



Factors predicting long-term changes in refraction after lamellar keratoscleroplasty in children with limbal dermoids

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Abstract

Objectives The objective of this study is to determine the factors that predict long-term changes in refraction after lamellar keratoscleroplasty in paediatric patients with limbal dermoids.

Methods A retrospective study of 66 children with limbal dermoids who had lamellar keratoscleroplasty correction with more than 1-year follow-up. Univariate and multivariate regression analyses were performed to investigate factors associated with the long term in refractive parameters, including spherical equivalent, astigmatism, and mean keratometry. The change value was defined as the postoperative refractive value minus the preoperative refractive value. The lower the value of changes, the more satisfied the effects on the correction of the preoperative refraction.

Results A total of 66 patients (mean surgical age: 3.5 ± 2.1 years) were assessed with at least 1-year follow-up. Amblyopia treatment duration was the only independent factor predicting the long-term changes in spherical equivalent between baseline and last follow-up visit ($\beta = -0.030$, $P < 0.001$). Lesion encroachment on the central and paracentral cornea ($\beta = 0.502$, $P = 0.024$), suture-related complications ($\beta = 1.571$, $P < 0.001$) and graft rejection ($\beta = 0.983$, $P = 0.035$) were significantly correlated with long-term changes in astigmatism. The long-term changes in refraction were not correlated with surgical age, lesion size, lesion depth, steroid-induced high intraocular pressure and changes in mean keratometry.

Conclusion Suture-related complications and graft rejection should be carefully observed and appropriately treated in order to avoid the possible postoperative increase in astigmatism, especially for patients with lesion encroachment on the central and paracentral cornea. The long-duration amblyopia treatment after surgery appears to have a better correction effect on spherical equivalent in the long term, compared with astigmatism.

Introduction

Corneal limbal dermoids are the most common choristomas arising from an early embryological anomaly [1]. They mainly consist of keratinised epithelium, an underlying dermal layer containing fibrous fatty tissue, and occasionally contain hair with sebaceous glands [2, 3]. Enlarging limbal dermoid may cause low visual acuity by the encroachment in the visual axis, corneal infiltration with fatty component and gradually induced corneal astigmatism; impaired vision may finally result in amblyopia [3, 4]. Previous reports have described the high tendency of amblyopia, especially anisometric amblyopia in patients with limbal dermoids [5–7].

Traditional surgical approaches for limbal dermoids included simple excision, penetrating keratoscleroplasty and lamellar keratoscleroplasty with full-thickness central corneal grafts or partial-thickness corneoscleral button [5, 6, 8]. The adequate choice depends on the size, depth and location

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of the lesion [8]. Although the cosmetic and visual outcomes of various surgical techniques have been reported in several studies, limited data are available on long-term postoperative refractive status in children with limbal dermoids. Besides, whether baseline characteristics and postoperative complications have any influence on postoperative refraction is not known. The purpose of this study is to assess the refractive outcomes and identify the preoperative or postoperative factors associated with long-term changes in refraction between baseline and last follow-up visit after lamellar keratoscleroplasty in children with lamellar keratoscleroplasty.

Materials and methods

Patients

A retrospective record review was performed for 66 patients who were pathologically proven limbal dermoids and underwent lamellar keratoscleroplasty with partial-thickness anterior corneoscleral button between January 2011 and January 2019 at Eye, Ear, Nose & Throat Hospital of Fudan University in Shanghai. All patients were regularly followed up and received ongoing amblyopia treatment duration with all sutures removed. Treatment of amblyopia included spectacles correction and occlusion therapy. The data were collected, including patients' gender, age, lesion size, lesion encroachment on the central and paracentral cornea, lesion depth, surgical age, follow-up period, amblyopia treatment duration, suture-related complications, graft rejection and steroid-induced high intraocular pressure [IOP > 21 mmHg], preoperative and postoperative mean keratometry [$1/2(K1 + K2)$], preoperative and postoperative spherical equivalent, preoperative and postoperative astigmatism. Suture-related complications following lamellar keratoplasty were recorded, including epithelial erosions, sterile infiltrates, suture abscesses, suture-tract vascularisation and suture loosening or breakage [9–11]. Patients who had the unsuccessful surgical outcomes and fewer than 1 year of postoperative follow-up were excluded. The study received the approval of the ethical committee of Eye, Ear, Nose & Throat Hospital of Fudan University in Shanghai, and was conducted according to the tenets of the 1964 Declaration of Helsinki. Informed consent for inclusion was waived because of the retrospective nature of the study.

