



# Supraciliary Incision as a Modified Approach for Asian Blepharoptosis Patients

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## Abstract

**Background** Blepharoptosis may result in an unattractive appearance and vision problems. According to the severity of ptosis, patients may undergo correction surgery using upper eyelid retractors. The conventional incision for surgical procedures was the double-eyelid incision, potentially resulting in an obvious and unnatural scar or long-lasting edema and prolonged recovery time.

**Objectives** The aim of this study was to introduce a supraciliary incision as an alternative to the double-eyelid incision for blepharoptosis correction that creates a scarless, natural appearance with a quick recovery time.

**Methods** From June 2019 to June 2021, 32 patients (36 eyelids) underwent blepharoptosis correction through a supraciliary incision. MRD1, the height of the eyelid fissure, and the patient's satisfaction with the shape and scar

as well as postoperative complications (eyelid insufficiency, conjunctival prolapse, inadequate correction of ptosis, and excessive correction of ptosis).

**Results** All 32 patients (36 eyelids) were followed up for 6 to 18 months, with an average follow-up of 11.6 months. The postoperative satisfaction rate was 96.43%. There was no overcorrection, but one patient (1 eyelid, 2.8%) was under correction that required secondary correction. One patient (1 eyelid, 2.8%) experienced conjunctival prolapse. Sixteen patients showed lagophthalmos early after surgery, in which one patient experienced early-stage keratitis and completely recovered within two months.

**Conclusion** Blepharoptosis correction via supraciliary incision allows for broader indications and fewer surgical scars without disrupting eyelid integrity, resulting in quick recovery after surgery.

**Level of Evidence IV** This journal requires that authors assign a level of evidence to each article. For a full description of these Evidence-Based Medicine ratings, please refer to the Table of Contents or the online Instructions to Authors [www.springer.com/00266](http://www.springer.com/00266).

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**Keywords** Blepharoptosis · Supraciliary incision · Scar · Edema · Eyelid anatomy

## Introduction

Blepharoptosis is defined as an upper eyelid margin covering the limbus of more than 2 mm or a length of MDR1 less than 4 mm [1]. The ptotic eyelid may result in an unattractive appearance and vision problems [2]. Blepharoptosis, as a result of dysfunction of the levator complex, can be unilateral or bilateral and is classified as mild,

moderate, or severe based on the extent of the covered pupil.

The fundamental goal of surgery is to lift the upper eyelid to increase the visual field. The incision site for blepharoptosis was often designed at the double-eyelid crease, approximately 6 mm to 8 mm from the palpebral margin for Asian patients [3]. Many surgical techniques that increase suspension strength involving levator aponeurosis, Müller's muscle, conjoint fascial sheath, and frontalis muscle have been reported [4–6]. The levator aponeurosis–Müller's muscle composite flap, for the physiological elevation of the upper lid, is the most frequently selected method [5]. The amount of correction toward different degrees of ptosis has not yet been established. However, some literature suggests that the levator strength is usually weak or absent in cases with severe ptosis. In such circumstances, conjoint fascial sheath (CFS) suspension and the frontalis muscle may be involved in correcting severe ptosis [2, 7, 8].

Patients' main concerns about the double-eyelid incision are visible surgical scarring, long-lasting edema, and prolonged recovery time. This approach may not be suitable for patients who prefer to retain their single-lid features. Therefore, mini-incision correction and nonincision or transconjunctival incision procedures have been proposed [9, 10]. The advantages of mini-incision correction include concealed incision and insignificant trauma with flexible adjustment during the operation. Since the correction is achieved by tension sutures, the correction cannot be achieved for severe ptosis. The transconjunctival procedure may face a higher risk of suture-induced granuloma or infection. Patients can complain about abnormal sensations after surgery [10, 11]. According to the authors, mini-incision correction and nonincision/transconjunctival incision procedures may only be suitable for patients with mild-to-moderate ptosis without excessive upper eyelid skin and prominent fibroadipose tissue.

These limitations led us to explore an alternative surgical procedure with a broader range of indications while maintaining the advantages of both full-incision and minimally invasive techniques. In this paper, we present a modified surgical approach for blepharoptosis by using supraciliary incision. The supraciliary incision is combined with an appropriate suspension approach for treating mild to severe blepharoptosis, bringing the advantages of full-incision surgery and minimally invasive surgery together to achieve a natural appearance with effective correction.

