Selective Endothelialectomy in Peters Anomaly: A Novel Surgical Technique and Its Clinical Outcomes in Children

Muralidhar Ramappa, MBBS, MS,*†‡ Sunita Chaurasia, MBBS, MS,*†‡
Ashik Mohamed, MBBS, MTech, PhD, MAMS,*§ Divya Sree Ramya Achanta, BS,*†‡
Anil Kumar Mandal, MBBS, MD, DNB, FAMS,¶ Deepak Paul Edward, MD, FACS, FARVO,||
Nikhil Gokhale, MBBS, MD, DNB,** Rishi Swarup, MBBS, DOMS, FRCS, †† and
Ken K. Nischal, MD, FAAP, FRCOphth†‡§§

Purpose: This study describes the surgical outcomes of selective endothelialectomy in Peters anomaly (SEPA), a relatively new technique to manage Peters anomaly (PA).

Methods: This study included 34 eyes of 28 children who had a visually significant posterior corneal defect due to PA and underwent SEPA between 2012 and 2019. A selective endothelialectomy from the posterior corneal defect was performed while preserving Descemet membrane. The primary outcome measure was the resolution of corneal opacification. The secondary outcome measures were functional vision, complications, and risk factors for failure.

Results: At a mean postoperative follow-up of 0.96 ± 0.20 years, 29 eyes (85.3%) maintained a successful outcome. Mean preoperative and postoperative best-corrected visual acuities were 2.55 ± 0.13 and 1.78 ± 0.13 (P < 0.0001), respectively. Ambulatory functional visual improvement was seen in 97%, and 23% attained vision ranging between 20/190 and 20/50. Corneal opacification failed to clear in 5 eyes (15%). Risk factors associated with surgical failure were female sex (P = 0.006), disease severity (P < 0.0001), glaucoma (P = 0.001), and additional interventions after SEPA (P = 0.002). In multivariate analysis, only disease severity (ie, a type 2 PA) was a significant risk factor for the failure of SEPA. There were no sight-threatening complications.

Conclusions: SEPA is a safe and effective technique in select cases of posterior corneal defect due to PA. SEPA could be a potential surgical alternative to pediatric keratoplasty or optical iridectomy in children with central corneal opacification smaller than 7 mm due to PA.

Key Words: corneal scar, optical iridectomy, Peters anomaly, resolution, selective endothelialectomy

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Peters anomaly (PA) is the most common indication for penetrating keratoplasty (PK) among congenital corneal opacities.1 PA is a developmental abnormality in which the corneal defect is mostly limited to the cornea’s posterior layers and, if untreated, can result in sensory deprivation amblyopia.1 A step ladder clinical categorization based on clinical signs includes type 1 disease depicted by a central corneal opacity with peripheral iridocorneal adhesions extending from the iris collarette to the perimeter of the corneal opacity (Fig. 1A) and type 2 disease featuring keratolenticular adhesions, which may result in a rudimentary, fragmented, or partially resorbed lens (Fig. 1B).2–4 In Peters plus anomaly, bilateral peninsular-like corneal opacification in the posterior stroma and corresponding defects in Descemet membrane (DM) endothelium complex are noticed besides typical systemic features.5–7 Bilateral disease is seen in 80% of PA,5 and type 2 disease is more often associated with poor visual outcomes than type 1 disease.2,5,8–14 Anterior segment optical coherence tomography (AS-OCT) observation has shown a double-layered DM in PA,15 explaining a reason for spontaneous closure of these defects. Histopathology of PA shows focal abnormal posterior corneal stromal architecture with focal absence of DM (Fig. 1D) and markedly attenuated endothelium with uveal pigment deposits around the defect’s edges.16,17
In the past two decades, the understanding of corneal endothelial cell biology and endothelial transplantation techniques has evolved considerably. For instance, when the peripheral endothelium is healthy, corneal endothelial defects heal rapidly after an injury or insult. However, in PA, the corneal endothelium at the edges and under the defect is abnormal and might inhibit centripetal expansion and normal healing. The absence of central corneal endothelium results in persistent corneal edema and opacification.18 Recent literature supports the idea that the peripheral corneal endothelium is capable of self-renewing after a descemetorhexis in Fuchs endothelial dystrophy.19 Management options in PA include a conservative approach in mild central corneal opacification, with mydriatics and occlusion therapy.20 PA with more extensive central opacities can be surgically managed with a variable success rate. Optical iridectomies,20 rotational keratoplasty,21 conventional full-thickness keratoplasty,2,8,9,11,12,22 and primary keratoprosthesis are the various surgical options used in severe cases.

Visually significant PA treated with PK is highly variable with suboptimal long-term outcomes. Graft failure rates have been reported to be 50% to 100% at 10 years,2 and there is a high incidence of postoperative complications such as allograft rejection, suture-related issues, wound dehiscence, and secondary glaucoma that further compromise the long-term outcomes.2,8,11 Therefore, the surgeon’s preference rather than scientific evidence usually determined the technique to be adopted.

