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Osteo-odonto-keratoprosthesis according to Strampelli original technique: A retrospective study with up to 30 years of follow-up

Short Title: Long-term follow-up in Strampelli original Osteo-odonto-keratoprosthesis

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ABSTRACT

Purpose: To describe clinical, anatomical, and visual outcomes obtained from a long-term follow-up of 59 patients who underwent osteo-odonto-keratoprosthesis (OOKP) using the original Strampelli technique.

Design: retrospective clinical cohort study.

Methods: 82 eyes of 59 patients who underwent OOKP surgery between 1969 and 2011 were included. Patients' clinical characteristics before surgery as well as complications and further surgeries until the end of follow-up were recorded. BCVA was revised before surgery and at 1 month, 1 year and every 5 years until the 30th year of follow-up.

Results: Mean follow-up post-OOKP was 27.4±11.2 years (2.4-52). The most frequent cause of blindness was chemical injuries (71%). OOKP integrity was maintained in 77 out of 82 eyes until the end of follow-up (94%). Excluding the cataract, acquired glaucoma was the most frequent complication with a prevalence at 10 years of 36%. Mean BCVA improved from 2.60±0.32 at presentation to 0.40±0.65 at 1 year and 1.21±1.19 logMAR at 30 years. Overall, 51% of the included eyes attained a BCVA better than 0.05 logMAR and a stabilization of BCVA was observed for the first 10 years of follow-up post-OOKP. Better BCVA outcomes were observed in the Stevens-Johnson Syndrome or Toxic Epidermal Necrolysis (SJS/TEN) group, while glaucoma showed not to significantly affect visual acuity.

Conclusions: The original OOKP still represents a valid surgical choice, durable over time, for restoring vision in end-stage corneal blindness patients not eligible for a corneal transplant.

1. INTRODUCTION

During the last century, surgeons developed several different techniques to restore vision in end-stage corneal blindness not eligible for a cornea transplant. The most widespread are, nowadays, the osteo-odonto-keratoprosthesis (OOKP), tibial bone keratoprosthesis (Tibial bone KPro), and the Boston keratoprosthesis (Boston KPro) Type 1 or Type 2. Whilst the OOKP employs a lamina made from autologous osteodental tissue, to harbor an optical cylinder made of polymethyl methacrylate (PMMA) in its center, the Tibial bone KPro employs a lamina obtained from the anterior surface of the tibial bone. The tibial bone KPro is thought for patients who do not have available teeth to undergo OOKP.[1] Conversely, Boston KPro employs a titanium plate to host the optical cylinder in combination with a carrier graft.[2,3]

The OOKP, first introduced by Strampelli in 1963 and later modified by Falcinelli, represents one of the best surgical approaches to end-stage corneal blindness, that oftentimes allows to achieve good visual outcomes.[4,5] Patients eligible for this procedure are bilateral blind patients not suitable for corneal transplantation. Good dental health is also required to harvest tissue to create a valid dental lamina. The most common indications are Stevens-Johnson syndrome (SJS), chemical or thermal burns, ocular cicatricial pemphigoid (OCP), but also end-stage dry eye disease, bullous keratopathy, and trachoma. **(Fig.1)** Highly motivated patients should also be selected as the procedure is long and elaborated and requires a life-long follow-up.[6] Several studies have reported good anatomical and functional outcomes with different follow-ups. Anatomical survival of the prosthesis was obtained in more than 80% of the patients throughout almost all published papers. Visual acuity of more than 3/10 was also obtained in around 50% of the patients followed.[7–9] Moreover, histological examination of the osteo-dental laminae showed a consistent grade of preservation of the laminae themselves even after 20 years from the procedure.[10]

OOKP is an ingenious and complex surgical procedure that is burdened by a wide range of complications. A relatively common intraoperative complication is vitreous hemorrhage, usually self-

resolving. However, postoperative complications are more challenging to manage. Glaucoma is the most common and requires a life-long follow-up. Other complications may occur even after several years from the surgery, including vitreoretinal pathologies, as well as reabsorption of the lamina or extrusion of the optical cylinder. **(Fig.2)** Unfortunately, most published studies do not exceed the 10-year mark follow-up. Therefore, the long-term OOKP visual outcomes and survival still need to be determined.[11,12] The aim of the present retrospective study is to evaluate OOKP long term functional and anatomical durability and to report the most common complications.

2. MATERIAL AND METHODS

We conducted a retrospective clinical cohort study reviewing clinical records of patients who underwent OOKP surgery between 1969 and 2011 in an ocular surface referral center. All patients were operated at Villa Benedetta Clinic (Rome, Italy) by an expert surgeon in OOKP (Dr. Francesco Iannetti ┼) and clinically followed by M.L. and L.I. All patients were treated with the Strampelli original technique[13], as almost all the surgeries were performed before the implementations suggested by the Rome-Vienna Protocol in 2005.[5] This retrospective study was approved by the Institutional Review Board of Villa Benedetta Clinic. The study was conducted in accordance with the tenets of the Declaration of Helsinki and data accumulation was performed in conformity with Italian laws.

2.1 Inclusion criteria

The inclusion criteria were as follows: (1) bilateral corneal blindness not eligible for penetrating keratoplasty (PK) or with previous failed PK, (2) BCVA equal or worse than 1.70 logMAR before surgery, (3) follow-up time after surgery $\geq$ 24 months, (4) good dental health. We excluded patients with extinguished flash visual evoked potential (VEP) response and with evidence of retinal detachment, history of retinal vascular occlusion, phthisis bulbi, and compromising systemic diseases (e.g., terminal neoplasm or terminal kidney failure) before surgery.

2.2 Ophthalmological evaluation and data collection

All patients underwent a full ophthalmic examination before surgery and subsequent follow-ups that included: BCVA, intraocular pressure (IOP) evaluated by a Draeger tonometer or Schiotz tonometer, ophthalmic ultrasound test (to investigate the anatomical integrity of the posterior segment), and flash VEP stimulation. After OOKP all patients were treated with antibiotic ointment and lubricants lifelong for mucosa protection.

Patients' clinical characteristics before surgery as well as complications and further surgeries until the end of follow-up were recorded. BCVA was revised before surgery and at 1 month, 1 year, and every 5 years until the 30th year of follow-up. A BCVA of 2.3 logMAR (Snellen equivalent ~ 20/4000) and of 2.6 logMAR (Snellen equivalent ~ 20/8000) was assigned for vision of hand motion and light perception, respectively; no light perception was defined as 3.0 logMAR (Snellen equivalent ~ 20/20000). Diagnosis of glaucoma after OOKP surgery was performed based on IOP value, VEP response, and clinical assessment of optic disk excavation grading.

Surgical technique

The surgical procedure to perform an OOKP follows three main steps. The first phase involves the corneal re-covering with a buccal mucosal flap, after the resolution of eventual symblepharon and the reconstruction of the fornices. During local or general anesthesia, fixation sutures are placed in the upper and lower lids and in the 4 rectus muscles. Subsequently, a peritomy of the conjunctiva is performed, and the corneal epithelium is removed. A marking 3.0 silk suture is fixed to the center of the cornea, and eight chromic catgut 6.0 sutures are placed in the episclera, 1 cm from the limbus. A thick flap of buccal mucosa, comprising the adipose tissue, is taken from the lower cheek. It should be larger than the corneal surface to recover. This flap is positioned on the ocular surface and sutured to the episclera and to the conjunctiva with catgut stitches. Closing sutures in silk 7.0 are positioned in the lids. The surgery is concluded with medication and a compressive bandage. **(Fig.3)**

The second step can be performed simultaneously with the corneal re-covering. A pocket is created in the lower lid, between the skin and the muscular tissue, to host the osteo-odonto-acrylic piece as soon as it is ready. A monoradicular tooth such as incisor, canine, or premolar has been previously chosen, preferably in the upper arch to avoid mandibular fracture. The tooth is excised together with the alveolar and spongy maxillary bone, using a saw. The tooth is cut parallel to the pulp canal, to obtain an osteo-dental slice, including a part of the root, the dental alveolar ligament, the bone, and

the periosteum. The pulp and the dentine are removed and the dental cuspids are blunted to get a comfortable shape. With a dentist's supersonic drill aerator, a hole is created in the osteo-dental slice, centered on the pulp canal, in which the optic cylinder will be inserted. The optic cylinder is made of PMMA. The dioptric power is about 50 to 60 diopters. The optic cylinder length is from 8.0 mm to 8.25 mm and is divided into two segments, anterior and posterior. The length of the anterior segment is from 5.75 mm to 6.0 mm, and the length of the posterior segment is from 2.25 mm to 2.50 mm. The diameter of the anterior segment varies from 2.45 mm to 3.75 mm, the diameter of the posterior segment is about 0.3 mm larger than the anterior part. To obtain a perfect adherence, both the hole in the osteo-dental slice and the acrylic lens should be washed in physiological solution and then dried with a jet of pure oxygen. The lens is definitively fixed with zinc oxide-based cement. When the cement has hardened, the complete osteo-dental-acrylic lamina is washed with fresh blood and introduced into the palpebral pocket. **(Fig.4)**

