJ confirm the authenticity of all the raw data. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The present study adheres to the tenets of The Code of Ethics of the World Medical Association (Declaration of Helsinki) for research involving humans and was reviewed and approved by the Ethics Committee of Hebei Eye Hospital (approval no. 2020KY013; Xingtai, China). Written informed consent for participation was obtained from the participant and the minor(s)' legal guardian, for the publication of any potentially identifiable images or data included in this article.

Patient consent for publication

Written informed consent for publication of their clinical details and clinical images was obtained from the legal guardian of the participants aged <18 years.

Competing interests

The authors declare that they have no competing interests.

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