Surgical procedure

All of the surgeries were performed by one surgeon (JX). The conjunctiva was cut open around the lesion to fully expose to the lesion. The lesion was then cut using the smallest size trephine that encompassed the entire lesion

and dissected in a lamellar fashion until the clear cornea was reached. The corneal graft was trephined from the anterior corneoscleral button, with the same size as the size of corneoscleral bed. The graft was secured with 10–0 nylon interrupted sutures onto the corneal side. The conjunctiva was anchored to the limbus with 10–0 nylon. All patients received topical corticosteroids and antibiotics after surgery. Suture removal was performed after surgery ~3 months or earlier for any suture-related problems such as loosening or suture-tract vascularisation.

Outcome measurement

Refractive error was measured by cycloplegic retinoscopy and keratometry was performed with a Nidek handheld keratometer (HandyRef-K; Nidek, Japan). The postoperative refractive data were collected and analysed after suture removal. The depth of lesion involvement (OCT; Tomey, Japan) was recorded. We used the partition method presented by Maseedupally et al. [12], dividing cornea into a central circular zone of 5 mm in diameter and paracentral annular zone ranging between 5 and 8 mm in diameter (based on corneal topography data). Whether the lesion encroached on the central and paracentral cornea was assessed by topographic pattern (Topographic Modeling System; Tomey, Japan). For the cosmetic outcome, graft opacity was graded clinically on a 0–4+ scale [13] (0 = completely clear; 1+ = minimal haze seen with difficulty under direct illumination; 2+ = mild haze seen easily; 3+ = moderately dense opacity partially obscuring iris details; 4+ = dense opacity completely obscuring all details of intraocular structure).

Statistical analysis

Data were analysed using SPSS statistical software version 22 (IBM Corp, New York, USA). The mean and standard deviation, range, frequency and percentage were used to express data. We defined the postoperative refractive value minus the preoperative refractive value as the change value. The negative change value represented the postoperative decrease, it meant that the surgery had a corrective effect on the preoperative refraction; the positive change value represented the postoperative increase, it meant that the surgery could aggravate the preoperative refractive parameters instead. The lower the value of changes, the more satisfied the effects on the correction of preoperative refraction. Wilcoxon signed-rank test was used when we compare the preoperative refractive parameters to long-term refractive outcomes. Spearman's rank correlation analysis was used to initially analyse the influence of preoperative parameters (surgical age, lesion size, lesion encroachment on the central and paracentral cornea, lesion depth, changes in

postoperative mean keratometry) and postoperative-related factors (amblyopia treatment duration, suture-related complications, graft rejection and steroid-induced high IOP) on the refractive outcomes (changes in spherical equivalent, changes in astigmatism). Candidate variables ($P < 0.05$) tested by Spearman's rank correlation analysis were included in multiple stepwise regression analysis. The significance levels were corrected using the Bonferroni method for multiple comparisons. A P value < 0.05 was considered to be significant. All reported P values are two sided.

Results

Baseline characteristics and clinical outcomes

A total of 66 patients with at least 1-year postoperative follow-up were included for analysis. The baseline characteristics are presented in Table 1. Suture-related complications in the five patients included suture abscesses ($n = 1$, 1.5%), suture-tract vascularisation ($n = 1$, 1.5%) and premature loosening ($n = 3$, 4.5%). Steroid-induced high IOP was identified in 12 patients (18.2%) and graft rejection occurred in 4 patients (6.1%). All surgical complications were controlled medically and treated successfully. The majority of patients had an overall improvement in cosmetic appearance. Eighteen patients (27.3%) had grade 0 graft opacity. Forty-four patients (66.7%) had grade 1+ graft opacity, including three patients with loose suture and two patients with mild rejection episodes. Slight interface vascularisation and grade 2+ graft opacity are present in the one patient with suture-tract vascularisation and two patients with rejection. Only one patient with suture abscesses had grade 3+ graft opacity after medical therapy with surgical debridement. The mean preoperative spherical equivalent was $+2.10 \pm 1.49$ D, while the mean postoperative value was $+1.54 \pm 1.49$ D. Spherical equivalent decreased by 0.56 ± 0.88 D ($P < 0.001$). The mean astigmatism before and after surgery was 2.93 ± 1.46 D and 2.92 ± 1.92 D, respectively. There was no significant change in astigmatism (the mean change, -0.02 ± 1.01 D; $P = 0.983$). The mean preoperative axis of astigmatism was $103.8 \pm 55.2^\circ$, and the mean postoperative value was $106.7 \pm 54.0^\circ$. The mean change in the axis of astigmatism after surgery was $2.9 \pm 5.4^\circ$ ($P = 0.641$). The mean keratometry before surgery was 42.14 ± 1.40 D, while the postoperative value was 41.89 ± 1.29 D. The mean keratometry decreased by 0.26 ± 0.40 D ($P < 0.001$).