Having performed more than 200 full-thickness corneal transplantations in PA with variable results (unpublished), we chose to adopt selective endothelialiectomy in Peters anomaly (SEPA), a novel technique for treating corneal opacification in PA in the year 2012. This technique showed that the selective removal of abnormal corneal endothelial cells underlying the posterior defect could reverse corneal edema and promote corneal scar remodeling, eliminating the need for full-thickness keratoplasty. Our initial unplanned experience of spontaneous regression of corneal opacification in keratolenticular dysgenesis after lens removal with endothelial scraping had prompted us to critically review our previous cases that had undergone synechiolysis with endothelialiectomy. In addition, we found an anomalous layer over the PA consistently, which was corroborated on AS-OCT (Fig. 1C) and histopathology (Fig. 1D–F). Furthermore, 2 independent studies have published successful outcomes by selective endothelial removal and descemetorhexis.23,24 However, the results needed validation in a large sample with a longer follow-up for broader acceptance of this new technique. Therefore, we report the surgical outcomes of the novel technique SEPA in a large cohort of children with PA.

**MATERIALS AND METHODS**

This was a retrospective, nonconsecutive, interventional clinical case series. A total of 34 eyes of 28 children with nonresolving corneal edema that underwent SEPA at L V Prasad Eye Institute, Hyderabad, India, between 2012 and
2019 were included. The affected eyes of children with PA were evaluated for size and density of the posterior corneal opacity, improvement in visual functions, and AS-OCT of the posterior corneal defect performed before and after surgery in cooperative children. The Institutional Ethics Committee of L V Prasad Eye Institute, Hyderabad, India, approved this study. This study was conducted in strict adherence to the tenets of the Declaration of Helsinki. All legal guardians of children who underwent SEPA and additional interventions (optical iridectomy or endocapsular lens aspiration (LA) with limited anterior vitrectomy) gave written informed consent for all procedures described in this study.

Grading of Disease Severity

We classified the disease severity and zonal involvement as previously defined by Yang et al. Clinically, PA is classified based on a constellation of clinical signs. Mild disease was characterized by the presence of a normal iris and lens. Moderate disease was defined by the presence of focal iridocorneal adhesions (anterior synechiae) or other iris defects such as atrophy, abnormal vasculature, or coloboma. Severe disease was defined by the presence of corneolenticular adhesions or corneal staphyloma with or without corneolenticular adhesion.

Zone of Corneal Opacity

The location and extent of the opacity were ascertained based on digital photographs, surgical videos, drawings, and other descriptive information in the medical records. The location of the opacity was described in 3 zones centered on the geographic center of the cornea. Zone 1 (central cornea) was circular with a diameter of 5 mm. Zone 2 (peripheral cornea) extended from zone 1 up to the limbus. Zone 3 (limbal zone) comprised the limbus. The zone of involvement was defined by the most peripheral location of the opacity. Zone 3 involvement was subdivided into subtotal (zone 3A) or total (zone 3B) based on limbal opacification.

Designation of Laterality

The eyes of patients with visually significant corneal opacity involving both eyes were designated as having significant bilateral disease. The eyes of patients with unilateral disease or asymmetrical bilateral disease in which the corneal opacity in the lesser affected eye was minimal, extraaxial, and visually insignificant were designated as having unilateral disease.

All children who underwent SEPA met the following inclusion criteria: Children with type 1 or 2 PA with a posterior corneal defect limited to zone 3A and affecting visual function and precluding retinoscopy or fundus view under undilated circumstances were considered for SEPA. The eyes excluded were those with panocular involvement, zone 3B corneal opacity, anterior staphyloma, secondary glaucoma, microphthalmia, persistent fetal vasculature, aniridia, and those unwilling to undergo a conservative surgical intervention.

Preoperative vision testing, corneal pachymetry, and AS-OCT were performed in all cooperative children. Parents consented with emphasis that this was a conservative surgical intervention that did not need a long-term stringent follow-up and medications and that there was no risk of graft failure. All parents understood that this innovative surgical intervention might have a modest outcome, and definitive intervention such as full-thickness corneal grafting might be necessary in the future. Alternative options including optical iridectomy, rotational autograft, and additional lens removal with concurrent or subsequent PK were discussed with the parents.

Surgical Technique of SEPA

The surgeries were performed under hypotensive anesthesia by experienced corneal surgeons (MR and SC). The anterior chamber was filled with sterile air, and this carefully delineated the actual extent of corneal opacification, any iris strands, and any lens opacity. Trypan blue (Aurovisc, Auro Laboratories Inc, Madurai, India) was used to delineate the extent of corneal opacification and DM reduplication. Using a bimanual irrigation aspiration cannula, the unhealthy corneal endothelium from the opacity’s undersurface and at edges was gently scraped off up to 1 mm into normal cornea without disturbing DM’s integrity. At the end of the intervention, trypan blue remaining along with a chandelier light pipe was used to identify any focal DM tears or detachment (Video 1, http://links.lww.com/ICO/B441).