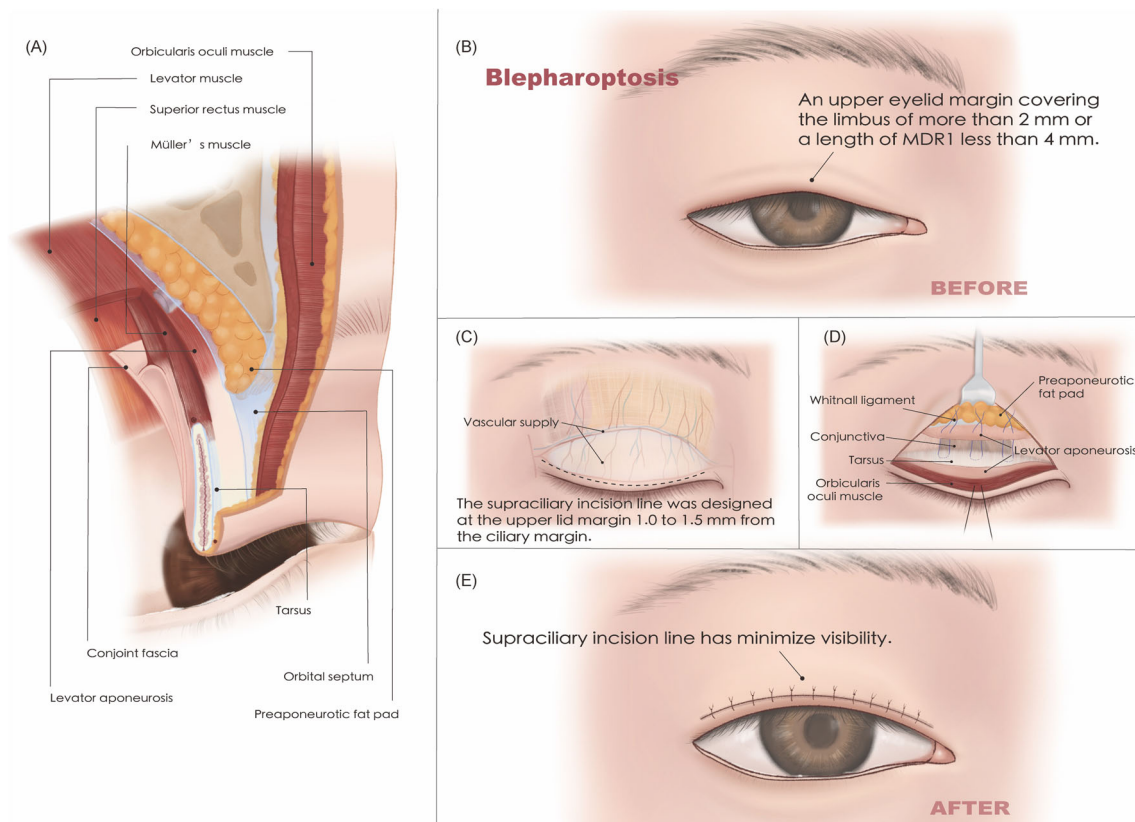
## Methods

### Patients

From April 2019 to June 2021, 32 patients (4 male and 24 female patients, 36 eyelids) with blepharoptosis who underwent blepharoptosis correction through a supraciliary incision performed by the same surgeon were enrolled. This study was a prospective study conducted at West China Hospital of Sichuan University and approved by the Ethics Committee of West China Hospital of Sichuan University. Unilateral or bilateral blepharoptosis, consent for primary eyelid surgery, and 12-month follow-up were the inclusion criteria. Patients with positive Bell's phenomenon, superior rectus dysfunction, dysthyroid ophthalmopathy, myasthenia gravis, or Marcus Gunn's jaw-winking syndrome were all excluded. All patients or their guardians gave written informed consent to use clinical data, and the study followed the standards of the Declaration of Helsinki.

### Preoperative Evaluation

A thorough medical history was obtained, and an ophthalmologic examination was performed. The marginal reflex distance-1 (MRD1), degree of ptosis, and levator muscle function were assessed before surgery (Figure 1B). MRD1, the distance between the corneal light reflex and the center of the upper lid margin in neutral gaze, was considered the gold standard for assessing correction. When the drooping eyelid obscured the light reflex, it was elevated until the reflex was visible, and the elevated distance was recorded as MRD1 in negative digits. We set the following standard to confirm the severity of ptosis: the difference between the level of the ptotic and normal eyelid was used to determine the degree of blepharoptosis in unilateral cases. If the eyelid drooped 2 mm or less, ptosis was classified as mild, 2 mm to 4 mm as moderate, and 4 mm or more as severe. The typical eyelid level in bilateral cases was arbitrarily set at 1 mm below the superior limbus of the cornea, according to Stasior and Ballitch. We used Berke's approach to assess the function of the levator muscles, which estimates the difference in the height of the upper eyelid margins when the patient looks lowest and highest after the surgeon has pushed the eyebrows together to stop the work of the frontalis muscle. If the eyelid excursion was 8 mm or more, it was considered good, moderate if it was between 5 and 7 mm, and poor if it was less than 5 mm. In certain cases, visual acuity



**Fig. 1** Illustration of the anatomy of the upper eyelid (A) and the key steps of the supraciliary incision for blepharoptosis correction (B–E)

and field tests were used to assess the functional deficit caused by ptosis.