The third step, performed usually at least 3 months after the second step, involves the removal of the osteo-dental-acrylic lamina from the palpebral pocket. The mucosa is partially detached from the ocular surface. The lamina is introduced in the pocket between the cornea and the buccal mucosa. The acrylic lens is inserted exactly in the central corneal hole previously obtained with a trephine. It should not protrude into the anterior chamber more than 1-1.5 mm to avoid the formation of retrolenticular membranes or cataracts. The buccal flap is then placed back on the corneal surface and fixed with detached stitches in chromic catgut 6.0. Closing sutures in silk 7.0 are placed on the lids. These stitches will be removed after three days, and the eye is regularly medicated with antibiotic ointment. After the healing of the surgical wounds, a cosmetic prosthesis can be applied. **(Fig.5)** In case of cataract, if it is pre-existing, it can be removed through the central corneal hole during the operation of OOKP, also removing the remains of the membrane and performing an ample iridectomy if the iris is attached to it. If the cataract forms afterward, either it can be removed in a second operation, intra or extracapsular.[13]

Glaucoma surgery was often associated with OOKP in the preoperative or postoperative phase. Apart from the medical treatment, some patients underwent a procedure known as cyclodiastasis. This intervention allows the creation of a cyclodialysis kept open with a supramid thread. The thread is inserted through a full-thickness scleral incision and slowly pushed toward the anterior chamber. It is then pulled from a corneal incision on the opposite side of the limbus. The two ends are knotted to keep the thread in place. This procedure forces a separation between the choroid and the sclera, allowing the filtration of the aqueous in the subchoroidal space. Moreover, this technique determines an increase in the permeability of choroidal vessels and a reduction of aqueous production, through the mechanical detachment of the ciliary body from the sclera.[14]

2.4 Statistical analysis

To identify parametric values, normal distribution of data was assessed using the Shapiro-Wilk test. All categorical data were reported as percentages, whereas continuous ophthalmologic data were reported as mean and standard deviation. Descriptive statistics of the included eyes were reported according to the cause of blindness. A linear regression analysis was performed to investigate the relationship between preoperative factors (age at surgery, months of blindness before surgery, previous cataract extraction, previously acquired glaucoma, previous PK, previous cyclodiastasis) and BCVA at presentation or at subsequent data points in all included eyes. Differences in BCVA values between enrollment and other follow-up times in the included eyes were tested by a linear panel regression analysis reporting marginal effects. Similar analyses were performed to estimate the differences of BCVA between 1 and 30 years (12 and 360 months): one according to the presence of glaucoma (previous, acquired, and no glaucoma), another according to the cataract extraction (previous, simultaneous and post-OOKP) and a third according to the causes of blindness. A panel regression analysis was also run to test for the differences of BCVA in the included patients taking into account the visual acuity of the best eye in order to have an estimate of visual autonomy for

every patient. When appropriate we reported *p* values, standard errors (Std Err), ranges, estimated differences or effects as well as confidence intervals (95%). In order to avoid potential biases due to intra-eye correlation in regression analyses, Std Err were calculated allowing for intragroup correlation at the patient level. A robustness check has been performed using a multilevel mixed-effect model accounting for patients with bilateral OOKP.[15] Data distribution, statistical analysis and graph generation were performed using STATA, v. 14.0 (StataCorp, TX, USA).

3. RESULTS

We reviewed the clinical records of 62 patients of whom 3 were excluded for a follow-up < 24 months due to physical trauma prejudicing OOKP integrity. Overall, 82 eyes of 59 patients (49 males and 10 females) were included in the study. The mean patients' age was 34.0±11.9 years (range 13-59) at the time of presentation and 61.9±13.4 years (range 35-88) at the last evaluation, with mean follow-up of 28.3±10.4 years (339±125 months) ranging between 2.8 and 52 years (34-624 months). Considering all the included eyes, patients' age at the time of surgery was 35.0±11.3 years (range 15-59), while mean follow-up post-OOKP was 27.4±11.2 years (328±135 months) ranging between 2.4 and 52 years (28-624 months). The most frequent cause of blindness was chemical injuries (including alkali, acids, molten metals, war related), other causes included: Stevens-Johnson Syndrome or Toxic Epidermal Necrolysis (SJS/TEN), unknown keratitis, bullous keratopathy, and ocular pemphigoid. Preoperative diagnoses with patients' demographic data and eyes' clinical features are summarized in **Tables 1 and 2**. Thirty-four eyes (42%) underwent penetrating keratoplasty (PK), with a mean of 1.47±0.72 failed PK, 20 eyes (24%) developed glaucoma before presentation and 14 eyes (17%) underwent cataract extraction before OOKP: 7 eyes intracapsular cataract extraction (ICCE), 6 eyes extracapsular cataract extraction (ECCE) and 1 eye phacoemulsification with intraocular lens (IOL) implantation. In 12 eyes (15%) cyclodiastasis was performed a few months before and in 11 eyes (13%) cataract extraction was performed during

OOKP surgery: 5 eyes ICCE and 6 eyes ECCE. No relationship was found between preoperative factors and BCVA at presentation or subsequent data points in the linear regression analysis.

3.1 Anatomical survival and complications of OOKP

OOKP integrity was maintained in 77 out of 82 eyes until the end of follow-up (94%). The loss of OOKP integrity was recorded in 5 cases (6%). In particular, 2 eyes required enucleation for phthisis bulbi secondary to retinal detachment and choroidal detachment at 5.1 years (61 months) and 28.7 years (345 months) after OOKP respectively; 1 eye underwent OOKP replacement at 21.7 years (260 months) due to prosthesis extrusion, and 2 eyes at 23 years (276 months) and 25.7 years (308 months) due to lamina reabsorption. Due to the low rate of the anatomical failure of the prosthesis, no difference in OOKP survival could be estimated when considering the different causes of blindness or other pre-operative conditions.

Excluding the onset of cataract, acquired glaucoma was the most frequent complication. At the end of follow-up, it occurred in 41 out of the 62 eyes that had not developed glaucoma before surgery (66%) on average at 12.1±7.4 years (145±89 months) ranging between 0.6-26 years (7-312 months) after OOKP. Prevalence of acquired glaucoma at 2 years was 7% and at 10 years was 36%. Furthermore, we recorded 21 out of 82 eyes that never had glaucoma before or after surgery (26%). Other complications were retinal detachment in 4 out of 82 eyes (5%), choroidal detachment in 3 eyes (4%), optic neuritis in 1 eye (1%), endophthalmitis in 2 eyes (2%) and mucosal fistula in 1 eye (1%).

During follow-up time, patients underwent a wide range of surgical procedures as shown in **Table 3**. Moreover, with regard to parasurgical procedures, 13 out of 82 eyes (16%) underwent a mean of 2.4±1.6 YAG (Yttrium Aluminum Garnet) laser sessions in order to remove retrolental membranes.

3.2 Visual outcomes

Achieved mean spherical equivalent (SEQ) obtained 12 months after OOKP surgery was 5.3±3.5 (range -3 to 14). No substantial differences in SEQ were observed between right and left eye in those patients who received bilateral OOKP surgery (p=0.285, diff. 1.04, CI 95% -0.9-3.0).

Mean BCVA of the included eyes varied from 2.60±0.32 (Snellen equivalent ~ 20/8000) at presentation to 1.49±1.21 logMAR (Snellen equivalent ~ 20/625) at the end of follow-up (30 years-360 months). Overall, 51% of the included eyes attained a BCVA better than 0.05 logMAR (Snellen equivalent ~ 20/23). BCVA was ≤1.00 logMAR (Snellen equivalent ~ 20/200) in 0 eyes before surgery, in 72 eyes (88%) at 12months, in 69 eyes (85%) at 5 years (60 months), in 63 eyes (81%) at 10 years (120 months), in 55 eyes (75%) at 15 years (180 months), in 47 eyes (69%) at 20 years (240 months), in 33 eyes (58%) at 25 years (300 months) and in 24 eyes (55%) at 30 years (360 months) after OOKP. Descriptive BCVA data stratified by the cause of blindness are available in **Table 4**.