Additional Interventions

Lysis of visible iris strands was performed when noted to arise from the iris collarette and extend to the perimeter of corneal opacity. Selective endothelialectomy in Peters anomaly with optical iridectomy (SEPAO): Optical iridectomy or sphincterotomy was performed where the corneal opacity was >6 mm or seen obscuring the retinal red reflex without dilation. Optical iridectomy (size of at least 3 clock hours) was performed using a vitrector and aimed to achieve a decent red reflex intraoperatively. Selective endothelialectomy in Peters anomaly with lenectomy (SEPAL): LA along with primary posterior capsulotomy and a limited anterior vitrectomy was performed when the lens was adherent to the posterior corneal surface. All incisional sites were closed using 10-0 nylon sutures. After the procedure, a drop of topical moxifloxacin 0.5% eye drops (Alcon Labs, Fort Worth, TX), prednisolone acetate 1% eye drops (Alcon Labs, Fort Worth, TX), and atropine sulfate 1% eye drops (Aurolab, Madurai, India) were instilled.

Postoperative and Follow-Up Schedule

Postoperatively, all children underwent comprehensive ophthalmic examinations at every follow-up visit either in the outpatient department using the slitlamp when cooperative or in the operating room using a handheld slitlamp under short general anesthesia. The examination included assessing corneal clarity, DM status, lens status, and intraocular pressure (IOP). Visual acuity assessment and refraction were
performed when possible. The side ports’ sutures were removed 3 to 4 weeks after the surgery. In the postoperative period, the child was maintained on topical moxifloxacin 0.5% eye drops 4 times a day until side ports’ sutures were removed. Prednisolone acetate 1% drops 6 times a day were followed by tapering doses of topical steroids over the next 6 weeks. The children were followed up 1, 4, 12, 24, and 52 weeks after the intervention and after that yearly. At each visit, examination under anesthesia was performed for younger children when necessary. If IOP was elevated, topical and, if needed, systemic glaucoma medications were used. Glaucoma filtering surgery was reserved for eyes where IOP was found to be unacceptable on maximal tolerated medical therapy. Retinoscopy was performed at every follow-up visit, either in the outpatient or under anesthesia. Spectacles were prescribed between 1 and 2 weeks after surgery or as soon as corneal clarity allowed a reliable retinoscopy reading. Amblyopia was managed using occlusive therapy, and optical correction with glasses or contact lenses or both was aggressively pursued under the attending surgeon’s direction or pediatric ophthalmologist. Intraoperative or postoperative complications were reviewed for all patients. During the first year after surgery, parents were contacted by telephone if they missed a scheduled visit and the next earliest appointment was arranged for them. This was performed proactively to ensure that all patients completed at least 1 year of follow-up.

**Optical Coherence Tomography Scan (AS-OCT)**

AS-OCT imaging was performed before the intervention either using handheld spectral domain optical coherence tomography (Bioptigen, Inc, Research Triangle Park, NC) under general anesthesia or preoperatively using RTVue-100 Fourier domain optical coherence tomography (Optovue, Fremont, CA) OCT in the office setting in cooperative children. The evaluated parameters included the zone of the extent of corneal opacity, iridocorneal or corneolenticular adhesions, and anterior chamber depth.

**Data Collection**

Data collected included patient age, sex, laterality, detailed pedigree, details of prior eye surgeries if any, duration of corneal opacification, preoperative visual acuity and IOP, intraoperative surgical details, postoperative complications, length of follow-up, and status of DM, IOP, and optic nerve head health at each visit. Visual acuity was measured using age-appropriate grating acuity in infants and Teller Acuity Cards in young children or linear Sloan letters in older children. Blink or grimace to light was defined as light perception. Centered/steady/maintain or fix and follow were defined as hand motion. Visual acuity values were converted to the logarithm of the minimum angle of resolution (logMAR) equivalence. The significant postoperative primary outcome measures included corneal clarity (cleared, partly cleared, and not cleared). The secondary outcome measures included best-corrected visual acuity (BCVA). The impact of laterality, preoperative age at surgery, size of opacity, additional intervention, and postoperative factors on the clinical resolution of corneal opacification was analyzed.