## Surgical Technique

### *Preoperative Design and Preparation*

The intended supraciliary incision line (Line a) was designed at the upper lid margin 1.0 to 1.5 mm from the ciliary margin parallel to the curvilinear shape of the upper eyelid processing from the upper lacrimal punctum to the lateral canthus (Figure 1C). Then, forceps were used to measure the laxity of the upper eyelid skin. The degree of redundancy determines the amount of skin removed. The crease height (Line b), where the double-eyelid crease is located, was designed according to the patient's desire and contralateral condition, usually 2.0 to 6.0 mm above the ciliary margin. Line b was drawn parallel to Line a. All procedures were performed by the same surgeon.

### *Surgical Procedures (Supplementary Video)*

**Anesthesia and Müller's Muscle-Levator Aponeurosis Composite Flap Advancement** Local anesthesia was injected under the dermis with 2% lidocaine hydrochloride

with a 1:100,000 epinephrine bitartrate solution. The skin was incised along Line a deep to the subdermal layer. Excess skin was removed according to the preoperative design. Subcutaneous dissection was carried out between supraciliary line a and the crease fixed line (Line b). A strip of pretarsal orbicularis muscle and subcutaneous tissue was trimmed inferiorly to the lower border of the tarsus and remained 1 mm above the lash follicle. The superior palpebral vascular network and the lymphatic system were carefully preserved. For patients with thick pretarsal tissue, the pretarsal orbicularis muscle from the inner canthus to the outer canthus can be selectively trimmed to form a ladder-like structure thicker above and thinner below the crease line. The orbital septum was breached, and the orbital fat was dissected to expose the levator complex, including the levator aponeurosis and Müller's muscle.

Then, the upper eyelid inside was turned out to expose the conjunctiva, and the local anesthetic solution was administered between the levator muscle and the conjunctival surface. A longitudinal incision was made at the superior margin of the tarsus. A mosquito vascular clamp was inserted to separate the levator aponeurosis and the Müller's muscle from the conjunctiva. The levator system was detached from the superior margin of the tarsus. Patients were asked to downgaze to expose the levator

muscle between the lid conjunctiva and the posterior wall of the orbital septum. Three mattress sutures of the folded aponeurosis were made using 6-0 nylon sutures at the medial, middle, and lateral points of the upper third of the tarsus (Figure 1D). Then, patients were told to sit up to check the upper eyelid margin level and curve. The thread was tightened until an ideal outcome was achieved.

For patients with severe ptosis, conjoint fascial sheath suspension (CFS) was applied. The dissection between the conjunctiva and the septum went further to the level of the superior conjunctival fornix. The CFS was exposed and fixed at the upper one-third of the tarsus using 6-0 nylon sutures. Likewise, the patient must confirm the eyelid margin level and curve in the sitting position before the thread is knotted. For patients not requiring double-eyelid blepharoplasty, several interrupted 8-0 nylon sutures or continuous 8-0 nylon sutures along the supraciliary incision were taken. Frost suturing of the lower eyelid was performed for severe ptosis patients to protect the cornea.

**Blepharoplasty** Blepharoplasty was performed according to the preoperative design. The double-eyelid crease was designed approximately 6.0 mm above the ciliary margin. The first 7-0 nylon suture was placed at the mid-pupillary point at the designed crease to anchor the skin to the levator aponeurosis and the pretarsal aponeurosis. Patients were asked to open their eyes to check the symmetry and curve of the double-eyelid crease. Then, several interrupted 8-0 nylon sutures or continuous 8-0 nylon sutures were taken to form the crease. Then, the supraciliary incision was closed using 8-0 nylon sutures.

### Postoperative Care and Evaluation

The surgical region was left exposed postoperatively. Oral antibiotics were given for three days after surgery. The sutures were removed on the seventh day after surgery. Patients were followed up from 3 to 16 months. Both patients and surgeons evaluated the surgical outcomes. The evaluation metrics included the differences in MRD1 values, palpebral fissure length, levator muscle strength, Bell's phenomenon, and Hering sign before and 12 months after surgery. Patient satisfaction with the shape and scar formation after surgery was rated from 0 to 10 points. Postoperative complications were collected, including lagophthalmos, conjunctival prolapse, and under- and overcorrection.