By a linear panel regression analysis, the estimated value of BCVA obtained as marginal effect improved from 2.60 logMAR at presentation (Std Err 0.04, p <0.001, CI 95% 2.52-2.68) to 0.40 logMAR (Snellen equivalent ~ 20/50) at 12 months (Std Err 0.08, p <0.001, CI 95% 0.25-0.55). Even though a worsening trend of BCVA was observed during the whole follow up, no significant difference from 12 months to 120 months (0.63 logMAR, Std Err 0.10, p <0.001, CI 95% 0.44-0.81) was noted, meaning an adequate maintenance of visual outcomes for at least the first 10 years of follow-up post-OOKP. The marginal effects of BCVA in all included eyes from the regression analysis are shown in **Figure 6**. Considering only the eye with the best BCVA in each patient at every follow-up stage, no significant difference was observed from 12 (0.32 logMAR, Std Err 0.08, p <0.001, CI 95% 0.17-0.48) to 300 (0.70 logMAR, Std Err 0.12, p <0.001, CI 95% 0.47-0.93) months after OOKP as shown in **Figure 7**. Comparative analysis in a series of panel linear regressions among different diagnostic groups showed better results in terms of visual outcomes in the SJS/TEN group during the entire follow-up period (**Figure 8**). We further performed a similar regression analysis to

estimate differences between patients who underwent cataract extraction before, after or during the OOKP surgery. As shown in **Figure 9,** even if the eyes that underwent cataract extraction before OOKP show a worse BCVA from 12 months to the end of follow-up, no significant differences were found between the three groups. Finally, an analogous regression analysis (**Figure 10**), showed no significant differences between patients who already had glaucoma before OOKP, patients who acquired it after OOKP and patients who did not develop it during the entire follow-up - although the latter group showed generally better BCVA from 20 years (240 months) after surgery.

DISCUSSION

The present retrospective study describes the clinical, anatomical, and visual results obtained from the long-term follow-up of 82 eyes in 59 patients who underwent OOKP using the original Strampelli technique.[4,13] The results were evaluated in patients with different clinical types of severe corneal blindness not treatable by corneal transplant.

Anatomical results showed that this surgical technique provided a long-term maintenance of the OOKP in most cases. In 5 cases OOKP did not survive, but in only 3 of those the failure was strictly connected to the prosthesis integrity (one prosthesis extrusion and two lamina reabsorption), whilst in the two other cases the physical loss of prosthesis was due to enucleation secondary to phthisis bulbi. In 94% of the cases, OOKP integrity was retained until the end of post-operative follow-up (mean follow-up time: 27.4 years or 328 months). As far as we know the present follow-up is the longest ever reported in the literature for a keratoprosthesis. Since no correlation between preoperative factors (i.e., cause of blindness, previous cataract extraction or/and cyclodiastasis, etc.) and anatomical retention of the OOKP could be found, the observed differences may be attributed to the quality of the surgical technique itself. In this regard the primary fundamental element to obtain a good anatomical result over time could be the dental tissue vitality, to create a graft and not a simple inclusion. The use of a non-vital dental fragment, or rather with a poorly vascularized pulp, could

lead to a higher percentage of prosthesis failure (i.e., lamina reabsorption or extrusion). To ensure permanent attachment of the graft, Strampelli preferred to include part of the dental root and cement tissue. He used to perform a surgical cut of the root longitudinally to the radicular canal, to dissect the dentine on one side only, and avoid the risk of necrobiosis associated with the presence of two zones of section. A longitudinal cut, compared to a perpendicular one, may have also reduced the risk of damage to the alveolar dental ligament. The tooth during the preparation must remain perfused as much as possible, except at the moment of the insertion of the acrylic lens, which requires a dry surface. The dental graft obtained, needs to be placed in a skin pocket created in the inferior eyelid, to develop a satisfactory covering of vascularized connective tissue.[13]

Reported anatomical survival rates of Tibial bone KPro at 18 years are 43%.[1] De la Paz et al performed a comparative study between OOKP and Tibial bone KP on a group of 227 patients, describing a 10 year anatomical survival of 60% and 48% respectively.[16] Concerning Boston KPro type I, a chance of prosthesis extrusion has been shown. A recent meta-analysis published by Priddy et al in 2019 reported retention rates of the device at 2 and 5 years of 88% and 74% respectively.[17] A large multicentric study demonstrated a retention rate of 76% after 7 years of follow-up in 139 eyes that underwent Boston KPro type I.[18] Regarding OOKP, previously reported survival rates attested around 88% at 5 years. The longest-term follow-up study showed survival rates of 81% at 20 years for OOKP.[6] Compared to formerly published papers, we report higher retention rates of 99% at the 20-year mark and of 94% at the 30-year mark. Interestingly, the patient with the longest follow-up in our cohort has been retaining the prosthesis for 624 months (52 years).

In our study, functional results show a reasonably good outcome at the end of follow-up with a significant visual improvement compared to the time of presentation. Visual acuity tended to be stable at least for the first 10 years (120 months) of follow-up, then it started to significantly decrease. Considering the BCVA of the best eye for every patient during the follow-up, we observed

a good visual acuity maintenance until the 25th year with a subsequent significant progressive decrease. Therefore, self-sufficiency was guaranteed for a very long time in patients who were otherwise destined to remain blind.

BCVA results in Boston KPro type I showed that 45-77% of patients retained a BCVA better than 1.00 logMAR (Snellen equivalent ~ 20/200) after 2 years of follow-up. However, Boston KPro type I seemed to have lower performances in autoimmune diseases.[19] The different surgical indications between OOKP and Boston KPro make challenging to directly confront these two techniques.[17] As for the Boston KPro type II, early reports show a visual acuity better than 1.00 logMAR (Snellen equivalent ~ 20/200) in 38% of eyes at the end of a mean follow-up of almost 6 years.[20]

Concerning the Tibial bone KPro, Charoenrook et al reported a BCVA better than 1.3 logMAR (Snellen equivalent ~ 20/400) in 33% and 19% of included eyes at 5 and 10 years after surgery respectively. Similar results were reported by De La Paz with a BCVA better than 1.3 logMAR (Snellen equivalent ~ 20/400) in 17% of eyes at 10 years.[16] However, it is important to mention that patients eligible for Tibial bone KPro may not have any alternative option for treatment as they lack dental or oral tissues sufficient to perform OOKP.[1]

Regarding OOKP, a systematic review reported an achievement of BCVA better than 0.48 logMAR (Snellen equivalent ~ 20/60) in 52% of patients (range 46-72%)[6], while we report 51% of the included eyes attaining a BCVA better than 0.05 logMAR (Snellen equivalent ~ 20/23). Falcinelli et al reported a mean BCVA at 12 years of follow-up ranging from 0.13 (in the bullous keratopathy following glaucoma surgery group) to 1.0 logMAR (in the Stevens-Johnson Syndrome and graft versus host disease).[21] De La Paz et al reported a BCVA better than 1.3 logMAR (Snellen equivalent ~ 20/400) 5 years after the surgery in 84% of the observed patients.[22] The same authors achieved a visual acuity better than 1.3 logMAR in 39% of the patients after 10 years of follow-up.[16] Conversely, our study showed better results at the same of follow-up times, where BCVA was ≤1.00

logMAR (Snellen equivalent ~ 20/200) in 69 eyes (85%) at 5 years (60 months) and in 63 eyes (81%) at 10 years (120 months) after OOKP.

Of note, in our study the group with SJS/TEN diagnosis is associated with better visual outcomes compared to the other diagnostic groups. In this respect, some case reports showed that OOKP provides good visual rehabilitation, with long-term anatomically stable prosthesis, in patients with end-stage ocular surface disorders and corneal blindness secondary to SJS.[23,24] One explanation could be that in SJS patients the corneal injury may have been more focal compared to the chemical burns that most often involve the entire ocular surface. However, better outcomes in those patients are not completely explainable and further investigations will be needed to fully understand its scientific reasons.

In our study, we observed potentially worse visual outcomes in patients who underwent cataract surgery before OOKP. We can suppose that a larger number of surgical procedures played a role in the functional long-term outcomes of the prosthesis due to repeated anterior segment stress. However, nowadays, the impact of cataract extraction could have a different relevance due to the modern less invasive surgical techniques like phacoemulsification.