**Outcome Measures of Efficacy**

The primary outcome measure was the clinically significant resolution of corneal opacification after SEPA. Successful resolution of corneal opacification was defined as a partial to near-total stromal clearing without epithelial or stromal edema allowing a clear view of iris features, retinoscopy, and fundus evaluation (Figs. 2A–L and 3A–F). Successful SEPA was also described as a reduction in corneal opacification’s size and density at the last follow-up without a later surgical procedure. Failure was defined as posterior corneal opacification failing to show clinical resolution even after 3 months after SEPA (Fig. 3D–F), precluding the visibility of iris details, retinoscopy, or retinal examination and a need for additional intervention for visual rehabilitation. The secondary outcome measure of efficacy was the improvement change in BCVA at each postoperative follow-up visit.

Cases were categorized based on a clinical resolution of corneal edema and scar remodeling: cleared, partly cleared, and not cleared. Cleared was considered when there was a complete resolution of corneal edema with a discernible scar remodeling by 3 months that allowed a decent retinoscopy reading in undilated condition (Figs. 2A–L and 3A–C). Not cleared had no change in corneal opacity’s density and size and where refraction was possible only after complete dilation or through the optical iridectomy opening and was classified as nonresponders (Fig. 3D–F). Partly cleared had a significant clearing but needed pupillary dilation for a decent retinoscopy reading by postoperative month 3 visit (Fig. 3E).

**Validation of Diagnosis and Outcome by Independent Masked Evaluators**

Five proficient ophthalmologists (2 glaucoma specialists, a pediatric cornea specialist, and 2 cornea surgeons) volunteered as evaluators to validate the investigators’ assessment of the type of PA and the outcome of surgical intervention in every case. The evaluators were provided preoperative and postoperative photographs of patients, and they were asked to evaluate the photographs based on the following objective criteria: visual acuity, grading of disease severity, zone of corneal opacity, designation of laterality, and outcome measures of efficacy. The evaluators were masked to the patient’s identity and the type of surgical intervention performed. In cases where there was disagreement between the evaluators or surgeons, an independent evaluators’ consensus opinion was taken as the final diagnosis or treatment outcome.

**Statistical Analysis**

The statistical analysis was performed using STATA v14.2 (Stata Corp, College Station, TX). The distribution of
Continuous data was tested for normality using the Shapiro–Wilk test. Continuous, normally distributed variables were represented as mean ± standard deviation. Median and interquartile range were used to describe continuous nonparametric data. Categorical data were expressed in proportions. A mixed-effects model with a random intercept at the subject level was used to account for the correlation between the fellow eyes of the same patients in the comparison of data between visits and in the analysis of risk factors for failure. In addition, the outcome data were compared among the types of surgical intervention: SEPA alone with/without synechiolysis, SEPAO, and SEPAL. A \( P \) value of <0.05 was considered statistically significant.

RESULTS

During the study period (2012–2019), a total of 34 eyes of 28 children diagnosed with posterior corneal opacity due to PA underwent SEPA with or without additional procedures (optical iridectomy or endocapsular LA with limited anterior vitrectomy), as summarized in Supplementary Digital Content 1, http://links.lww.com/ICO/B438. Seventeen children (60.7%) were male. Parental consanguinity was noted in 6 of 19 children (31.6%). Nineteen eyes of 13 children with a visually significant bilateral disease accounted for 55.9% of the study cohort, while 15 eyes of 15 children (44.1%) had unilateral involvement.

Table 1 summarizes the baseline demographics by the type of procedure performed. Mean age at presentation, sex, laterality, consanguinity, zone of involvement of the opacity, and preoperative BCVA were comparable among the 3 interventions SEPA, SEPAO, and SEPAL. All eyes with type 2 PA underwent SEPAL.

The mean age at the time of SEPA was 2.06 ± 0.51 years. Twenty-four eyes (70.6%) were in children who were younger than 12 months at first intervention. The post-interventional mean follow-up period was 0.96 ± 0.20 years. Table 2 summarizes the outcomes by the type of procedure performed. SEPA was performed significantly earlier than SEPAO. SEPAO had a significantly shorter follow-up duration than SEPA and SEPAL. SEPAL with limited vitrectomy was performed in 9 eyes. In most of these eyes, the adherent lens was clear (2 eyes), rudimentary (3 eyes), cataractous (3 eyes), or partially resorbed (1 eye). Diligent care was taken to avoid inadvertent lens matter spillage into the vitreous cavity.

Efficacy of Selective Endothelialectomy Cleared

Of the 34 eyes, 11 eyes (32.4%) had significant clearing of the corneal opacification. These eyes maintained a clear optical axis with a gradual reduction in the density of corneal haze, which was evident 3 months postintervention, besides expansion of overall corneal diameter, and no further
reintervention was necessitated. The proportion of eyes with corneal clearing was comparable among the 3 intervention groups (Table 2).

Partly Cleared
Eighteen eyes (52.9%) had a discernible change in corneal clarity and an acceptable functional vision. Refraction was possible in these patients after pupillary dilation or through an iridectomy opening. In this subset postoperatively, we did not observe any glare or photophobia. The proportion of eyes with partly cleared cornea was also comparable among the 3 intervention groups (Table 2).