### Statistical Analysis

The data are expressed as the mean  $\pm$  standard deviation (SD). Student's *t*-test and the Mann–Whitney U test were used for data comparisons preoperatively and

postoperatively. SPSS version 21.0 (IBM Corp, Armonk, NY, USA) software was used for statistical analysis. A *p* value  $< 0.05$  demonstrated statistically significant differences.

### Results

A total of 32 patients (4 male and 24 female patients, 36 eyelids) with blepharoptosis were enrolled in our study. The patients were between 16 and 48 years old (average age of 26 years old). The characteristics of the patients are summarized in Table 1. According to the severity of ptosis, 19 eyelids were mild, ten were moderate, and seven were severe. Among them, eight patients underwent levator advancement, 14 underwent levator resection, 10 underwent levator-CFS suspension, and 4 underwent frontalis suspension.

All patients were followed up for 6 to 18 months, with an average follow-up period of 11.6 months. From the measurement, the mean  $\pm$  SD preoperative and postoperative MRD-1 were  $0.30 \pm 2.729$  and  $4.28 \pm 0.439$ , respectively. The mean  $\pm$  SD preoperative and postoperative palpebral fissure lengths were  $4.81 \pm 2.729$  and  $8.88 \pm 0.524$ , respectively. The mean  $\pm$  SD preoperative and postoperative levator muscle strength were  $4.98 \pm 2.942$

**Table 1** Preoperative characteristics of patients

Characteristics	Results
Age (mean), years	28.34 (16–48)
Gender, <i>n</i> (%)	
Men	6 (18.75%)
Women	26 (81.25%)
Involved eyes, <i>n</i> (%) ( <i>n</i> =32 cases)	
Unilateral	29 (90.63%)
Bilateral	3 (9.37%)
Blepharoptosis severity, <i>n</i> (%) ( <i>n</i> =36 eyelids)	
Mild	19 (52.78%)
Moderate	10 (27.78%)
Severe	7 (19.44%)
Levator function, <i>n</i> (%) ( <i>n</i> =36 eyelids)	
Good	8 (22.22%)
Fair	14 (38.88%)
Poor	14 (38.88%)
Operation methods, <i>n</i> (%) ( <i>n</i> =36 eyelids)	
Levator advancement	8 (22.22%)
Levator resection	14 (38.89%)
Tarsus–levator–CFS suspension	10 (27.78%)
Frontalis suspension	4 (11.11%)