Excluding the onset of cataract, post-operative glaucoma was the most frequent complication observed in our cohort, similarly to previous studies.[25,26] It is uncertain if glaucoma is connected to the surgery or otherwise is a consequence of pre-existing abnormalities of the anterior segment, involving trabecular meshwork and angle, caused by the original etiology (e.g., severe chemical injuries). Concerning the functional results, we did not observe substantial differences between patients with or without glaucoma - contrarily to what observed by other authors - even if panel regression analysis showed promising long-term outcomes in eyes without glaucoma.[10,27] However, as already pointed out by Tan et al, the effect of glaucoma on the visual acuity caused by visual field

loss, may not be apparent until the disease is advanced since the visual field width is already limited in those patients.[6]

The prevalence of acquired glaucoma in our study increased over time during the follow-up (36% at 10 years and 66% at the end of follow-up) and seems to be higher than in previous studies. However, Falcinelli et al considered the glaucomatous disease only if it occurred within 24 months from the second surgical step. Thus, their reported estimated incidence of 10.4% should be considered as a prevalence of acquired glaucoma at 2 years which is higher than in our cohort (7%).[21] De La Paz et al reported an occurrence of glaucoma of 10%. This percentage refers to a mean follow-up of 8.4 years from OOKP and includes patients with a follow-up of only 1 month. Furthermore, the same authors state that the existence of glaucoma prior to surgery could not be ruled out, therefore the impact of OOKP surgery on this complication could not be fully clarified.[16] Finally, different reported incidence or prevalence rates could be also due to a non-standardized criteria of glaucoma diagnosis in eyes with OOKP.[21]

CONCLUSIONS

As far as our knowledge this is the OOKP study with the longest mean follow-up, providing an analysis as extensive and detailed as possible in terms of anatomical survival, complications, and visual outcomes. This study shows that well-performed OOKP, although it is a long and complex procedure, may allow patients to retain vision even after 50 years from the original surgery. Nevertheless, further studies are desirable to confirm the evidence of our research, and to determine whether modern day glaucoma medications, new diagnostic tools and innovative surgical techniques may improve the life-long outcome of OOKP. Despite being invented during the ’60s, the Strampelli original technique still represents a viable and valid choice for restoring vision in end-stage corneal blindness patients when traditional keratoplasty is not indicated or already failed.

Figure 1 Clinical photograph of a patient with a history of severe chemical burn caused by acidic agents.

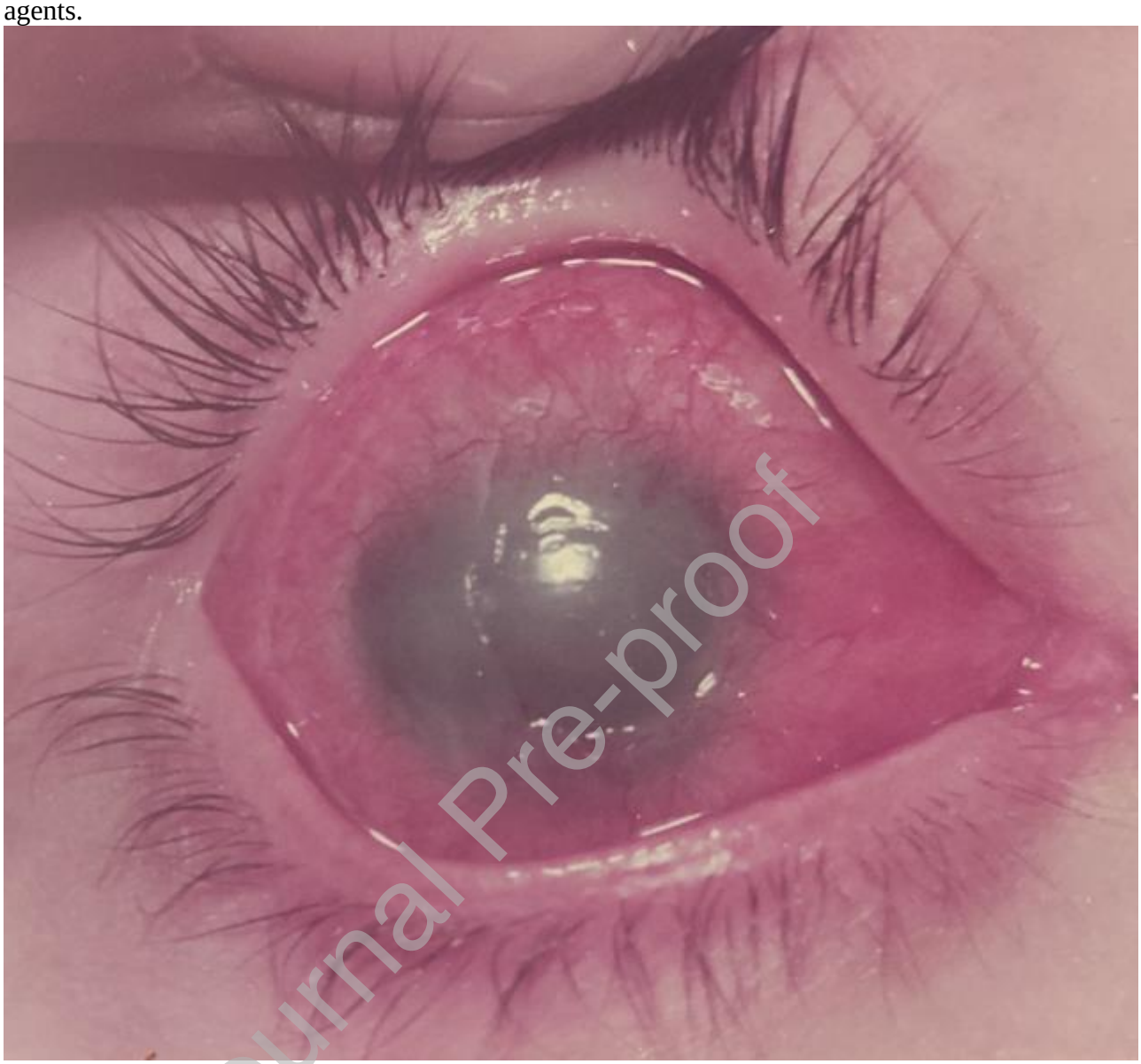


Figure 2 Clinical photograph of a patient who suffered from optical cylinder extrusion.

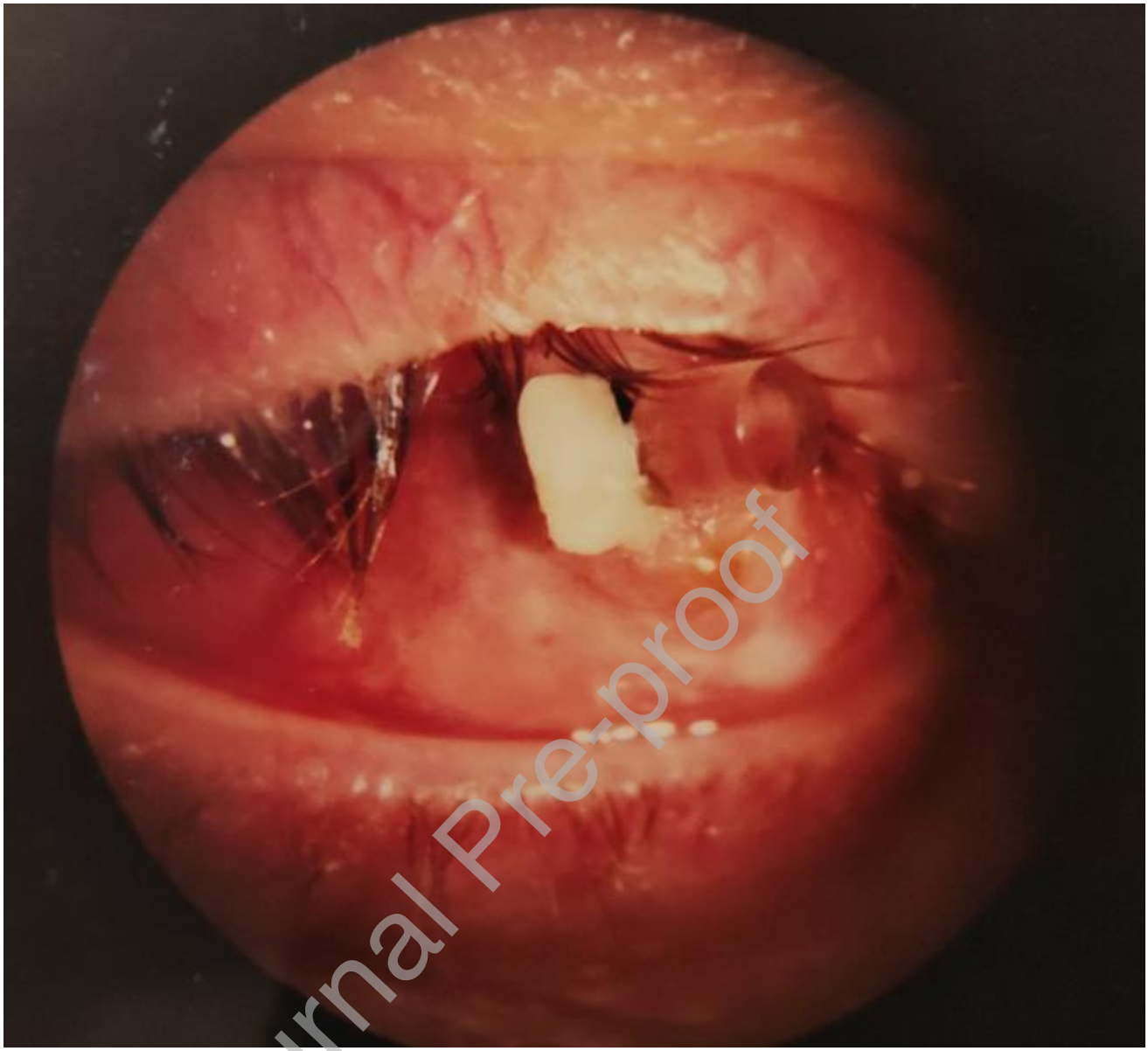


Figure 3 Intraoperative photographs of the first surgical step. (A) Conjunctival peritomy and removal of corneal epithelium/corneal covering tissues. (B) Fixing of the buccal mucosal flap to the episclera.