Spearman's rank correlation analysis

Spearman's rank correlation analysis revealed that long-term changes in spherical equivalent between baseline and last

Table 1 Baseline characteristics of 66 children with limbal dermoids.

Variable	Mean \pm standard deviation	Range/%
Sex		
Male, n	37	56.1%
Female, n	29	43.9%
Age (year), mean	7.5 ± 2.8	3.1–12.5
Surgical age (year), mean	3.5 ± 2.1	1.2–10.2
Amblyopia treatment duration (month), mean	34.5 ± 22.8	3.6–84.6
Lesion size (mm), mean	5.54 ± 0.73	4.30–7.20
Lesion encroachment		
Presence, n	30	45.4%
Absence, n	36	54.6%
Lesion depth (um), mean	373.39 ± 70.13	227–500
SE (D), mean	$+2.10 \pm 1.49$ D	−0.88 to +5.38
Astigmatism (D), mean	2.93 ± 1.46	0.25–5.75
Axis of astigmatism (degrees), mean	103.8 ± 55.2	14–180
Mean keratometry (D), mean	42.14 ± 1.40	39.01–46.93

D dioptre, *SE* spherical equivalent.

follow-up visit had a significant association with amblyopia treatment duration ($r = -0.772$, $P < 0.001$). Long-term changes in astigmatism were significantly associated with lesion size ($r = 0.268$, $P = 0.029$), lesion encroachment on the central and paracentral cornea ($r = 0.317$, $P = 0.010$), suture-related complications ($r = 0.258$, $P = 0.037$), graft rejection ($r = 0.400$, $P = 0.001$) and amblyopia treatment duration ($r = 0.277$, $P = 0.025$).

Multiple stepwise regression analysis

In multiple stepwise regression analysis, the only independent factor predicting long-term changes in spherical equivalent between baseline and last follow-up visit was amblyopia treatment duration ($\beta = -0.030$, $P < 0.001$). The correlation between long-term changes in spherical equivalent and amblyopia treatment duration was high, with an R^2 for the model fit of 0.607, indicating robust predictive value. Figure 1 shows the regression between amblyopia treatment duration and changes in spherical equivalent. Having longer amblyopia treatment duration was associated with the lower change value, presenting the postoperative decrease in spherical equivalent. The same analysis showed that lesion encroachment on the central and paracentral cornea ($\beta = 0.502$, $P = 0.024$), suture-related complications ($\beta = 1.571$, $P < 0.001$) and graft rejection ($\beta = 0.983$, $P = 0.035$) significantly influenced long-term changes in astigmatism. Lesion encroachment on the central and paracentral cornea, suture-related complications and graft rejection was associated with the higher change value,

presenting the postoperative increase in astigmatism. In addition, long-term changes in refractive outcomes were not correlated with surgical age, lesion size, lesion depth, steroid-induced high IOP and changes in mean keratometry. The results of this analysis are shown in Table 2.

Discussion

Astigmatism, refractive amblyopia and poor vision caused by limbal dermoids were regarded as not only indications for surgical intervention, but also remaining problems after operation [8]. We found that all cases had hyperopia and astigmatism after surgery, roughly the same as preoperative

refractive status. The overall refractive outcomes after lamellar keratoscleroplasty in children with limbal dermoids were also reported by previous studies [6, 14], while the residual and surgically induced spherical equivalent for individual patients during the long-term follow-up were associated with multiple factors, which were analysed in our study. Factors that may influence the corneal refractive error after keratoplasty included donor-recipient disparity and suture tension [15, 16]. In the current study, the same donor-recipient disparity and surgical technique were applied in all cases by one surgeon; thus, the possible influence of these two surgical variables was not included in our analysis.