Not Cleared
In our surgical cohort, 5 eyes (14.7%) failed to show any discernible resolution in corneal opacification. All these eyes had severe disease involving zone 3A and had undergone SEPAL. In patients (21 and 22) with severe bilateral disease affecting zone 3A, it was found 3 months after the first surgery that the clear optical zone was small, and therefore, optical iridectomy did not give an adequate red reflex. In this patient, the children’s parents did not consent for keratoplasty given severe hydronephrosis, but after a repeat large sectoral iridectomy, child had regained decent ambulatory vision. There was a trend toward improved corneal transparency with longer follow-up.

Postoperative Visual Function
Among 34 eyes at presentation, only 1 (2.9%) eye had vision better than 20/190, 20 (58.8%) had an ambulatory vision, and 13 (38.2%) had nonambulatory vision. Post-intervention, 24 eyes (70.6%) had ambulatory vision, and 8 (23.5%) achieved a BCVA of 20/190 or better at the final follow-up. Suboptimal visual improvement was due to dense amblyopia and near-total corneal opacification. Case numbers 21 and 22, a patient with bilateral type 2 PA, had a 2-line improvement in visual acuity compared with baseline after a repeat large sectoral iridectomy. The mean spherical equivalent refraction at the final visit was 5.08 ± 1.18 D. The eyes undergoing SEPA and SEPAL had significant improvement in the visual acuity at the final visit when compared with preoperative. In SEPAO, BCVA seemed to improve, but it did not achieve statistical significance (Table 3).

Safety of SEPA in the Operated Eye
None of the eyes that received SEPA and its one of iterations had a DM detachment, persistent corneal edema, lens touch, or uveal trauma. The most common observation in the operated eye was corneal edema at the site of SEPA intervention. The corneal edema resolved spontaneously within 1 month postoperatively, as demonstrated on AS-FIGURE 3. Digital photographs showing the dynamics of stromal healing pattern chronologically after SEPAL in a child with type 2 PA. A, Right eye of a 7-year-old girl (patient 28) showing corneal opacity involving the zone 1 with keratolenticular adhesion. B, Day 30 postoperatively, after SEPAL with anterior vitrectomy showed marked improvement visual axis clarity. C, Last visit, 7.6 years postintervention, showed a significant decrease in opacity and vision improvement over time to 20/50. D–F, Captures a similar timeline of events in the left eye of the same child (patient 29) with a severe disease that necessitated SEPAL with an optical iridectomy. Corneal opacity did not regress postoperatively. Finally, the cornea decompensated after Ahmed glaucoma valve implantation.

| TABLE 1. Baseline Characteristics of SEPA, SEPAO, and SEPAL |
|-------------------|-------------------|-------------------|
| Variables         | SEPA              | SEPAO             | SEPAL              |
| Age at presentation (yr), mean ± standard error | 1.2 ± 0.4          | 1.0 ± 0.6          | 0.7 ± 0.5          |
| Sex, male:female  | 11:7              | 5:2               | 2:7                |
| Bilateral presentation, n (%) | 8 (44.4%)          | 4 (57.1%)          | 7 (77.8%)          |
| Consanguinity     | 2/11 (18%)        | 1/6 (16%)         | 4/6 (66%)          |
| Zone of opacity, n (%) | Zone 1 8 (44.4%)    | Zone 1 2 (28.6%) | Zone 1 2 (22.2%) |
| Zone 2            | 3 (16.7%)         | Zone 2 2 (28.6%)  | Zone 2 1 (11.1%)  |
| Zone 3            | 7 (38.9%)         | Zone 3 3 (42.8%)  | Zone 3 6 (66.7%)  |
| Severity (type 2 PA), n (%) | 0 (0%)            | 0 (0%)            | 8 (88.9%)          |

FIGURE 3. Digital photographs showing the dynamics of stromal healing pattern chronologically after SEPAL in a child with type 2 PA. A, Right eye of a 7-year-old girl (patient 28) showing corneal opacity involving the zone 1 with keratolenticular adhesion. B, Day 30 postoperatively, after SEPAL with anterior vitrectomy showed marked improvement visual axis clarity. C, Last visit, 7.6 years postintervention, showed a significant decrease in opacity and vision improvement over time to 20/50. D–F, Captures a similar timeline of events in the left eye of the same child (patient 29) with a severe disease that necessitated SEPAL with an optical iridectomy. Corneal opacity did not regress postoperatively. Finally, the cornea decompensated after Ahmed glaucoma valve implantation.
TABLE 2. Postoperative Outcomes After SEPA, SEPAO, and SEPAL