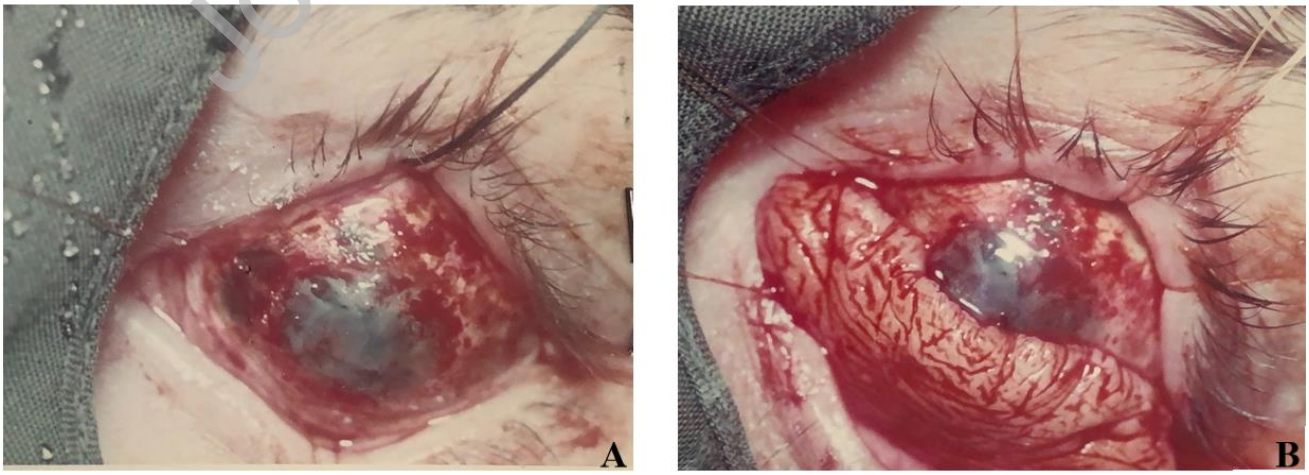


Figure 4 Intraoperative photographs of the second surgical step. (A-B) Photographs of prepared osteo-dental lamina with a central hole of 1.75mm in diameter. (C-D) The acrylic cylinder lens is held inside the central osteo-dental lamina's hole.

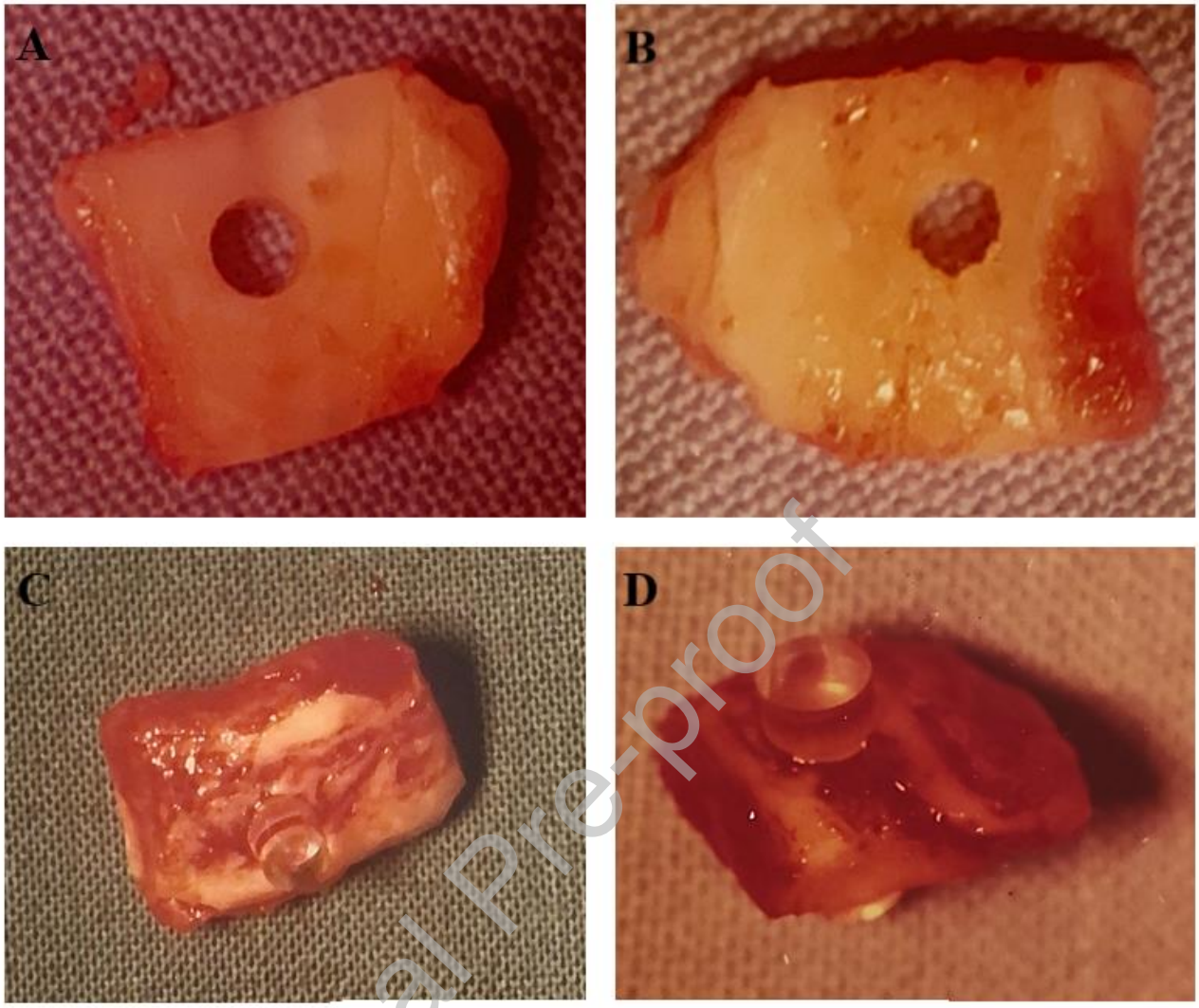


Figure 5 Intraoperative photographs of the third surgical step. (A-B) Placement of the acrylic osteo-dental lamina. (C-D-E) Fixing of the buccal flap on the corneal surface. (F) Complete healing of all the wounds.

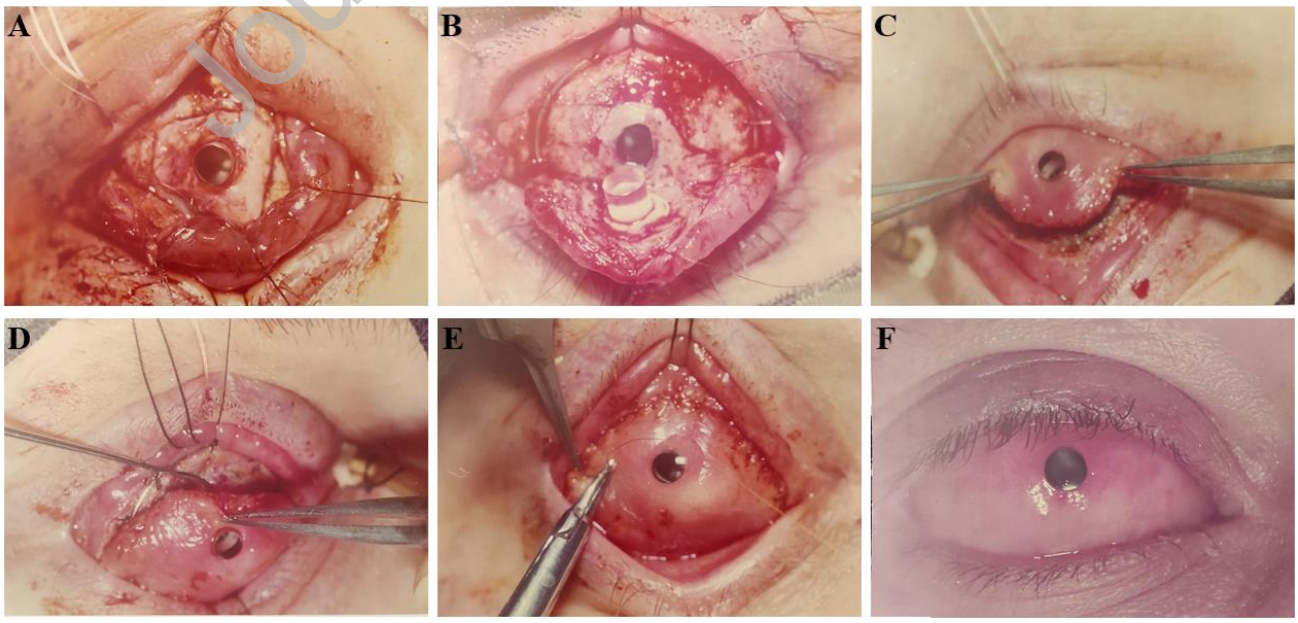


Figure 6 Margins plot of BCVA of all included eyes over time, as resulted from the panel regression analysis (CI 95%). Dashed gray line shows no significant difference between 12 to 120 months.