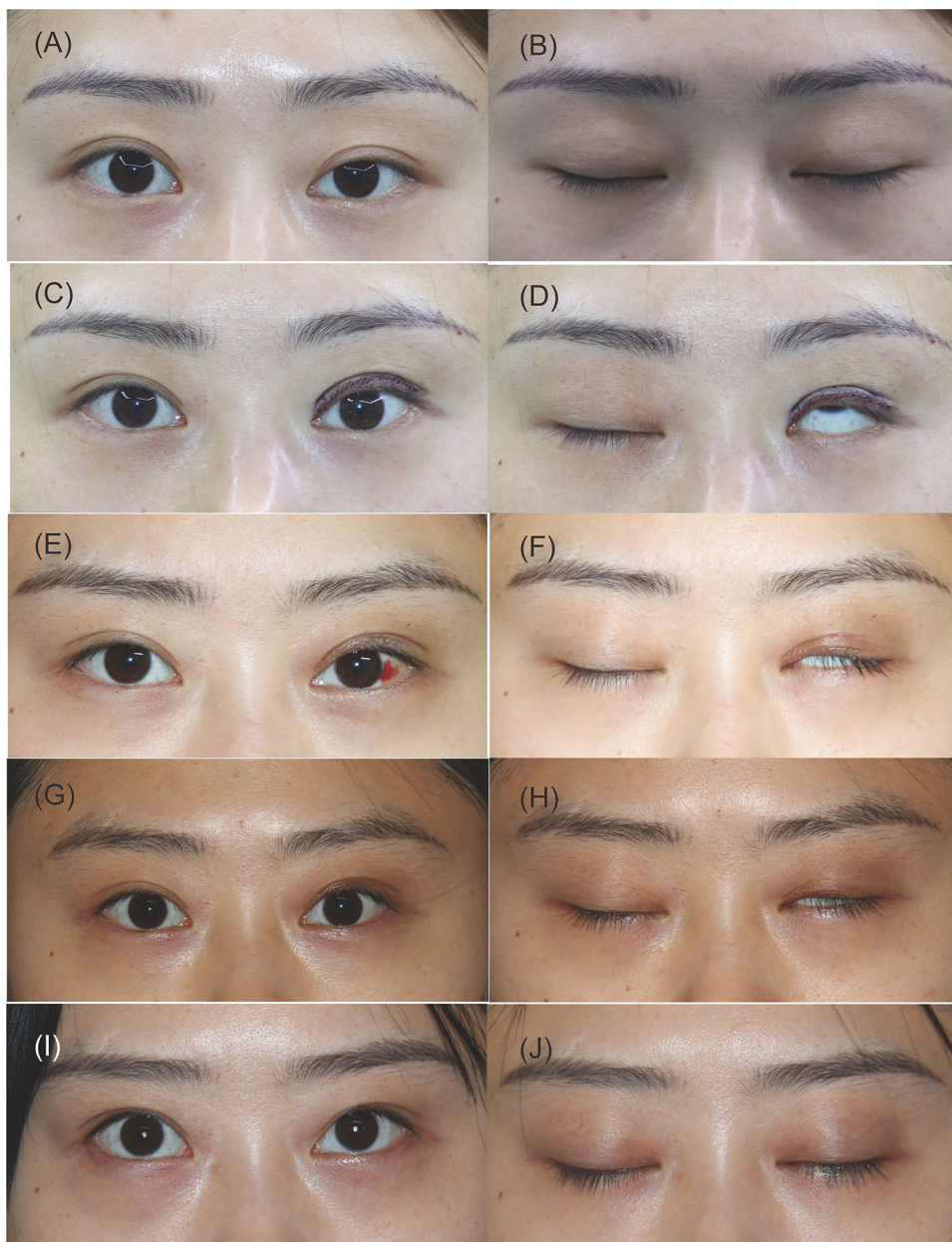


and  $8.47 \pm 2.274$ , respectively. In the long-term postoperative follow-up, there was no overcorrection, but one patient (1 eyelid, 2.8%) was under correction that required secondary correction. One patient (1 eyelid, 2.8%) experienced conjunctival prolapse. Sixteen patients (16 eyelids, 44.4%) showed lagophthalmos early after surgery, in which one patient experienced keratitis two months after surgery. The postoperative satisfaction rate was 96.43%. The satisfaction degree of the eyelid shape of all patients was  $9.04 \pm 0.92$ , and the satisfaction score of the incision scar was  $9.57 \pm 0.57$ .

## Case Report

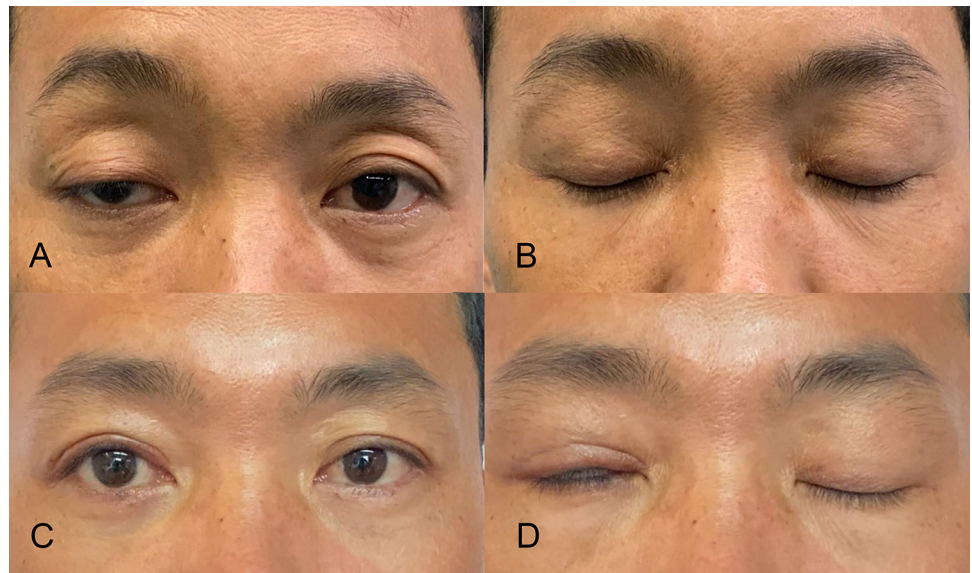
**Case 1** A 32-year-old female was diagnosed with moderate left blepharoptosis. On examination, the MRD-1 was 2.0 mm on the left and 4.0 mm on the right (Fig. 2A and B). Figure 2C–J shows the postoperative results after left levator advancement through the supraciliary incision line at 7 days (Fig. 2C, D), 1 month (Fig. 2E, F), 3 months (Fig. 2G, H), and 1 year (Fig. 2I, J) postoperatively. The patient developed incomplete closure of the left eye within 3 months postoperatively, and the symptoms disappeared after conservative treatment two months later. One-year postoperative results showed that MRD-1 was 4.5 mm on both sides (Fig. 2I, J).