| Variables                  | SEPA 18 Eyes | SEPAO 7 Eyes | SEPAL 9 Eyes | P*          |
|----------------------------|--------------|--------------|--------------|-------------|
| Age at surgery (yr.), mean ± SE | 1.6 ± 0.6   | 2.0 ± 0.6   | 3.4 ± 1.1   | <0.0001†    |
| Follow-up duration (yr.), mean ± SE | 0.8 ± 0.2   | 0.5 ± 0.2   | 1.8 ± 0.4   | <0.0001‡    |
| Corneal clarity, n (%)       |              |              |              |             |
| Cleared                    | 7 (38.9%)    | 2 (28.6%)   | 2 (22.2%)   | 0.85§       |
| Partly cleared             | 11 (61.1%)   | 5 (71.4%)   | 2 (22.2%)   | 0.16§       |
| Not cleared                | 0 (0%)       | 0 (0%)      | 5 (55.6%)   | <0.0001§§   |

*A P value of <0.01 was considered statistically significant after applying Bonferroni correction for multiple comparisons.
†In post hoc analysis by multiple pairwise comparisons, only SEPA was significantly different from SEPAO (P < 0.0001) and not SEPA versus SEPAL (P = 0.14) nor SEPAO versus SEPAL (P = 0.23).
‡In post hoc analysis by multiple pairwise comparisons, SEPAO was significantly different from SEPA (P < 0.0001) and SEPAL (P = 0.003) and not SEPA versus SEPAL (P = 0.026).
§Adjusted for age at surgery.
¶In post hoc analysis by multiple pairwise comparisons, only SEPAL was significantly (P < 0.0001) different from SEPA and SEPAO and not SEPA versus SEPAO (P = 0.98).

OCT analysis (Fig. 4A–D). AS-OCT confirmation was available in 23% eyes (8). There were no sight-threatening complications documented. None of the eyes had a decline in visual function postoperatively.

Five eyes had persistent elevation of IOP after intervention despite excluding eyes with preoperative glaucoma. Four eyes had severe disease, and the other two had a mild-moderate disease. In patients 1 and 2, who had severe disease, but corneal involvement limited to zone 1, have shown a marked improvement in the corneal haze. Ahmed glaucoma valve implantation in the left eye was required to achieve adequate IOP control. Post-Ahmed glaucoma valve intervention, the cornea decompensated, and corneal grafting was deferred in view of dense amblyopia and contralateral aphakic eye that had a BCVA of 6/15 or better (0.40 logMAR) vision. The remaining cases were managed with topical antiglaucoma medications alone.

AS-OCT Analysis

AS-OCT images of preintervention and postintervention were available in 8 eyes (23%). Preoperative image analysis revealed that the Bowman membrane over the corneal defect appeared either disrupted or absent, while the rest of the anterior stromal architecture was comparatively preserved. Overlying the DM defect, the posterior stroma had a denser reflectivity with varying degrees of stromal thinning and excavation. The edges of defects were thickened and rolled out, and few cases showed a presence of anomalous pre-Descemet layer occupying the posterior concavity. There were numerous, delicate iris strands extending between the iris collarette and edges of the corneal defect in most cases. In an example, duplication of DM was observed (Fig. 1C). Type 1 PA (Fig. 4A) corneas that underwent SEPA showed the presence of corneal edema in the immediate postoperative period (Fig. 4B), and an intact DM was seen (Fig. 4C). In summary, AS-OCT analysis suggested a healing pattern after SEPA over the original site of posterior excavation (Fig. 4D).

Resolution of Opacity After SEPA

Table 4 presents associated risk factors for SEPA failure. Using bivariate analysis (P value <0.006), female sex (P = 0.006), disease severity (P < 0.0001), glaucoma (P = 0.001), and additional interventions after SEPA (P = 0.002) were significant risk factors for the failure of SEPA. In multivariate analysis, disease severity (ie, a type 2 PA) was a significant risk factor for the failure of SEPA.

Agreement Between Primary Surgeons and Independent Masked Evaluators

The overall agreement between masked evaluators and primary surgeons for the primary diagnosis and PA type was 100% (95% confidence interval (CI), 87.4%–100% see Supplementary Digital Content 2, http://links.lww.com/ICO/B439). The concordance ‘kappa’ measures between the primary surgeon and masked evaluators for the treatment outcome ranged from 0.51 to 0.61, suggesting they were fair to good.