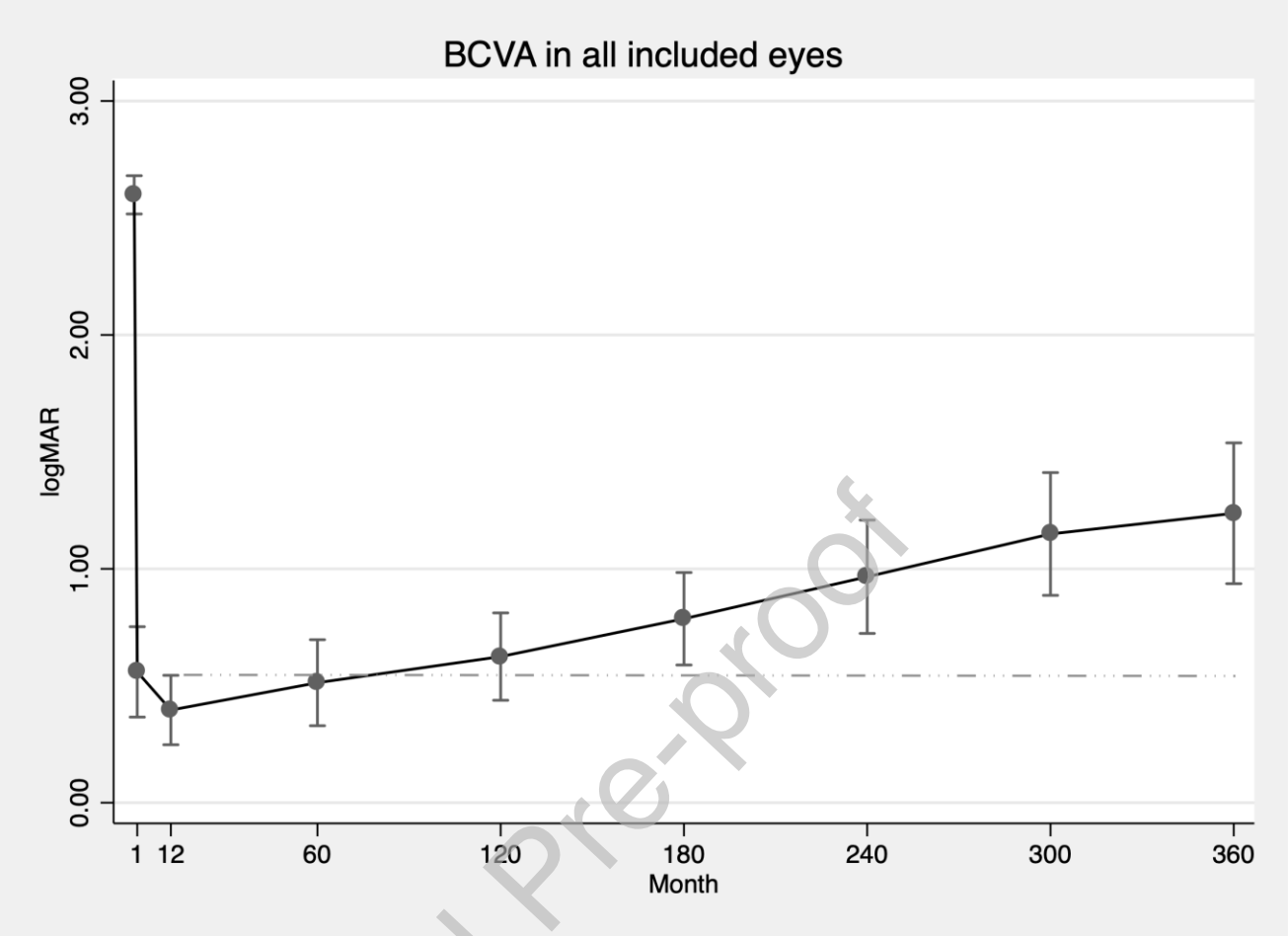


Figure 7 Margins plot of BCVA taking into account only the patients' eye with the best visual acuity over time. Dashed gray line shows no significant difference between 12 to 300 months.

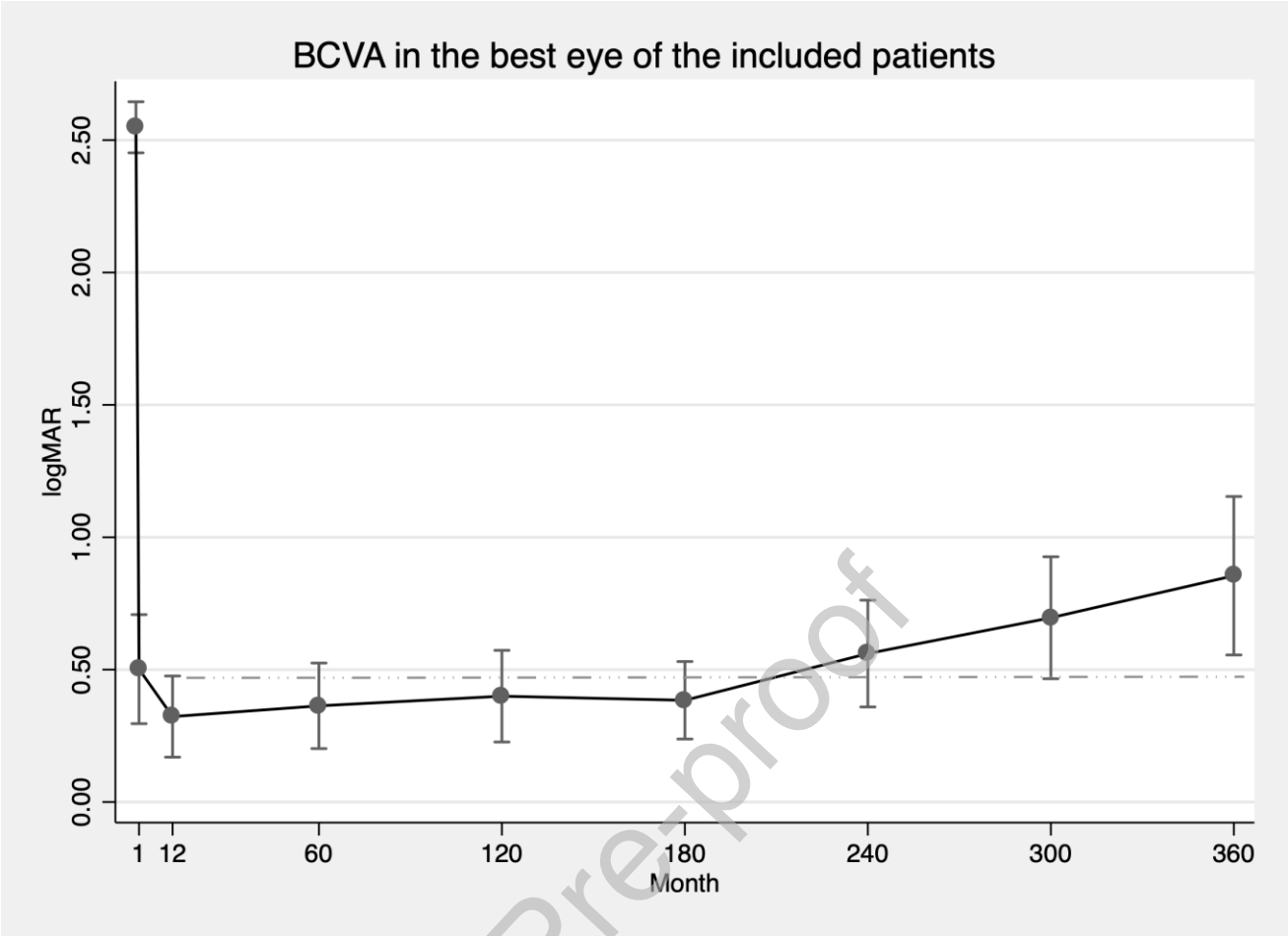


Figure 8 Margins plot of BCVA of all included eyes over time, comparing SJS/TEN group with all the other diagnostic groups.