**Fig. 2** Preoperative view of a 32-years-old female with unilateral moderate left blepharoptosis with eyes open (left column) (A) and with eyes closed (right column) (B), who underwent left levator advancement technique through the supraciliary incision line. Photographs 7 days before suture removal (C, D), 1 month (E, F), 3 months (G, H), and 1 year (I, J) postoperatively showed the patient is exhibiting a stable and symmetrical correction result with invisible surgical scar in supraciliary incisions

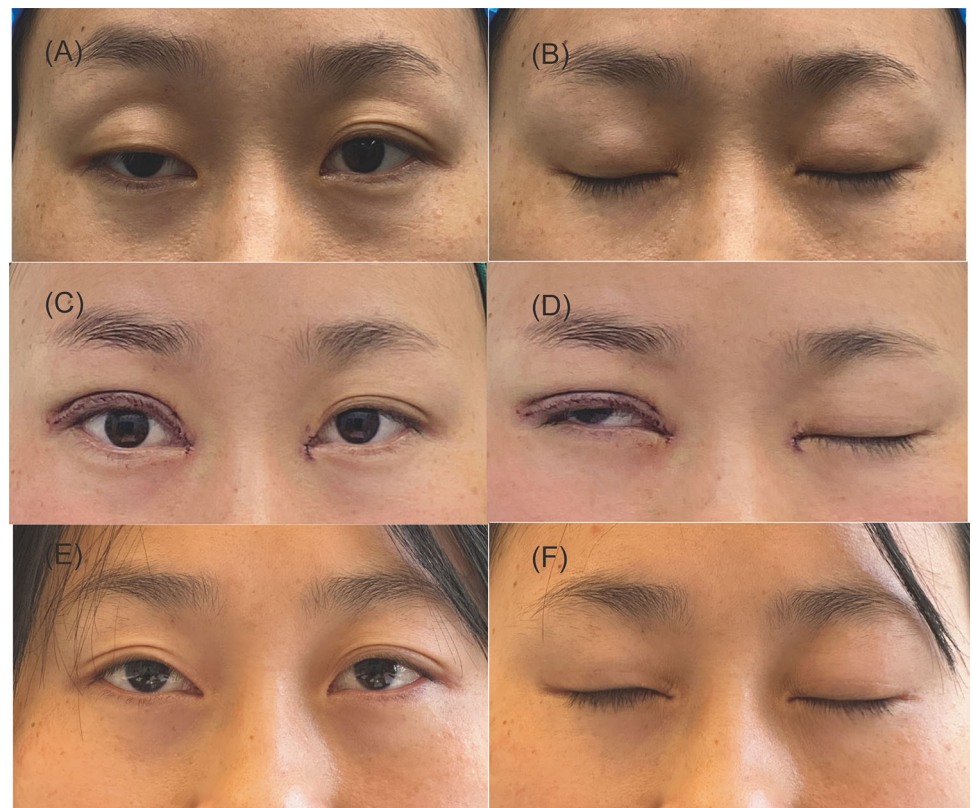




**Fig. 3** Preoperative view of a 35-years-old male with unilateral severe right blepharoptosis with eyes open (left column) (A) and with eyes closed (right column) (B). On examination, the MRD-1 was 4.0 mm on the left and 0 mm on the right. Photographs 1 year after right CFS suspension through the supraciliary incision line and right buried suture blepharoplasty (C, D) showed that MRD-1 was 3.0 mm on both sides (C, D). A depression was observed in the inner third of the blepharoplasty line at 1-year postoperative follow-up



**Fig. 4** Preoperative view of a 29-years-old female with unilateral severe right blepharoptosis with eyes open (left column) (A) and with eyes closed (right column) (B). On examination, the MRD-1 was 4.0 mm on the left and 0 mm on the right. C and D showed immediate results after left levator advancement technique through the supraciliary incision line, right buried suture blepharoplasty, and left epicanthoplasty. One year postoperatively showed the patient is exhibiting a stable and symmetrical correction result with invisible surgical scar in supraciliary incisions. MRD-1 was 4.0 mm on both sides (E and F)



**Case 2** A 35-year-old male was diagnosed with severe right blepharoptosis. On examination, the MRD-1 was 4.0 mm on the left and 0 mm on the right (Fig. 3A and B). One-year postoperative results after right CFS suspension through the supraciliary incision line showed that MRD-1 was 3.0 mm on both sides (Fig. 3C and D). A depression surgical scar at the medial third of the double eyelid line was found 1 year after surgery (Fig. 3D). Since the patient was

satisfied with the postoperative results, we did not carry out follow-up treatment of the scar.