Our study found the statistically significant changes ($P < 0.001$) in both postoperative spherical equivalent refractive error and keratometry from preoperative value, with the reductions that were clinically not significant (0.56 ± 0.95 D in mean SE, 0.26 ± 0.40 D in mean keratometry). Besides, our results showed no marked improvement in astigmatism. Cylinder power ($P = 0.983$) and the axis of astigmatism ($P = 0.641$) at the last follow-up visit were not significantly changed compared with preoperative value. In general, no significant differences were observed in refraction between baseline parameters and postoperative outcomes in our series. These findings may support previous reports concluding that limbal dermoid-induced astigmatism and hyperopic spherical equivalent cannot be corrected by surgery, probably due to alteration or moulding of the intrinsic structure of the corneoscleral wall when lesions formed [7, 13, 17]. However, we still believe multiple factors besides surgery may also have affected the final refractive outcomes.

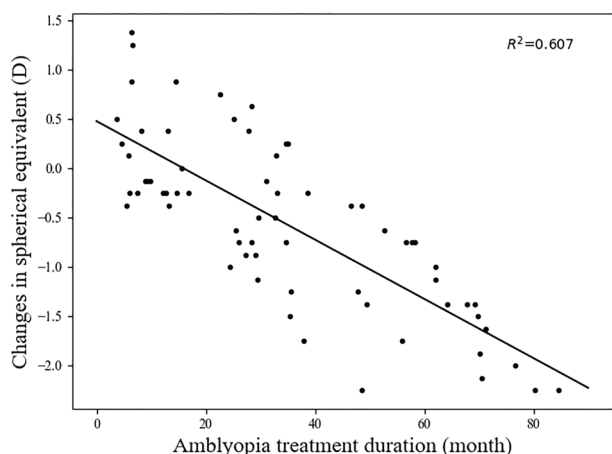


Fig. 1 Regression between amblyopia treatment duration and changes in spherical equivalent. Having longer amblyopia treatment duration was associated with the lower change value ($P < 0.001$).

Table 2 Spearman’s rank correlation analysis and multiple stepwise regression analysis to determine the factors predicting long-term changes in refraction after lamellar keratoscleroplasty in children with limbal dermoids.

Variables	Changes in spherical equivalent				Changes in astigmatism			
	Spearman’s rank correlation analysis		Multiple stepwise regression analysis		Spearman’s rank correlation analysis		Multiple stepwise regression analysis	
	<i>r</i>	<i>P</i> value	β	<i>P</i> value	<i>r</i>	<i>P</i> value	β	<i>P</i> value
Surgical age	-0.128	0.306	Not included	NA	-0.214	0.085	Not included	NA
Lesion size	-0.131	0.295	Not included	NA	0.268	0.029	Not included	NA
Lesion encroachment	0.035	0.779	Not included	NA	0.317	0.010	0.502	0.024
Lesion depth	0.036	0.772	Not included	NA	-0.094	0.455	Not included	NA
Changes in mean K	-0.174	0.163	Not included	NA	-0.132	0.291	Not included	NA
Graft rejection	0.045	0.719	Not included	NA	0.258	0.037	0.983	0.035
Suture-related complications	-0.137	0.273	Not included	NA	0.400	0.001	1.571	<0.001
Steroid-induced high IOP	0.039	0.754	Not included	NA	-0.044	0.723	Not included	NA
Amblyopia treatment duration	-0.772	<0.001	-0.030	<0.001	0.277	0.025	Not included	NA

r = Spearman’s rank correlation coefficient, β = regression coefficient.

NA not associated, *K* keratometry, *IOP* intraocular pressure.

Ametropic or anisometric amblyopia caused by astigmatism and hyperopic spherical equivalent in eyes with limbal dermoid usually persists after surgery, which should be corrected with the standard treatment with spectacle correction and occlusion therapy [7, 14, 18]. In this study, we found that the only independent factor predicting long-term changes in spherical equivalent was amblyopia treatment duration. It suggested that adequate amblyopia treatment was associated with decreased hyperopic spherical equivalent of lesion eye in the long-term follow-up. Previous researchers found that spectacle correction can lead to a relatively small decrease in hyperopia [19, 20]. Animal models revealed that spectacle lenses can compensate refractive changes in the hyperopic direction by affecting eye growth, which provided a possible mechanism responsible for refractive correction [21, 22]. Also, it has been reported that spectacle correction can lead to longitudinal changes in cylinder power [23]. However, no correlation between amblyopia treatment and changes in spherical equivalent was observed in our series. The effect of spectacle prescription and occlusion therapy on refractive changes and visual improvements needs further investigation, focusing on children with limbal dermoids.