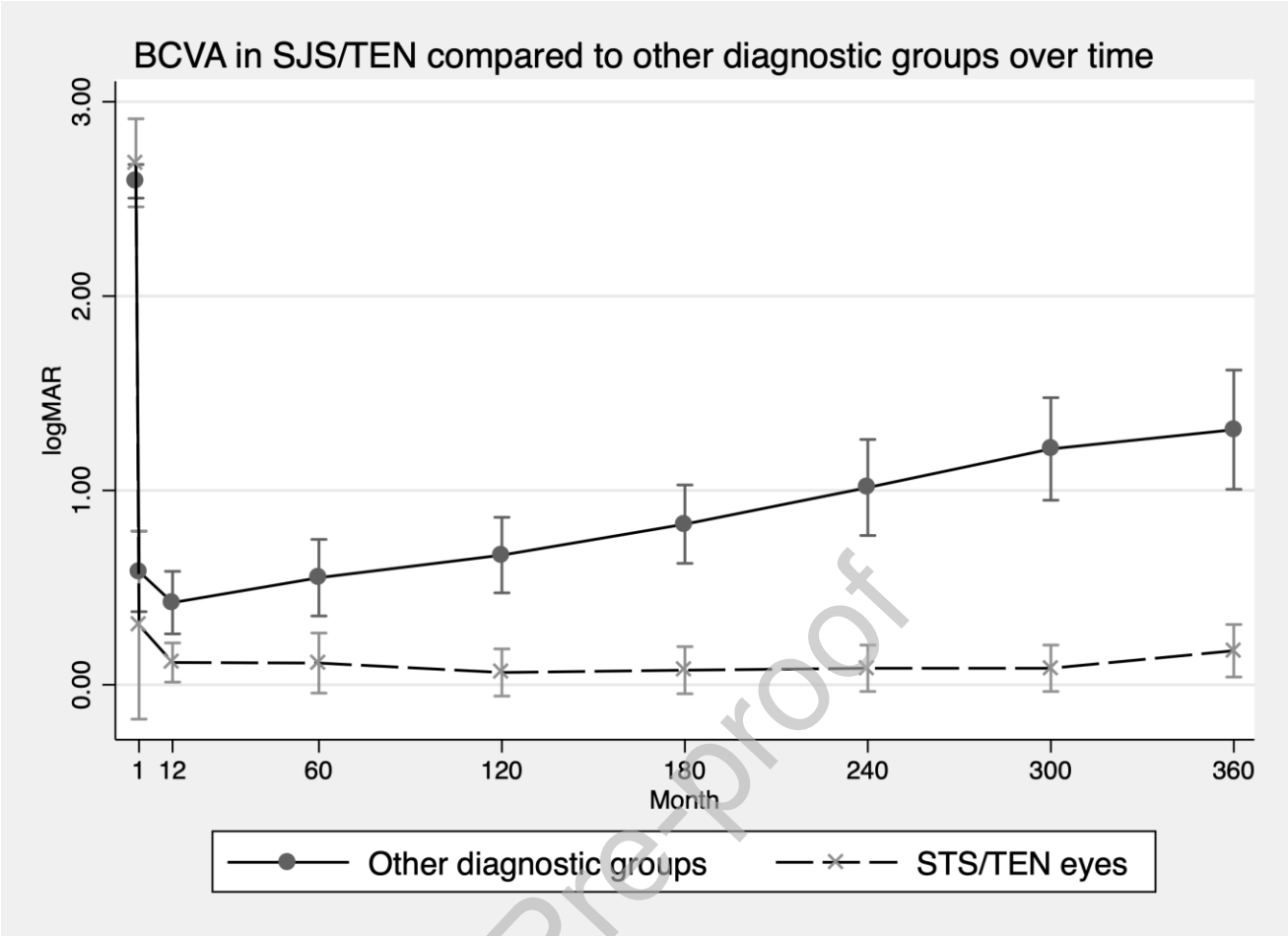


Figure 9 Margins plot of BCVA of all included eyes over time, comparing patients that underwent cataract surgery before, after or during OOKP surgery.

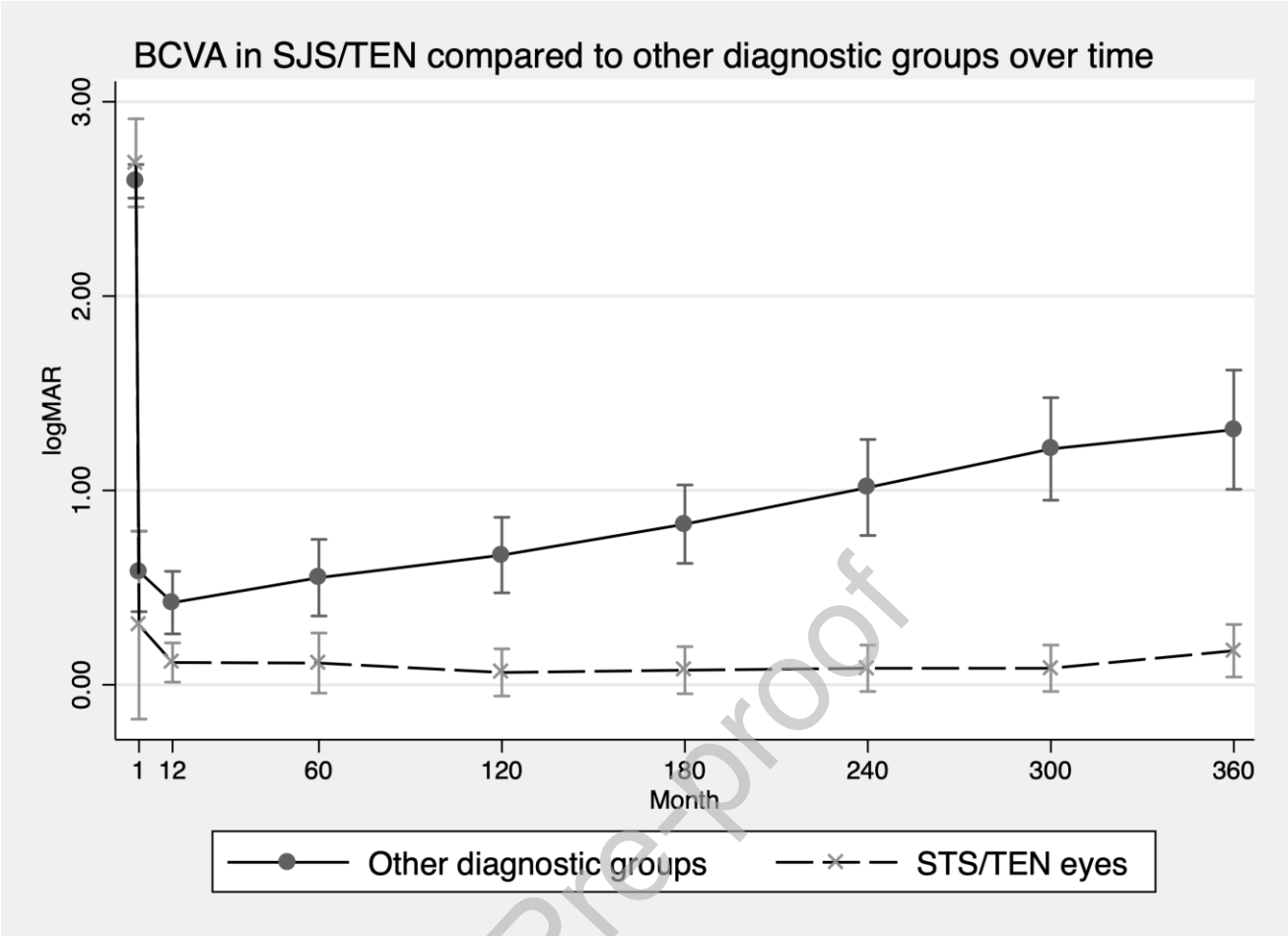
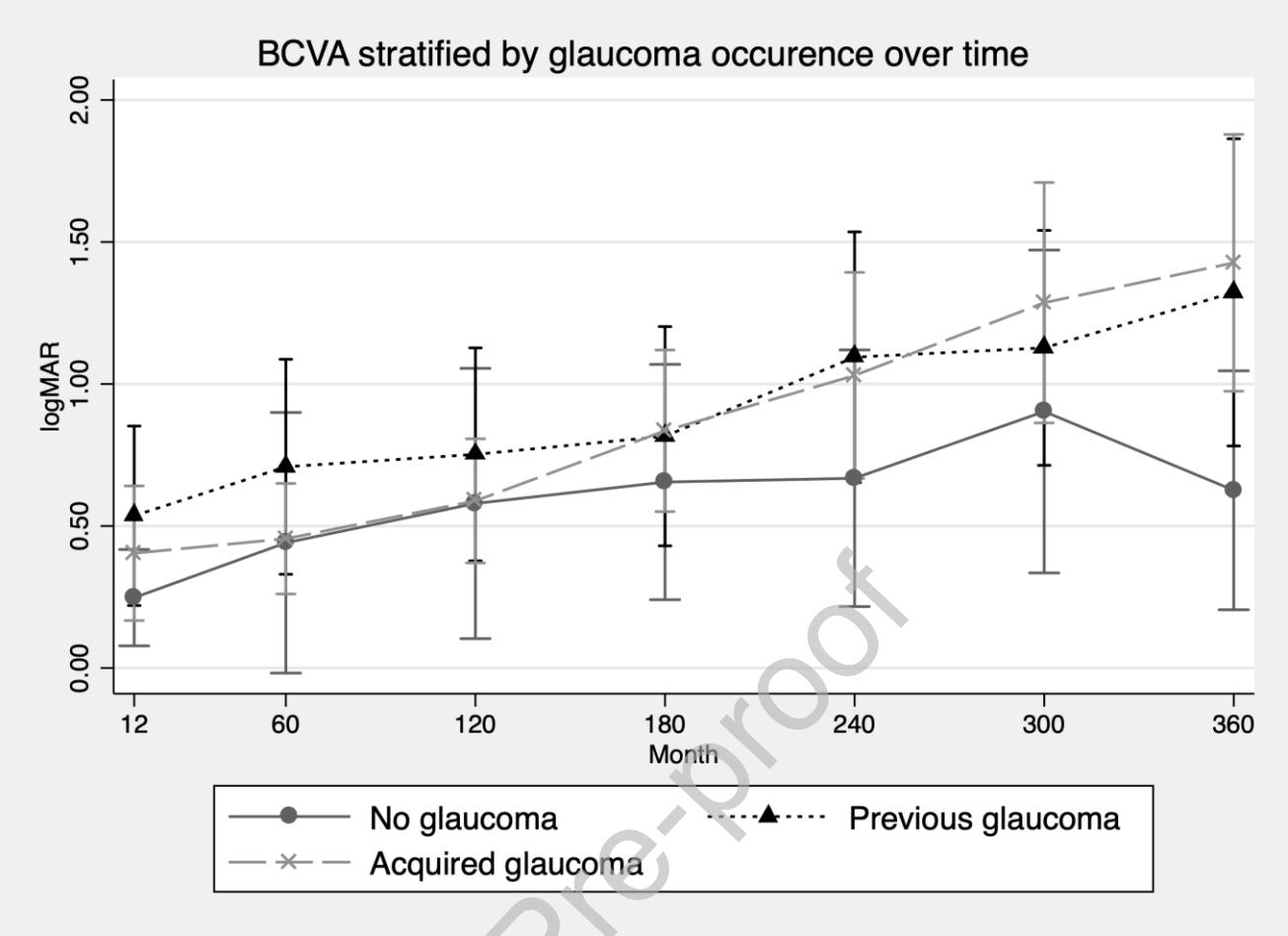