**Case 3** A 29-year-old female was diagnosed with severe right blepharoptosis. On examination, the MRD-1 was 4.0 mm on the left and 0 mm on the right (Fig. 4A and B). Figure 4C and D showed immediate results after right blepharoptosis correction through the supraciliary incision line, right buried suture blepharoplasty, and left

epicanthoplasty. One-year postoperative results showed that MRD-1 was 4.0 mm on both sides (Fig. 4E and F).

## Discussion

Ptosis is one of the common diseases of plastic surgery and is manifested by an upper eyelid margin covering the limbus of more than 2 mm or a length of MDR1 less than 4 mm in the primary gaze position. Based on the etiology, blepharoptosis can be categorized as myogenic, aponeurotic, neurogenic, and mechanical ptosis [12]. Most of the published articles on the etiology of congenital ptosis have demonstrated that the primary cause of simple congenital ptosis is the levator palpebrae superioris muscle, the origin of the levator aponeurosis and Müller's muscle. According to previously published reports, the underlying pathological changes include dysgenesis or dystrophy associated with oculomotor nerve damage or disrupted innervation within LPS or fibrotic changes within the levator aponeurosis [13]. Lee et al. [14] reported the age-specific etiology among Taiwanese ptosis patients, with younger patients presenting with myogenic ptosis, while older groups tended to have aponeurotic ptosis. This observation proposed similar demographic features with a Korean national study [15].

A thorough preoperative examination of the ocular and eyelid is essential for the selection of surgical procedures. Upper eyelid retractors are composed of three primary structures: the levator palpebrae superioris (LPS) muscle, the levator aponeurosis, and Müller's muscle [16]. The LPS muscle is the origin of the levator aponeurosis superiorly and the Müller's muscle inferiorly [17]. The levator aponeurosis then separates into two layers. The digital end of the anterior layer is fused with the posterior layer of the orbital septum and attaches to the subcuticular tissue. The posterior layer is inserted into the anterior-inferior one-third of the tarsus [18]. According to recent research, Müller's muscle can also originate from the orbital smooth muscle network underneath the LPS muscle [19]. It inserts in the superior aspect of the tarsal plate [16].

On the basis of the anatomy of the levator system of the upper eyelid, the two primary procedures for correcting ptosis are to shorten the levator complex or to perform frontalis suspension. The levator advancement technique is one of the most frequently used techniques for blepharoptosis correction for mild-to-moderate blepharoptosis [20, 21]. The correlation between the amount of correction and the LPS is 3–4 mm LPS muscle advancement for each millimeter of correction [21]. Frontalis suspension or levator-CFS suspension are viable options for severe ptosis [22, 23]. However, conventional incision for blepharoptosis correction leaves a visible surgical scar, long-lasting

edema, and prolonged recovery time. Mini-incision correction and nonincision or transconjunctival incision procedures have been proposed. These techniques cannot remove redundant skin or protruding subcutaneous tissue, such as preaponeurotic fat and orbicularis oculi muscle. This method is especially inapplicable to elderly patients with loose skin and swollen upper eyelids. Moreover, the suture force may be gradually eroded away in the later stage of recovery.

The supraciliary incision for the blepharoptosis correction procedure is modified according to the anatomic features of Asian upper eyelids. The supraciliary incision has several advantages compared to the full-incision and non-incision or transconjunctival methods for blepharoptosis correction.

## Minimized Scar Formation

Skin thickness is thought to be closely related to scar formation. The thickness of the eyelid skin is a gradual and continual change from the ciliary margin to the eyebrow. The thickness of the eyelid skin is a gradual thickening progression from the ciliary margin to the eyebrows [3]. The thinnest skin of the upper eyelid (0.3–0.5 mm) is near the ciliary margin with fewer elastic fibers, while the infrow skin is thickest (1.0–1.3 mm) [24, 25]. For patients with redundant skin, a strip of skin will be removed. As in the conventional double-eyelid incision, the suture may result in an uneven eyelid crease [26].

Based on the growing understanding of the anatomy of Asia, the dermal thickness and the content of collagen are higher in Asian skin than in Caucasian skin [27], which implies that Asians are more likely to suffer from postoperative scarring and unnatural results created by a conventional double-eyelid incision [3]. In light of these foundations, hypertrophic scar formation can be minimized within the periciliary incision. This is confirmed by surgeries using the supraciliary or subciliary incision [4, 28–31]. However, only a few studies have reported the implication of supraciliary incisions in blepharoptosis correction.