In addition, multiple regression analysis suggested that lesion encroachment on the central and paracentral cornea, rather than lesion size or lesion depth, was significantly and independently associated with long-term changes in astigmatism. On the one hand, this finding supported that of Yamashita et al. [7], in which postoperative astigmatism was not influenced by the size of the graft; on the other hand, it offered new insight into the effect of lesion characteristics on postoperative refraction. It indicated that dermoids location relative to the critical optical zone had a greater effect on postoperative astigmatism than its size and depth. Some previous studies have concluded that in order to address the amblyopia and acquire better visual acuity, surgery at an early age is preferred [12, 18, 24, 25]. In our study, we did not find any significant association between surgical age and changes in refractive error during the long-term follow-up visit.

Other factors predicting changes in astigmatism were postoperative complications including suture-related complications and graft rejection, which were significantly associated with the postoperative increase in cylinder power. It could be assumed that stitch-associated abscesses, suture-tract vascularisation and corneal vascularisation related to graft rejection will act like the external compressive force, which would flatten the topical cornea and hence exacerbate astigmatism. High IOP may induce corneal oedema, which can affect cylinder power in the short term. While this study failed to demonstrate any significant correlation between steroid-induced high IOP and changes

in astigmatism. In this series, we found that suture-related complications in five patients were premature loosening, suture abscesses and suture-tract vascularisation. Previous studies have suggested that corneal deturgescence, wound remodelling, scar contraction and biodegradation caused by enzymatic factors and ultra-violet light exposure of the suture occurred during wound healing. As wound healing proceeds, these conditions caused the suture to loosen, become exposed and serve as a nidus for infection [11, 26, 27]. Children's stronger wound healing can make it easier for them to have premature suture loosening. Lack of regular monitoring, patient education and compliance may lead to prolonged retention of loose sutures and secondary infection, leading to suture-related complications founded in our study. In addition, we reported four cases of rejection (6.1%) in children after lamellar keratoscleroplasty, which exhibited a relatively high rejection rate compared with other investigations [13, 28]. Graft rejection in our series may be attributed to a lack of medication compliance with a relatively topical corticosteroid dosing regimen and a more active immune response in younger patients. Although graft rejection and suture-related complications in our study were reversed medically, marked postoperative increase in astigmatism inevitably occurred. Therefore, continuing patient education should be given to enhance adequate awareness of complications and improve medication compliance. Furthermore, a novel tissue called gamma-irradiated sterile cornea has been provided for use in lamellar keratoscleroplasty [29]. Gamma irradiation kills antigen-presenting cells of donor tissue, thereby reducing the risk of rejection by preventing the direct pathway of allosensitization [30]. Besides, multiple studies have also demonstrated its availability, easy handling, sterility advantage and improved cosmetic outcome [31–34]. These suggested that gamma-irradiated sterile corneal lenticules may be a suitable alternative to fresh tissue in order to reduce the stromal rejection in children with limbal dermoids.

In conclusion, our study identified factors that independently and significantly influence long-term changes in refraction after lamellar keratoscleroplasty in paediatric patients with limbal dermoids. These factors included lesion encroachment on the central and paracentral cornea, suture-related complications, graft rejection and amblyopia treatment duration. When planning for lamellar keratoscleroplasty in children with limbal dermoids, surgeons should take into account the higher tendency toward astigmatism among patients with lesion encroachment on the central and paracentral cornea. Careful observation and proper management of suture-related complications and graft rejection may avoid the postoperative increase in astigmatism. Although adequate amblyopia treatment after surgery appeared to decrease both residual and surgically induced

spherical equivalent in the long term, its effect on correcting postoperative astigmatism was disappointing.

Summary

What was known before

- Astigmatism and refractive amblyopia caused by limbal dermoids are regarded as not only indications for surgical intervention, but also remaining problems after operation.
- The overall refractive outcomes after lamellar keratoscleroplasty in children with limbal dermoids have been reported, while factors associated with the residual and surgically induced spherical equivalent in the long term remain unclear.

What this study adds

- Our study identified factors that independently and significantly influence long-term changes in refraction after lamellar keratoscleroplasty in paediatric patients with limbal dermoids.
- Suture-related complications and graft rejection should be carefully observed and appropriately treated in order to avoid the significant postoperative increase in astigmatism, especially for patients with lesion encroachment on the central and paracentral cornea.
- The long-duration amblyopia treatment after surgery appeared to decrease both residual and surgically induced spherical equivalent in the long term, while its effect on correcting postoperative astigmatism was disappointing.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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