DISCUSSION

Our study validates the outcomes of SEPA, a novel and less-invasive surgical strategy to treat corneal opacities in children with PA, and provides surgical outcomes in a large cohort. SEPA is based on the following assumptions in PA: 1) focal area of anomalous DM endothelial complex underlying posterior corneal defect, 2) perilesional healthy endothelium

TABLE 3. Preoperative and Postoperative Visual Functions After SEPA, SEPAO, and SEPAL

| Visual Acuity              | At Presentation | Last Visit | P*          |
|----------------------------|-----------------|------------|-------------|
| Number of Eyes (%)         | Number of Eyes (%)|            |             |
| Overall visual functions   |                 |            |             |
| n = 34                      |                 |            |             |
| Nonambulatory†             | 13 (38.2%)      | 2 (5.9%)   | <0.001      |
| Ambulatory‡                | 20 (58.8%)      | 24 (70.6%) | 0.27        |
| 20/190–20/50               | 2 (6.0%)        | 8 (23.5%)  | 0.004       |
| Overall: BCVA (logMAR), n = 34, mean ± SE | 2.55 ± 0.13 | 1.78 ± 0.13 | <0.001 |
| SEPA: BCVA (logMAR), n = 18, mean ± SE | 2.45 ± 0.17 | 1.70 ± 0.17 | <0.001 |
| SEPAO: BCVA (logMAR), n = 7, mean ± SE | 2.68 ± 0.18 | 2.28 ± 0.15 | 0.051      |
| SEPAL: BCVA (logMAR), n = 9, mean ± SE | 2.79 ± 0.19 | 1.71 ± 0.19 | <0.001 |

*Adjusted for age at surgery and follow-up duration, and a P value <0.007 was considered statistically significant after applying Bonferroni correction for multiple comparisons.
†Nonambulatory: hand motions, light motions, light perception or no light perception.
‡Ambulatory: 20/200 to 20/800, counting fingers, or fixes and follows.
has regenerative potential to fill in the denuded area, 3) robust scar remodeling in children, and 4) relatively well-preserved overlying anterior stromal architecture. The anomalous endothelium inhibits normal expansion of the surrounding peripheral corneal endothelium, leading to localized loss of endothelial pump function and corneal edema. Therefore, it is logical to believe that there could be an improvement if the abnormal endothelium is removed, resulting in defects being replaced with healthy perilesional corneal endothelium. More recently, the corneal endothelial wound models have demonstrated that after a localized corneal endothelial removal, neighboring cells will enlarge and migrate to restore the anatomic and functional integrity of the corneal endothelial monolayer. Based on these findings, we believe that SEPA, while preserving the DM, might promote spontaneous endothelial migration, thus simply accelerating the spontaneous resolution of corneal edema and opacification, consequently evading limitations of PK in children with PA.

Although PA is the most common indication of corneal transplantation among childhood corneal blindness, it is challenging to visually rehabilitate these children, considering the complexity of corneal and anterior segment involvement. Type 2 variant often requires sequential lens-based intervention followed by PK. Associated comorbidities necessitate further intervention that in turn compromises the long-term graft survival. PA type 1 cases typically fare better than PA type 2. The visual and functional prognoses in both groups of patients are modest. Furthermore, there are several intraoperative challenges and postoperative complications that limit the long-term prospects of PK. The alternatives to PK include pharmacological dilation, rotational corneal grafts, optical sector iridectomy, and spontaneous resolution, which have had different success rates.

In our series, the surgical approach in each case was governed by disease severity, associated comorbidities, child’s visual potential, parents’ expectations, and surgeon’s preference. Several studies give importance to the anatomic and surgical results, and a small subset focuses exclusively on long-term functional outcomes of PK in children with PA. Supplementary Digital Content 3, http://links.lww.com/ICO/B440, provides an overall comparison of this study's results with that of other large series consisting of different surgical interventions for PA.

### Table 4. Risk Factor Analysis for Failure of Simple Endothelialectomy in Peters Anomaly

| Variable                      | SEPA Success (n = 29) | SEPA Failure (n = 5) | P*   |
|-------------------------------|-----------------------|---------------------|------|
| Age at surgery (yr), mean ± standard error | 2.07 ± 0.52           | 2.07 ± 0.51         | 0.99 |
| Sex, male:female              | 18:11                 | 0:5                 | 0.004|
| Laterality, unilateral:bilateral | 15:14               | 0.5                 | 0.02 |
| Severity of PA: Type 1 versus type 2 | 26:3                  | 0.5                 | <0.0001|
| Zone of opacity: 1, 2, or 3A | 12:6:11               | 0:0:5               | 0.009|
| Glaucoma, n (%)               | 3 (10.7%)             | 3 (60%)             | 0.001|
| Microcornea, n (%)            | 1 (3.5%)              | 2 (40%)             | 0.63 |
| Additional intervention, n (%)| 3 (10.7%)             | 3 (60%)             | 0.002|