## Quick Recovery

The intact vascular supply and lymphatic drainage guarantee recovery with limited hematoma, edema, and puffiness. Based on the anatomy of the upper eyelids, the arterial supply is derived principally from the palpebral branches of the ophthalmic artery. Kawai et al. [32] reported the arterial anatomic features of the upper palpebra. The upper palpebral artery is composed of four arterial arcades, including the marginal arcade (MA), the peripheral arcade (PA), the superficial orbital arcade (SOA), and

the deep orbital arcade (DOA), where the MA is located anterior to the inferior margin of the tarsal plate and the PA courses in the Müllers muscle along the superior margin of the tarsal plate. Their branches anastomose to form a vascular plexus on the superficial layer of the tarsal plate. The SOA and DOA originated mainly from the supra-trochlear artery and were located anterior and posterior to the orbicularis oculi muscle along the superior orbital rim, respectively.

Edema is a common complication of blepharoptosis correction. It occurs due to venous and lymphatic drainage. Zhang et al. [33] reported a higher incidence of eyelid edema in Asian participants than in Caucasian participants, which may be related to ethnic anatomic characteristics. The anatomical features of the Asian eyelids showed a lower fusing region of the transverse ligament and a narrower height of the tarsal plate than in Caucasians [34, 35]. In the conventional procedures for blepharoptosis correction, the palpebral arterial arch and drainage system will be interrupted by an incision. Since the supraciliary incision is located 1 mm above the lash line that maintains the vascular and lymphatic system of the upper eyelid integrity, the postoperative edema will be resolved faster than in the higher incision.

Eyelid numbness is also complained of by patients after conventional full-incision surgery. In a cadaveric microanatomical study, the upper palpebral sensory nerves were observed to travel vertically in the suborbicularis fascia until they end at the caudal part of the tarsus [36]. The supraciliary incision is located away from the caudal edge of the tarsus so that sensory nerve damage is avoided and sensation of the upper eyelid is preserved.

### Broader Indications

The eyelid is one of the most distinctive features of Asian eyes. Growing numbers of Asians are willing to preserve more personal characteristics during preoperative communication. However, the conventional incision for blepharoptosis correction is designed 6 to 8 mm above the palpebral margin of the upper eyelid, and rigidly connecting the skin to the tarsus often leaves visible surgical scars and a sinking double-eyelid crease with fewer ethnic characteristics.

The supraciliary incision is suitable for all kinds of blepharoptosis patients with or without eyelid creases, senile patients or patients with redundant skin and fibroadipose tissue, and patients requiring revision surgery. In our study, 32 patients underwent levator advancement surgery, levator resection surgery, levator-CFS suspension, or frontalis suspension according to the severity of ptosis. No major complications or undercorrection were reported during the follow-up. The postoperative satisfaction rate of

the incision scar and eyelid shape was promising. The supraciliary incision is not only suitable for blepharoptosis but can also be combined with buried suture double-eyelid blepharoplasty.

For those reasons, the supraciliary incision for blepharoptosis achieved scarless and natural results. However, this study may have some limitations. Our postoperative results were assessed by outpatient follow-up or online follow-up of the incidence of postoperative complications, subjective morphological observations, and patient satisfaction surveys. Although most patients were able to be followed up regularly for six months after surgery, they were not available for follow-up thereafter for a variety of reasons. We will enroll more patients in our follow-up studies and quantify the results. In addition, the photograph contains a great deal of valuable information. Our photos contained only anterior and closed-eye view. Two oblique and lateral views as well as upward gaze and downward gaze should also be included in subsequent shots. A controlled study will be performed comparing the supraciliary incision to the double-eyelid incision and non-incisional procedure for blepharoptosis correction.

### Conclusion

Blepharoptosis correction via supraciliary incision allows the preservation of the neurovascular network, thus avoiding disrupting the eyelid's integrity, resulting in quick recovery and reducing complications after surgery. In addition, the supraciliary incision is concealed near the lash line. Nevertheless, the indications for supraciliary incision are not limited to the current ptosis correction techniques, with the option of performing blepharoplasty.

**Author contributions** YC and HZ contributed equally to this work. Conceptualization, JW; validation, YC, HZ; investigation, YC; resources, HZ; original draft preparation, YC and HZ; review and editing, WAW; visualization, HZ; supervision, YQ and JW. All authors have read and agreed to the published version of the manuscript. All authors have accepted responsibility for the entire content of this manuscript and approved its submission.

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### Declarations

**Conflict of interest** The authors declare that they have no conflicts of interest to disclose.

**Human and Animal Rights** This study was approved by the Ethics Committee of West China Hospital of Sichuan University. This article does not contain any animal studies.



**Informed Consent** All participants in the study were informed and signed the informed consent form.

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