Figure 10 Margins plot of BCVA of all included eyes over time, comparing patients who already had glaucoma before OOKP, patients who developed glaucoma after OOKP and patients who never developed glaucoma.



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CRediT author statement

Ludovico Iannetti: Conceptualization, Methodology, Investigation, Validation, Writing-Reviewing and Editing, Supervision

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This 30-year follow-up retrospective study showed that the original Strampelli osteo-odonto-keratoprosthesis maintained its integrity in 94% of eyes until the end of follow-up.

Mean visual acuity improved from 2.60±0.32 to 0.40±0.65 at 1 year and 1.21±1.19 LogMAR at 30 years, with visual stabilization for the first 10 years of follow-up post-surgery.

This technique still represents a valid surgical choice, durable over time, for restoring vision in end-stage corneal blindness patients not eligible for corneal transplant.

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Table 1 Characteristics and follow-up of the included patients by sex

	Total (n. 59)	**Male**	**Female**
n (%)	59 (100%)	49 (83%)	10 (17%)
Age at presentation (mean±SD)	34.0±11.9	32.8±11.7	40.1±11.3
Months of blindness before presentation (mean±SD)	149.6±141.2	138.5±134.6	203.8±167.4
OOKP in both eyes n (%)	23 (39%)	20 (41%)	3 (30%)
Age at the end of FU (mean±SD)	63.3±13.1	61.6±12.8	65.7±14.5
Months of FU from presentation (mean±SD)	339.1±125.3	345.8±115.3	307.2±169.2

OOKP = osteo-odonto keratoprosthesis, FU = follow-up

Table 2 Characteristics and cause of blindness of the 82 included eyes

Cause of blindness	**Eyes n (%)**	**Age at surgery (mean±SD)**	**Months of blindness before OOK (mean±SD)**	**Months of FU after OOK (mean±SD)**
Chemical injuries	58 (70.7%)	35.9±12.1	165.2±152.1	346.9±123.3
Alkali	38 (46.3%)	34.9±10.5	154.0±152.4	359.6±132.7
Acid	5 (6.1%)	37.0±17.6	157.2±138.9	397.4±141.1
Molten metal	8 (9.8%)	35.6±15.8	149.0±129.1	275.9±135.0
War related	7 (8.5%)	41.0±13.6	250.3±185.8	323.3±62.9
Unknown keratitis	13 (15.9%)	31.8±9.6	205.2±131.7	290.8±119.1
SJS/TEN	7 (8.5%)	31.0±7.7	90.6±76.2	214.4±158.0
Other causes	4 (4.9%)	40.3±8.8	215.0±72.3	379.5±223.6
Total	82 (100%)	35.0±11.3	167.6±142.6	328.3±135.0

OOK = osteo-odonto keratoprosthesis, FU = follow-up, SJS/TEN = Stevens-Johnson Syndrome or Toxic Epidermal Necrolysis

Table 3 Surgical procedures following OOKP in all included eyes

Further interventions	**n 82 (%)**	**Mean±SD (months)**
Cataract extraction	52 (63.4%)	74.6±91.7
ICCE	*43 (82.7%)*	*79.2±97.9*
ECCE	*9 (17.3%)*	*52.8±51.6*
Strabismus surgery for horizontal or vertical diplopia	11 (13.4%)	20±23.6
Oculoplastic surgery for eyelids fornices reconstruction	23 (28.1%)	27.3±25.6
Glaucoma surgery	9 (11.0%)	148.1±113.6
SB for RRD	2 (2.4%)	57.0±46.7
Vitrectomy for retrolenticular membranes	7 (8.5%)	182.6±187.2
Mucosal plastic surgery for redundant mucosa around optic cylinder	13 (15.9%)	67.2±53.5

ICCE= intracapsular cataract extraction, ECCE= extracapsular cataract extraction
SB = scleral buckling, RRD = rhegmatogenous retinal detachment

Table 4 Descriptive BCVA data stratified by the cause of blindness over time (months)

Cause of blindness	**BCVA logMAR±SD (n. of eyes)**						
	0	**1**	**12**	**60**	**120**	**180**	**240**
Chemical injuries	2.62±0.31 (58)	0.51±0.81 (58)	0.33±0.63 (58)	0.41±0.63 (57)	0.52±0.69 (57)	0.68±0.91 (55)	0.89±1.0 (52)
Unknown keratitis	2.44±0.37 (13)	1.05±1.06 (13)	0.85±0.80 (13)	1.04±0.98 (13)	1.21±1.10 (13)	1.25±1.04 (12)	1.40±1.0 (10)
SJS/TEN	2.69±0.30 (7)	0.31±0.75 (7)	0.11±0.20 (7)	0.11±0.21 (7)	-0.01±0.02 (5)	0.01±0.01 (3)	0.02±0.0 (3)
Other causes	2.68±0.25 (4)	0.19±0.25 (4)	0.36±0.45 (4)	1.04±1.35 (4)	0.92±0.86 (3)	1.20±1.44 (3)	1.52±1.4 (3)
Total	2.60±0.32 (82)	0.56±0.85 (82)	0.40±0.65 (82)	0.51±0.76 (81)	0.62±0.80 (78)	0.77±0.96 (73)	0.96±1.0 (68)

SJS/TEN = Stevens-Johnson Syndrome or Toxic Epidermal Necrolysis