*A P value <0.006 was considered statistically significant after applying Bonferroni correction for multiple comparisons.*
In our surgical cohort, 29 eyes (85.3%; 95% CI, 68.2%–94.3%) that had undergone SEPA with or without additional intervention showed partial to near-total corneal clearing and discernible change posterior to stromal architectures indicative of endothelial cell healing pattern as observed using Fourier domain optical coherence tomography. In 5 eyes of 3 children where cornea failed to show the expected response by 3 months after SEPAL, a larger zone of involvement (Zone 3A) was seen in contrast to eyes that had a successful outcome (zones 1 and 2). A larger zonal involvement of 4 to 6 mm requires more than double the surface area for the remaining endothelium to repopulate (4π vs. 9π).19 By contrast, an 8 mm defect may require a repopulation of 4 times that of the area of a 4 mm of endothelial scraping.19 Therefore, the ideal case selection for this new technique is mild to moderate PA cases with smaller zonal involvement than 7 mm. Although most eyes with successful outcomes showed a marked reduction in corneal edema within 1 month of SEPA, the central corneal haze showed a gradual decline ranging from 6 to 18 months. This suggests that the eyes with denser opacity within the surgical cohort showed the considerable time for stromal clearing and scar remodeling. During this period, children must be monitored closely for amblyopia. If there is no significant improvement in corneal haze based on clinical judgment, consideration should be given to perform an optical iridectomy or PK.

The visual outcomes after SEPA are particularly impressive, and vision continued to improve in 32 eyes (94%) with a longer follow-up duration. Besides, the vision continues to improve with age, owing to visual maturation in growing children. It is known that after SEPA, corneal haze may regress much faster in younger patients because of superior stromal remodeling and better regenerative potential of the peripheral corneal endothelium. Correspondingly, the AS-OCT analysis revealed that a well-preserved anterior stromal architecture helps achieve faster refractive stabilization compared with PK. In addition, corneal diameter expands until the age of 2 years15; thus, a larger optic zone aids the visual rehabilitation. Besides the significant visual gains achieved from this minimally invasive surgical intervention, we have also circumvented long-term postoperative complications associated with keratoplasty, notably the need for stringent postoperative follow-up, the lifetime risk of allograft rejection, and eventual graft failure. To the best of our knowledge, this is the largest report of selective endothelialec- tomy in the PA being successfully investigated exclusively in children with visually significant corneal opacities.

Outcomes after SEPA are dependent on undisturbed anterior stromal architecture, an island of the transparent cornea in the center or midperipheral region, and healthy peripheral corneal endothelial cells. Endothelial migration requires breakage of contact inhibition of anomalous endothelial cells; hence, adhesiolysis alone would not have allowed cell migration of healthy cells and restoration of endothelial pump function with a lessening in stromal opacity. Although mild–moderate cases where opacity was limited to zone 1 tend to have excellent outcomes, severe cases limited to zone 1 or 2 may fare better if concurrent endocapsular LA with optical iridectomy is considered along with SEPA. Primary PK can be deliberated in cases with extensive corneal involvement (Zone 3B), corneal ectasias, or staphyloma formation after a perforation. Besides more extensive cornea involvement, the visual impairment in PA is frequently due to associated comorbidities; hence, although selective endothelialec- tomy may improve corneal transparency, the overall visual prognosis may remain poor without other interventions such as prompt amblyopia therapy and glaucoma control.

This study also sheds new light on the possible factors responsible for the failure of SEPA. The analysis revealed that severe disease, presence of microcornea, high IOP, concomitant LA with vitrectomy, and female sex were identified risk factors for nonclearing after SEPA. Inadvertent DM detachment at the time of SEPA should be avoided because it necessitates additional intervention, which in turn adversely affects SEPA outcome. Therefore, it may be advisable to preemptively identify those eyes with wider corneal involvement, corneolenticular attachment, ectasia, extremely thin cornea, perforation, and a staphyloma formation by performing an OCT or ultrasound biomicroscopy before surgery.16,36

This study’s major strengths are sample size, single-center design with experienced pediatric corneal surgeons, and long follow-up. Five independent masked evaluators validated the diagnosis, and outcomes were assessed in every case. Other more objective means such as AS-OCT or image analysis of postoperative outcomes could have been used. However, considering that 3/4th of the cohort constituted young children, it would have meant additional anesthesia examination at each follow-up visit to perform AS-OCT or capture images, and these were not feasible. The lack of events (nonclearing) among Type 1 PA suggests that the results may not be generalized to represent the entire cohort of SEPA.

The findings of this study question the paradigm whether this procedure should be offered as a preferred surgical modality in all children with PA or only in select cases, where PK is not the preferred alternative, such as in areas where there is a scarcity of donor tissues, noncompliance, inability to follow-up, or high-risk cases. We have demonstrated, to the best of our knowledge for the first time, that the SEPAL technique can be used even in cases of keratolenticular adhesion as long as the opacity is not greater than 6 mm or at least half of the peripheral cornea is clear. We have shown that, by being used in the manner described by us, SEPA may circumvent these limitations drawing from our favorable experience in infants and children with PA. This study showed that SEPA results are extremely promising, and SEPA can be an effective surgical alternative to optical iridectomy and full-thickness PK benefitting hundreds of children with PA-related blindness worldwide.

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